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THE
PROCTOR
MEDAL

Funds for the establishment of the Research Medal of the Association for Research in Ophthalmology were donated in 1947 by Mrs. Francis I. Proctor of Santa Fe, New Mexico, as a memorial to her late husband. Dr. Proctor, a Boston ophthalmologist, became intensely interested in the experimental side of ophthalmology after his retirement, and participated in numerous studies on the etiology and treatment of trachoma. The purpose of the medal is to stimulate research and to honor investigators who have made notable contributions in the basic fields of ophthalmology. The medal is to be awarded without regard to the nationality or professional status of the recipient.

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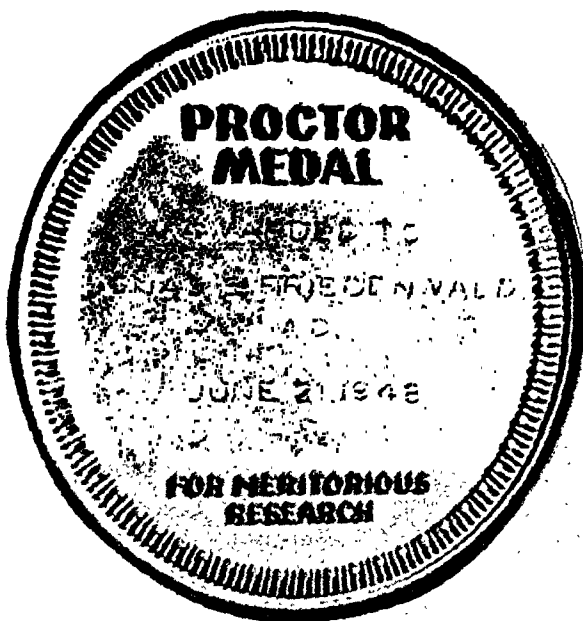
THE JONAS S. FRIEDENWALD
PROCTOR MEDAL AWARD
PROCEEDINGS
of the seventeenth meeting of the
Association for Research in Ophthalmology
Chicago, Illinois, June 21 and 22, 1948

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JONAS S. FRIEDENWALD

A SHORT BIOGRAPHY OF DR. JONAS S. FRIEDENWALD

Dr. Jonas S. Friedenwald was born in Baltimore, June 1, 1897, the son of the distinguished ophthalmologist, Dr. Harry Friedenwald, and Bertha Stein Friedenwald. He received his early education at Calvert and Friend's schools in Baltimore; entered The Johns Hopkins University in 1913, where he was graduated with honors in 1916. He entered The Johns Hopkins University, School of Medicine, in 1916, and was graduated with a distinguished record in 1920. Thereafter, he became house officer in medicine in The Johns Hopkins Hospital (1920-21) and, in 1921-22, studied eye pathology under Dr. Frederick Verhoeff, receiving an M.A. degree in pathology from Harvard University in 1922.

· He then went to Philadelphia, where for one year he studied in the out-patient department of the University and Wills Hospitals under Dr. de Schweinitz and Dr. Zentmayer. In 1923, he returned to Baltimore and since then has been associated with his father, Dr. Harry Friedenwald, in the practice of ophthalmology.

Although in active practice, Dr. Friedenwald did not abandon his interest in pathology and research. He took over the subdepartment of ophthalmic pathology in the Department of Pathology of The Johns Hopkins University, School of Medicine, under the late Dr. George MacCallum. With the founding of the Wilmer Institute in 1925, Dr. Friedenwald was appointed instructor in ophthalmology in charge of the pathological division. Here his flair for investigation found full opportunity for expression. His earlier work was chiefly in ophthalmic pathology, culminating in the publication of his textbook in 1928. During this period he became interested in the problem of the mechanism of the intraocular secretion, an investigation which since then has been his major work. However, his work was not confined to this field alone. His mathematical mind has led him into various physical problems, the results of which are the slitlamp ophthalmoscope, his theory of the relationship of intraocular pressure and ocular rigidity, the standardization of tonometers, and so forth. It is, however, in the broad fields of ophthalmic pathology and physiology that Dr. Friedenwald has made his major contributions.

He was appointed associate in ophthalmology in 1929, and associate professor in 1931, which position he now holds. Dr. Friedenwald is now in full charge of the pathological and physiological laboratories of the Wilmer Institute, and of the glaucoma research program.

Dr. Friedenwald received the Research Medal of the American Medical Association in 1935, and the Howe Medal of the University of Buffalo in 1948. He now is the recipient of the Proctor Award.

REMARKS ON ACCEPTANCE OF THE PROCTOR AWARD

June 21, 1948

Dr. Adler and Dr. Thygeson have left me quite speechless for the moment. Not that such embarrassment is unpleasant. It feels wonderful to have such things said about you even when you know they are untrue. I am reminded of the story about a Viennese artist whom a lady asked to paint a portrait of her husband,

"When can your husband sit for me?" asked the artist.

"Never," said the lady. "He is dead."

"Can I see a photograph?" the artist asked.

"I have none," answered the lady, "but I will describe him to you."

Noticing the look in the lady's eyes, the

artist concluded she was a bit cracked and, to pacify her, agreed to paint a picture according to her description. Two weeks later the lady came for the unveiling, and the artist wondered how she would react to his efforts. She sat before the picture and, as he removed the covering cloth, her face was enraptured. Finally she stretched out her hands toward to portrait and said, "August, how beautiful you are!—But how you have changed!"

If I may for the moment consider this award impersonally, I would like to suggest that the establishment of this award—not the choice of the present recipient—the flourishing state of this association, and the high caliber of its program, all indicate the increasing importance of basic research in ophthalmology.

Professor Northrop of Yale has pointed out in a recent book that every science goes through two phases. There is first what he calls the natural history phase of science in which facts are gathered and classified, the phase of taxonomy. In our science that phase is represented by the classification of ocular diseases, differential diagnosis, descriptive anatomy, morphologic pathology.

Northrop points out that when sufficient facts have been gathered in the natural history phase of a science, attempts are begun to place these facts in a rational order. This Northrop calls the mature phase of the science. In ophthalmology this phase is concerned with questions of etiology, pathogenesis, physiologic mechanisms.

Naturally, especially in the biologic sciences, the natural history phase of the subject is never done. There are still new distinctions to be made in the classification of disease, new disease pictures to be described. I do not wish to imply any disparagement to clinical research. The point is that the field of strictly clinical investigation has been so thoroughly harvested that really great effort, wisdom, and experience are required in order to make a genuinely new contribution to that field. Such a contribution is an achievement of high order. Its author has accomplished something much more difficult than did the illustrious fathers of clinical ophthalmology who in the 1860's and 1870's discovered a new disease at least once a month.

The point that I wish to make is not that clinical investigation is to be disparaged. It is, on the contrary, to be greatly admired, but its gleanings in the well-harvested field are few and far between.

By contrast the field of basic research is rich and ripe for the harvest. The slogan of our association should not be that basic research is recondite, solemn, austere,—but that it is easy, joyous and exciting. The orchard is full of golden fruit. One can hardly take a step without discovering something new and illuminating.

The natural history phase of a science requires increasing specialization. The taxonomists in different fields have little need of one another. Often their languages become mutually incomprehensible. In the mature phase of a science the interrelations of allied fields become, on the contrary, increasingly important. This means that there must be institutions within the framework of which men with different backgrounds of training can work and think together in intimate association. The work which has been cited for the current award would not have been possible but for the facilities supplied by The Johns Hopkins Medical School and its Department of Ophthalmology, the Wilmer Institute. I find it a little startling to realize that I have been working the same stall for a quarter of a century. I think that is an unduly long time, and wonder why they don't fire me. The reason why I don't resign is simply that I have the best job in the ophthalmological world.

But men are more important than institutions, and it has been my signal good fortune in the work which your committee has cited for the award to have had a series of collaborators who were really outstanding. I cannot mention all of them but there was, first

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THE FORMATION OF THE INTRAOCULAR FLUID*

PROCTOR AWARD LECTURE OF THE ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY

JONAS S. FRIEDENWALD, M.D.

Baltimore, Maryland

I met Dr. Proctor only once, and only briefly, but I formed the impression of him then as a gentle and deeply kind person whose interest in the science of ophthalmology was one of abiding devotion. It is a fitting memorial to his quiet but persistent zeal that an award should have been established by this association in his name. I am very proud and happy to be the recipient of this award, and I am deeply grateful to the association for this honor.

Knowledge of the mechanism of control of intraocular pressure is basic to any interpretation of the pathogenesis of glaucoma, and knowledge of the mechanism by which fluid and dissolved substances are transported into and out of the eye is important in any understanding of the metabolism of the lens. It is no wonder, then, that work in this field has engaged the attention of a great many investigators, and that the literature is voluminous and confusing. I shall not attempt a comprehensive review but shall merely outline those contributions of others, the interpretation of which constitutes the logical basis for my own point of attack.

One large group of investigators has approached the problem by studying the chemical composition of the aqueous, and the relations of this composition to that of the blood. The early results in this field, particularly those of Duke-Elder,[13] lent themselves to the conclusion that the composition of the aqueous resembles that of a dialysate of the blood plasma.† Duke-Elder and others concluded that the aqueous was in diffusional exchange with the blood plasma across a barrier whose chief relevant characteristics, like that of the capillary wall, were its impermeability to colloids and its permeability to crystalloids.

Later studies with the aid of more exact and refined techniques have shown that the chemical composition of the aqueous is not exactly that of a dialysate of the blood plasma. There are definite and important discrepancies. Nevertheless, the overall resemblance is approximately true, and the existence of some diffusional exchange between blood and aqueous may be accepted as thoroughly established. There is, indeed, a very strong a priori reason for expecting this to be true because, in the iris at least, the capillaries expose their naked walls to the intraocular fluid.

It follows that fluctuations in capillary blood pressure and in the osmotic composition of the blood would be expected to reflect themselves in fluctuations in intraocular pressure. Abundant experimental confirmation of these expectations has been presented by Duke-Elder[12] and by others. What is remarkable, however, is that persistent changes in blood pressure or in the osmotic pressure of the plasma colloids cause very

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the blood-aqueous problem, Duke-Elder, in 1927, left bicarbonate out of account. With this omission Duke-Elder calculated that the Donnan factor, that is, the ratio of aqueous sodium to plasma sodium and of plasma chloride to aqueous chloride, should be 0.84, although this value had previously been shown by Van Slyke to be approximately 0.95. Duke-Elder's experimental data agreed with his erroneous value for the Donnan factor. If the experimental data are correct, the aqueous is very far indeed from a dialysate of the plasma. For further analysis of these discrepancies see Meyer.[40,41]

little persistent effect on intraocular pressure. Some of the discrepancies and even paradoxes in this field have been emphasized, particularly by Robertson,[42] and it is plainly apparent both from experimental studies and from ordinary clinical experience that there are local compensating mechanisms which play important roles in the regulation of intraocular pressure, and that simple diffusional exchange between blood and aqueous merely furnishes the background, the important background, upon which these local mechanisms operate.

The existence of some diffusional exchange between blood and aqueous does not justify the conclusion, sometimes drawn, that the aqueous is or must be stagnant. It has been supposed, for instance, that if the aqueous were not stagnant, and if fluid were filtered into the ocular cavity from some bed of capillaries of higher than average pressure, the larger molecules of the solutes would be held back by the filtering boundary, and that a measurably hypotonic aqueous would result.

Since the aqueous is not measurably hypotonic, Magitot[38, 30] and others have concluded that it is stagnant. This conclusion is erroneous. If a solution is filtered through a barrier of sufficiently small pore size to retard the transport of the larger solute molecules, an osmotic pressure difference immediately arises on the two sides of the filtration boundary, retarding the movement of water relative to the solutes. Consequently the osmotic pressure difference between filtrate and mother liquor cannot be greater, and generally is much less than the effective filtration pressure.

It is easy to calculate, for instance, that a filtering mechanism yielding aqueous 1 percent hypotonic in electrolytes as compared with the plasma would require a filtering pressure in the capillaries of over 100 mm. Hg. So far no investigator has claimed that his measurements, for instance, for sodium or chloride in the aqueous are accurate within 1 percent, nor, in fact, that the expected composition of a dialysate of the plasma could be estimated within that degree of accuracy. Within the present limits of the experimental data, therefore, no assertion that the aqueous is stagnant is justified.

The only conclusive way to find out whether the aqueous circulates or is stagnant is by a direct measurement of the water flow. An effort which I made in this direction many years ago led to an estimate of through and through circulation in dogs' eyes of one cubic mm. per minute.[16] Kronfeld,[37] using a similar technique, reached the same estimate. More recent studies by Kinsey and Grant[34, 35] on the rate of exchange of solutes between blood and aqueous were found by them to be compatible with a flow of four cubic mm. per minute in the rabbit. It is gratifying that such widely differing experimental approaches led to estimates of the same order of magnitude.

The early chemical studies on the composition of the aqueous as noted above showed that, in a rough and approximate fashion, the aqueous resembles a dialysate of the plasma. With more modern and more nearly exact studies, discrepancies have appeared and it has become increasingly clear that many factors other than simple diffusional exchange play a part in the picture. Davson and Weld,[10] in their most recent studies, have found that the dog's aqueous is hypertonic in crystalloids by about 2 percent. Benham, Duke-Elder, and Hodgson[3] have extended these results. Similar findings are reported by Roepke and Hetherington.[43] Scholz and Wilde,[44, 50] using radio-sodium, found even more marked discrepancies in guinea pigs. Kinsey and Grant, however, do not find an excess of electrolytes in the aqueous of rabbits.

From their osmotic studies, Duke-Elder and Davson concluded that the aqueous is a secretion, or, more precisely, that electrolytes are secreted into the aqueous. This conclusion may indeed be true since, as will appear below, it is in accord with arguments

reached from quite different consideration.

The experimental data presented by Duke-Elder and Davson do not, however, in themselves justify this conclusion, for some water must be lost from the aqueous by evaporation through the cornea.[48] At least a part of the hypertonicity of the aqueous is to be attributed to this loss of water, but no quantitative data are available with which to estimate the magnitude of this effect. It is not certain, therefore, that any measurable hypertonicity would remain if losses by evaporation were eliminated.

Glucose has been shown by many investigators to be present in the aqueous at a lower concentration than in the plasma. The deficit is of the order of magnitude of 20 percent. No definite conclusions can be drawn from this finding as to the mechanism of formation of the intraocular fluid since the deficit in glucose could well be accounted for by local consumption. Adler[1] has demonstrated how large a factor local consumption can be by his analysis of the distribution of glucose in the vitreous, which indicates that the closer one gets to the retina, the lower the glucose concentration.

Recent studies by Kinsey and Grant[34] reveal that levulose, a sugar of the same molecular size as glucose and one which is surely less actively consumed by the intraocular tissues, is present in the aqueous in no greater concentration relative to the plasma than is glucose. Urea is another non-metabolized, nonelectrolyte that has been much more extensively studied than levulose. This is found in the aqueous in concentrations about 30 percent lower than in the plasma. Urea (molecular weight, 60) is a much smaller molecule than levulose (molecular weight, 180). Weld, Feindel, and Davson[49] found that the blood-aqueous barrier is almost impermeable to raffinose (molecular weight, 504), and Swan and Hart[46] found the barrier normally impermeable to inulin (molecular weight, 5,000). These are all un-ionized, not metabolized, water soluble, lipoid insoluble substances. The general

rule would appear that their transfer into the aqueous is retarded relative to electrolytes, and that the relative retardation is greater the larger their molecular size.

It would be natural, at first sight, to attribute the retardation of these substances to a filtering process. As noted above, however, the hypotonicity of a filtrate when computed in osmotic units cannot be greater than the effective filtration pressure. Several authors, particularly Kinsey and Grant, have explored the plasma-aqueous distribution of urea at artificially high plasma urea levels, and have reached figures for the aqueous deficit in urea that would require capillary pressures of over 100 mm. Hg if the deficit is to be explained solely on the basis of filtering out.

The anomalous behavior of these metabolically inert substances is not peculiar to the eye. Similar deficits of the same or similar substances have been found in the spinal fluid. The classical study of Amberson and Höber[2] on the salivary gland revealed that the transfer into the saliva of substances of this type is retarded increasingly as their molecular size increases. If, however, these substances are compared with their chemical derivatives of increasing lipoid solubility, the discrepancies tend to disappear. No satisfactory general theory has as yet been presented to explain the anomalous behavior of the group of substances of which urea may be taken as the prototype, but some conclusions are obvious.

The deficit of these substances in the aqueous and in various other body fluids cannot be accounted for *solely* by physicochemical processes of diffusion and ultrafiltration. Some contribution of cellular or tissue metabolic energy is required to account for the deficit, some sort of secretory phenomenon is involved. Either these substances are secreted out, that is, actively excluded by the blood-aqueous boundary—and this seems wholly unlikely in view of their metabolic inertness—or something else, that is, water or electrolytes or both, are secreted in.

In the latter case, the osmotic retardation of water movement would be overcome by the active secretory mechanism and the relative retardation of urea and other similarly acting substances *could* be attributed to a filtering process.

These conclusions have been greatly fortified by the work of Kinsey and Grant who studied not merely the equilibrium ratios between plasma and aqueous for urea and a variety of electrolytes, but their rates of transfer from plasma to aqueous and from aqueous to plasma. The mathematical formulation of the monumental mass of data which they obtained is necessarily complex, and the particular analysis used by Kinsey and Grant has been criticized by Duke-Elder and Davson.[14] I shall not burden the argument with a discussion of the various possible alternative mathematical equations.

What can be concluded from Kinsey and Grant's data[26] is: (1) The data are not compatible with an hypothesis of simple diffusional exchange with or without ultrafiltration into the eye, and ultrafiltration or leak out of the eye; (2) the data are compatible with the combination of the following hypotheses: (a) Electrolytes are transported into the eye by a secretory process, (b) in the presence of such electrolyte secretion, the retardation of urea can be accounted for by ultrafiltration; (3) the data demonstrate that reabsorption of the intraocular fluid occurs at least in part in the fashion of a leak, that is, by a mass transfer out of the eye of fluid with all its solutes undisturbed in the reabsorption process by diffusional exchange.

No doubt some other more complicated sets of hypotheses would also fit the data. However, until new data indicate that more complicated hypotheses are required, these studies of Kinsey and Grant add strong support to the conclusions outlined above from a consideration of the equilibrium levels of electrolytes and of urea, and, in addition, throw new and important light on how the reabsorptive mechanism may be conceived as operating.

Returning now to glucose, it would appear that this substance is somewhat out of line with the group of lipoid insoluble, water soluble, nonelectrolytes. If account is taken of intraocular consumption of glucose, the transfer of this substance may not be retarded at all. We have here, then, a *possible* suggestion that glucose is actively secreted into the eye. The exceptional position of glucose and of other metabolized sugars is, again, not unique for the eye. A large literature exists indicating an active transport of various metabolized sugars across the intestinal wall. It is thought that an active metabolic process by which these sugars are phosphorylated at one side of the boundary, and de-phosphorylated at the other side may explain their active transfer. There is, however, no necessary implication that this active transport of metabolized sugars is associated with an over-all movement of water. According to a currently held theory, glucose is present in the glomerular filtrate in the kidney by simple diffusion without any active secretion involved. It is reabsorbed by the tubules by an active secretory mechanism. Intravenous injections of glucose produce a marked diuresis. Therefore, the increase in the active transfer of glucose from the tubules back to the blood stream is not accompanied by a corresponding increase in tubular reabsorption of water.

Ascorbic acid is present in the aqueous of many mammals, including man, in concentrations very markedly higher than in the plasma. In rabbits the concentration ratio is about 10 to 1. The excess of ascorbic acid in the aqueous might be the result of local synthesis or of active transfer. Both these possible explanations have been advanced with some experimental support. Local synthesis, however, seems very unlikely because guinea pigs, monkeys, and man all show an excess of ascorbic acid in their aqueous, although animals of these species are unable to synthesize ascorbic acid and suffer from scurvy if vitamin C is eliminated from their diet. In fact, the disappearance of ascorbic acid from the aqueous is a *very early symptom of*

vitamin-C deprivation in guinea pigs, and this could not be true if it were being synthesized locally independent of the supply in the plasma.

Goldmann and Buschke[30-32] showed that over a wide range of concentrations, the aqueous ascorbic-acid level fluctuates in proportion to the plasma level. They concluded that the aqueous ascorbic acid was derived from that in the plasma, and that the excess concentration in the aqueous must be attributed to active transport rather than to local synthesis. Kinsey[36] has carried the argument still further. If ascorbic acid is actively transferred into the aqueous, then there must be some limit to the capacity of the transferring mechanism. Within the physiologic range he confirmed the findings of Goldmann and Buschke, but when the plasma ascorbic-acid level was pushed very far above the normal range, an upper limit of aqueous ascorbic-acid concentration was reached.

There seems no doubt, then, that ascorbic acid is actively transferred into the aqueous. Here also the ocular tissues are not unique. The concentration of ascorbic acid in the saliva, the tears, and in many other secretions is higher than that in the plasma. There is, however, no reason to assume in advance that the active transfer of ascorbic acid across these various tissue boundaries is linked with an active transfer of water. The two mechanisms, even when simultaneously present in the same organ, might in fact be wholly independent.

Finally, we come to hyaluronic acid, the mucoid component of the vitreous, which, as Karl Meyer[41] has shown, is present in appreciable concentration in the aqueous and not measurably present in the blood plasma. If aqueous is withdrawn from an eye, it is rapidly replaced by plasmoid aqueous in which the hyaluronic acid content is low, but from this low level the normal concentration is slowly reattained. If excess hyaluronic acid is injected into the anterior chamber, the excess, at first rapidly and then more slowly, disappears. One must conclude that

hyaluronic acid is normally secreted into the ocular cavity, and, since this substance is not present in the plasma, we must be dealing here with local synthesis rather than active transfer.

Again we must ask, and leave for the present unanswered, the question whether the local synthesis of mucoid is in any way linked with fluid transport. There are many tissues in the body in which mucoid synthesis occurs without any obvious relation to fluid transport, for instance, the umbilical cord, the synovial tissues, cartilage, and so forth. There are also some organs, for instance, serous glands, the kidney, and liver, in which fluid transport occurs without mucoid synthesis. There are, however, many mucous glands in which mucoid synthesis and fluid transport are conjoined, and in which the two processes may nor may not be integrally linked.

The conclusions which seem to me justified from studies on the chemical composition of the aqueous may be summarized as follows: (1) Hyaluronic acid is secreted into the ocular fluid in the sense that it is synthesized locally. (2) Ascorbic acid, certainly, and glucose, possibly, are secreted into the intraocular fluids in the sense of active transfer from plasma to aqueous. (3) The osmotic measurements of Duke-Elder and Davson and the transport measurements of Kinsey and Grant are compatible with the notion that electrolytes are actively secreted into the ocular fluid, that water follows by osmosis, that urea and like substances are filtered out in the process, and that the reabsorption of the intraocular fluid is by a process equivalent to leakage.[16,17]

If this seems unduly complex, I cannot apologize, for the state of the subject is complex. Rather I must apologize for making these studies seem unduly simple. Accurate chemical measurements on substances present in low concentration, in the minute volumes of fluid that can be obtained for analysis, present major problems in chemical technique for their solution. It is no wonder that the results of different investigators are

occasionally conflicting. Rather it is a great wonder and a great tribute to the meticulous care and diligent labor of this group of investigators that their results have achieved broad and substantial agreement. Also, it is no wonder that debate regarding the interpretation of the results has been lively, for the subject has intrinsic importance, and the persons concerned are lively.

Having reached thus far it seems appropriate to ask: if there are secretory contributions to the intraocular fluid, where do these several secretory acts take place, what are the mechanisms involved in these several secretory processes, are these mechanisms independent or integrally linked with one another, how are these mechanisms activated and how controlled? These questions form the logical background of those studies that I have been asked to summarize. I hasten to add that these questions were not, historically, the background of the studies that I undertook in this field, for information as to the chemical composition of the aqueous was at that time much less well defined than it is now. The most that I asked myself at that time was: Supposing there is secretion of the intraocular fluid, where and how does this take place?

A clue as to "where" came to us early from studies on the reabsorptive mechanism.[16] If the eye is connected with a fluid reservoir and the pressure raised far above normal, fluid runs into the eye from the reservoir at a steady rate, and is absorbed from or escapes out of the ocular cavity at a corresponding rate. It was easy to show that the escape or absorption occurs almost exclusively from the anterior chamber, that the tissues behind the iris do not participate appreciably in the absorption or provide the portal of escape.

If the ocular tissues are poisoned by cyanide, on the other hand, quite appreciable quantities of fluid are absorbed by tissues behind the iris at supranormal intraocular pressure. It was evident that some metabolic processes were involved in the resistance which the posterior ocular tissues offer to the absorption of fluid. When the intraocular pressure is brought below its normal level, the anterior chamber becomes shallow, and fluid enters the posterior chamber at a considerable rate. Under these circumstances, the fluid in the posterior chamber and in the Greef vesicles that form on the ciliary processes becomes plasmoid.

It is plain, then, that some tissue behind the iris exhibits in its unpoisoned state the phenomenon of irreciprocal permeability to water. Phenomena of this type have been widely found associated with secretory organs. We concluded that if there was an organ for the secretion of the intraocular fluid, it was probably located behind the iris, and since nothing pointed to the retina as a possible secretory organ, we concentrated our attentions on the ciliary body.

The supposition that the ciliary body might be an organ of secretion was strongly supported by our experience with the variety of dyes.[18] This tissue shows a remarkable and coherent set of phenomena of anomalous transport with respect to a large number of crystalloid dyes, tending to accumulate basic, that is, cationic dyes, in the epithelium and acid, that is, anionic dyes in the stroma. The final distribution of the dye is the same irrespective of whether it is introduced to the tissue on the epithelial side or into the stroma via the blood stream.

Phenomena of this type are always subject to the possible suspicion that they represent the result of selective staining rather than anomalous transport. We were very fortunate, therefore, to find that these phenomena could be studied in the excised tissue maintained supravitally. If the tissue was poisoned with cyanide, the anomalous behavior of the dyes disappeared. If the tissue was placed under nitrogen, the anomalous behavior of the dyes disappeared reversibly, and reappeared on readmission of oxygen. Such behavior could not possibly be attributed to selective staining.

It was concluded, therefore, that the anom-

alous distribution of these dyes in the ciliary processes represented a true example of anomalous transport, and that the anomalous transport was dependent upon the oxidative metabolism of the tissue. We concluded further that, if there was secretion of the intraocular fluid, the ciliary processes were a likely site of the secretory mechanism for here was a tissue that exhibited a veritable exuberance in pushing things around.

Having decided to search in the ciliary body for a possible secretory mechanism it was necessary first to clarify our own ideas as to what we were looking for. By a secretory mechanism concerned in water transport, we mean an arrangement of elements in the tissues, such that the chemical energy of cellular metabolism is converted into mechanical energy of water movements.

Let us consider this problem from the point of view of an engineer, and ask ourselves how the chemical energy of metabolism could conceivably be converted into the work of water movement. The chemical energy of metabolism becomes available primarily through the interaction of substrates with enzymes or enzyme systems. Insofar as the enzymes and substrates are considered as being suspended or dissolved in a fluid environment, no effective conversion of chemical energy to water transport appears possible, for the mechanical transport of water requires at least some sort of boundary across which the water is to be transported, such that the water, once moved through the boundary, will not immediately flow back to its original position. The first requirement for a water-secreting system, then, is a boundary across which the secretory work is to be performed.

Given such a boundary, the second requirement is that the metabolic processes on the two sides must differ from each other so as to generate a difference in the potential energy on the two sides of the boundary. Only when there is a difference in potential energy between two parts of a system is there free energy available to do mechanical

work. The difference in potential energy on the two sides of the boundary might exhibit itself in osmotic or electrical or other form.

It follows that the third requirement for a water-secreting mechanism is that the characteristics of the boundary must be such as to transform the free energy into the work of water movement. The particular characteristics required of the boundary depend on the form in which the energy is available, but, in any case, both a difference in potential energy across a boundary and a boundary whose special characteristics are appropriately related to the special form of available energy are required.

The significance of these basic requirements will become clearer if I digress briefly to indicate the present status of theories regarding water transport in the domain of general physiology. Work in this field has been enormous in its extent, and has engaged some of the best minds of our generation. Any brief compendium that I can make will necessarily present only a simplified and inadequate picture. Even the large monographs by Gellhorn,[29] Höber,[33] and Davson and Danielli[9] present each a truncated account of the matter. Nevertheless, the problem of ocular-fluid transport cannot be viewed in isolation but only against the background of knowledge and thought regarding fluid and solute transport in the domain of general physiology. The problems of ocular-fluid transport constitute but one small item in this general field. It may be stated at the outset that no satisfactory general theory of water secretion has so far been developed, largely, it seems to me, through neglect of consideration of the basic engineering requirements outlined above. Nevertheless, a vast number of careful and interesting observations have been made.

In serous glands the epithelial cells contain many cytoplasmic granules. Observations in vivo have revealed that during secretion certain of these granules, the so-called zymogen granules, grow rapidly in size and are discharged into the lumen. It is not clear

whether the contents discharged into the lumen are chiefly solid matter which is diluted and dispersed in the watery secretion provided by some other mechanism, or whether the swollen zymogen granules are in essence vacuoles, similar to the excretory vacuoles of the protozoa. In the latter case, the boundary of the vacuole would be that across which the secretory transport actually takes place. Even in the former case, the introduction into the lumen of water-soluble colloidal material could, through its colloid osmotic pressure, play a role in water transport.

In mucous glands the mucoid material can clearly be seen in a sharply outlined region in each goblet cell. Presumably the interior of the goblet contains enzymes capable of synthesizing the mucoid while the boundary is presumably permeable to the substrates out of which the mucoid is synthesized, but impermeable to the synthetic product. Mucoids are hydrophilic colloids and their synthesis must be accompanied by an accumulation of water in the goblet, and this water along with the mucoid is eventually discharged into the lumen. Since the molecular size of the mucoids is enormous, their colloid osmotic pressure is not very great, and the amount of water transported in this fashion is probably relatively small.

Some indication of the probable magnitude of the mucoid contribution to water transport may be reached in respect to the eye. The protein osmotic pressure of plasma, that is, the hydrostatic pressure at which plasma is in equilibrium with its dialysate is generally estimated at about 25 mm. Hg. This is the osmotic pressure of a 1.5 millimolar solution of a nonelectrolyte. Plasma contains about 6 percent of proteins or 60,000 mg. per liter. From these two figures one can estimate that the average molecular weight of the plasma proteins should be about 40,000, a figures which agrees well with more direct determinations.

According to Meyer, the vitreous contains 2.5 percent of mucoid. In order that the colloid osmotic pressure of the vitreous should equal that of the blood, the average molecular weight of the mucoid molecules would have to be about 1,500. The estimated molecular weight of hyaluronic acid is of the order of 100,000, consequently the synthesis of mucoid can contribute only a very small factor of water transport into the eye. As a matter of fact, if the colloid osmotic pressure of the vitreous mucoid were appreciable, there would necessarily be a corresponding excess of hydrostatic pressure in the vitreous as compared with the aqueous, since the latter contains only one sixth as much mucoid as the former.

Actually the difference in pressure, if any, is very small. While the aqueous cannot, therefore, be accounted for as a mucous secretion, this analysis reveals the role of a difference in potential energy, in this case colloid osmotic plus hydrostatic pressure, operating across a boundary, in this case a simple semipermeable membrane. In the synovial cavities, in which the mucoid concentration is very high, a mechanism of the type outlined might account for the whole of the water content.

The frog's skin has been the subject of extensive studies. When this tissue is placed as a diaphragm between two chambers of isotonic salt solution, fluid is transferred from the epithelial to the subcutaneous side. The transfer is inhibited by cyanide. An electric potential difference is measurable across the membrane and this is also suppressed by cyanide. Much has been made of the fact that under these postmortal conditions the corium tends to swell more actively than the epithelium, but there is no reason why such a local swelling should effect a net transfer of fluid.

It is, nevertheless, possible to conceive of a system in which reversible turgescence could play a role in water transfer. If the boundary material became alternatively hydrophilic and hydrophobic on reversible chemical change, for instance, if it became hydrophilic on oxidation and hydrophobic on reduction, and if the respiratory metabolism

of the tissues on the two sides was such that one tissue tended to oxidize the boundary, the other to reduce it, then water would be added to the boundary on the oxidizing side and removed from it on the reducing side, the boundary constituting at the same time a link in a hydrogen transport chain between a set of oxidases in one tissue, and reductases in the other.

Reversible oxidation and reduction is not the only chemical change that can be conceived of as related to reversible hydration and dehydration. Esterification and de-esterification might have a similar effect. Changes in pH are also notorious in their influence on water binding. A system in which such opposite chemical changes were continuously occurring on opposite sides of the boundary would transfer water toward the dehydrating side while at the same time transferring the reacting group in the same or in the opposite direction.

Another interesting field of physiologic study in this connection is that of the fresh-water fish. These animals maintain an internal environment hypertonic in electrolytes to their external environment. Water enters by osmosis through the gills which are presumably relatively impermeable to electrolytes, and the excess water is excreted by these animals in the form of very hypotonic urine This accounts for the homeostasis of the fish, although the renal mechanism is not understood, but leaves out of account the fact that some electrolytes have to be accumulated during growth, and also to make good the small renal losses. No mechanism for such accumulation has been proposed. If the fish get their inorganic salts from their food, the problem of salt accumulation is merely displaced to another species.

The process of electrolyte accumulation is again the key problem in respect to the movement of water in the sap of plants. The concentration of electrolytes, particularly of potassium salts, in the sap is much higher than in the soil water in which plants' roots are exposed. Thus water is drawn into the roots by osmotic forces and is lost from the leaves by evaporation. Consequently the water transport in plants presents no critical problems except in those special species whose leaves "sweat." But as the plant grows it increases its electrolyte content by accumulation out of a hypotonic environment. A possible explanation of this accumulation is available in the supposition that metabolic activity in plant cells produces organic acids which are either nondiffusible or unable to permeate through the cell wall. If the cell wall is, then, permeable to hydrogen ions and potassium ions, an exchange could occur leading to an accumulation of potassium within the cell. This hypothesis, however, requires that the pH of the cell should be below that of the soil, a requirement that does not appear to be generally fulfilled. We are left, therefore, with the need to explain an active transport of potassium ions.

Similar problems of accumulation confront the mammalian physiologist. While the total concentration of electrolytes inside and outside of the body cells is approximately equal, most cells (perhaps not all) contain potassium as their chief inorganic cation, while the body fluids contain chiefly sodium. In the red blood cell the ratio of potassium to sodium is 10 to 1, while in the plasma it is 1 to 50.

An easy explanation in the past has been that the red-cell membrane is impermeable to cations and, having been loaded with its quota of potassium, it holds this quota throughout its life by simple inert non-exchange with the adverse environment. This hypothesis, of course, fails to explain how the potassium got inside the red cell in the first place.

Recent studies with radioactive sodium, however, have shown that the red-cell membrane is not completely impermeable to sodium. If red cells are suspended in plasma containing radioactive sodium, either in vivo or in vitro, an exchange of normal sodium for radioactive sodium takes place, so that the small amount of sodium inside the cell,

only 10 percent of its total inorganic base, eventually contains the same fraction of radioactive isotope as is present in the plasma. According to Cohn and Cohn,[8] 50 percent of the equilibrium ratio is reached in 8 hours. These new experiments taken at their face value indicate that the theory that cell membranes are impermeable to cations does not suffice to explain the maintenance of the high intracellular K:Na ratio, just as it fails to explain the anomalous accumulation of potassium in the cell during growth.

The problems of renal physiology are even more complicated for here the glomerular filtrate which is in effect a dialysate or ultrafiltrate of the plasma, passes successively through at least 4 different tubular organs which transfer a variety of substances into and out of the urine. Although there is considerable knowledge of the net exchange, very little is as yet known about what substances are transported conjointly in a single functional segment of the renal tubule.

It is to be admitted in frank veneration of the enormous achievements of the general physiologists in these various fields, that the problems of water transport and of ionic transport are extremely difficult and complex, and that this complexity is still further compounded in many of the organs that have, for various reasons, engaged their special interest. Thus the kidney is not a single secretory organ but a whole group of such organs arranged in series.

The serous glands present not merely special problems in the special composition of their secretory product, but are further complicated by special start and stop mechanism involving neural or humoral controls. Study of the mucous glands is handicapped by lack of knowledge of the biochemical mechanisms of mucoid synthesis. The problem of salt accumulation in plants is inextricably linked with the still more recondite problem of growth.

It is the fortunate privilege of ophthalmologists that we have been forced to devote our attentions to a potential secretory organ in which the secretory product differs little from a dialysate of the plasma, in which special synthetic metabolic processes appear to play only a minor or indirect role, in which the special complexities of start and stop mechanisms appear not to be present, in which the perplexing problems of growth need not be held in the forefront of our minds. The chorioid plexus is, perhaps, an equally happy choice for introductory studies in this problem, but other comparably suitable test objects are few or at any rate hard to find.

Returning, then, to the ciliary body, we have as a firm beginning for our study the anomalous transport of anionic and cationic dyes. The boundary across which this transport operates is the boundary between stroma and epithelium. There is, at this point in the study, no reason to believe that water is also transported across this boundary, but we can at any rate attempt to disentangle the mechanism of dye transport, and see where this will lead us.

The argument set out above requires that we seek the source of energy for the dye transport in terms of a difference in potential energy on the two sides of the secretory boundary. Since the anomalous transport of dyes disappears reversibly under asphyxia, it is clear that the energy that we seek to identify is ultimately derived from the oxidative metabolism of the tissue. Such energy might become available to the secretory boundary in a variety of forms. There might be a difference in the redox potential on the two sides of the boundary. There might be a difference in the availability of substances with high energy phosphate bonds, or of some other reactive substances on the two sides of the boundary.

We chose initially to explore the first of these possibilities for several reasons. In the first place, there was available, particularly from the work of Clark and Cohen,[6] a series of indicator dyes with the aid of which intra-

cellular redox potentials could be estimated. In the second place, there was, in respect to the potential intraocular secretory mechanism, some a priori doubt as to whether a coherent theory of secretion on the basis of phosphate bond energy could be worked out.

In a secretory mechanism which derives its energy from high energy phosphate carriers, the boundary would, in accordance with the principles outlined above, be continuously phosphorylated on one side and de-phosphorylated on the other, the de-phosphorylation yielding the energy for the secretory transfer. This possible arrangement, however, would, of course, include an active transfer of phosphate across the boundary. A secretory organ that operated in this fashion should yield a secretion that was either very rich or very poor in phosphate unless there were associated with it some additional device for phosphate equilibration. Since the inorganic phosphate of the aqueous does not differ considerably from that of a plasma dialysate, explorations of this possibility appeared at best a second choice.

Experiments with redox indicator dyes,[18] introduced into the ciliary tissues without mechanical trauma, revealed that these tissues possessed well-poised potentials. The results with a large series of dyes of very varied chemical structure gave a consistent pattern, and one which was altered consistently by altered experimental conditions such as anoxia and cyanide poisoning. The interpretation of these results requires, however, great caution. The fundamental considerations involved in such interpretation have been indicated in the classical studies of Cohen and Chambers[5,7] on the intracellular redox potential of protozoa.

Redox indicator dyes are chemical substances which are readily and reversibly oxidized and reduced, and which change color on oxidation and reduction. They change from their reduced to oxidized state or vice versa in a characteristic fashion de-

pending on the redox potential of the environment in which they are placed, and with which they react. The redox potential at which an equal mixture of the oxidant and reductant of the indictor is present, that is, the midpoint of their color change, is characteristic for each indicator, and varies with pH.

The first requirement for the valid use of such indicators, therefore, is that the pH of the environment in which they are reacting should be known. In the ciliary body we used pH-indicator dyes, and tested the reliability of these pH indicators in the tissue by immersing the tissue with its indicator dyes in buffer solutions of known pH, and found that under these circumstances the pH-indicator dyes assumed the expected colors characteristic of the pH of the buffer solutions. There was, therefore, nothing in the tissue that violently disturbed the reliability of the pH indicators.

Using these indicators, then, without surrounding buffers we found that the pH of the tissue studied supravitally was in the reasonably expected range, close to pH 7.4. This was, then, the pH at which the redox potential was to be estimated.

The characteristic potential of each of the redox-indicator dyes in simple aqueous solution is well known. In the complex protein-laden internal environment of the cell, the thermodynamic activity of the indicator molecular special may not be the same as in the simple in vitro solutions, and errors may thus be introduced into the estimate of intracellular redox potential.

A similar problem, of course, arose in respect to the use of pH indicators for the determination of intracellular pH. It was for this reason that the experiments were made of immersing tissue with indicator-pH dyes in buffered solution. The fact that no significant difference in color was observed between the dyes in the tissue and in the surrounding buffer solution indicated that the difference in activity of the indicator within

the cell from that outside in the buffer solution was negligible within the range of accuracy of the measurement, in this case amounting to one to two tenths of a pH unit.

Similar variations in thermodynamic activity of the redox-indicator dyes would not introduce errors in the estimate of intracellular redox potential of more than ±10 millivolts. The observational error of the experiment itself left an uncertainty of ±15 millivolts. The substantial concordance of results with a whole series of dyes of very varying chemical configuration further supported the conclusion that errors in the estimate of intracellular redox potential due to unknown variation in thermodynamic activity of the indicators within the tissue were small. In any case the total uncertainty of the redox potential measurements would be smaller than ±30 millivolts, and would be small compared to the differences actually found in the different tissue regions.

A third consideration in the interpretation of these observations is somewhat more complicated. When oxidants and reductants are mixed in a test tube, they interact until they reach an equilibrium composition. If a small amount of indicator dye is introduced into the mixture, it reacts with the components and comes to equilibrium with them. The resulting color of the indicator is used to estimate the redox potential of the system. Within cells and tissues no such equilibrium exists. At most we can deal only with steady states. Some enzymes in the cells are continuously reacting with molecular oxygen and becoming oxidized in the process. The oxidized enzymes in turn react with other cellular components oxidizing these components, and themselves becoming reduced and capable of again reacting with molecular oxygen. The cellular components which have been oxidized in turn oxidize other components, and this chain of reactions continues by successive links until finally metabolites are reached. This chain of reactions has many links. Some of the links are proteins,

that is, enzymes. Other links are diffusible substances which carry the oxidation and reduction from one enzyme to another. Some of these diffusible links in the chain are independently reactive while others are sluggish in their reactions except when activated by association with the appropriate enzymes.

The independently reactive substances within the cell thus constitute a pool which will tend to be more oxidized or more reduced depending on the bottle necks in the reacting chain. If oxygen is not available or if the enzymes that normally react with oxygen are poisoned, for instance with cyanide, the level of oxidation in the pool will fall. If oxidizable metabolites are not available, or if the enzymes that normally catalyze their oxidation are poisoned, the level of oxidation in the pool will rise. In two tissues both of which have adequate supplies of oxygen and of metabolites, the oxidative levels in the pools will depend on the abundance and enzymatic activities of the various enzyme systems within them.

When redox-indicator dyes are introduced into cells, they react with and become a part of the intracellular pools of reactive substances. The redox potential determined by the indicator is that of the pool of substances with which they react. The existence of well-poised potentials within cells observable by this means does not at all imply that all the substances within the cell are in equilibrium with this potential. Nevertheless, the recorded potentials do in fact indicate the balance within the cells between oxidative and reductive processes. In the ciliary body, the measurements with indicator dyes showed that there was a difference in apparent redox potential between the epithelium and the stroma of almost one quarter of a volt, the epithelium being the more oxidizing tissue.

Such a difference between these two tissues might be due, as indicated above, to a difference in the enzymatic constitution of the two tissues. This proved to be the case. In a series of studies[22, 25, 27] in which the

epithelium and stroma of the ciliary body were mechanically separated from one another, and then analyzed separately for their enzyme content, it was found that the epithelium contained an abundant supply both of enzymes that react with molecular oxygen (the cytochrome oxidase system), and of enzymes that catalyze the oxidation of carbohydrate substrates (for example, lactic and malic dehydrogenases). The ciliary stroma, on the other hand, contained no detectable enzymes that react directly with molecular oxygen, but nevertheless contained an abundant supply of lactic and malic dehydrogenases, roughly as much per cell as in the epithelium.

The existence of adjacent tissues operating under different respiratory patterns has long been known. Like so many other aspects of modern cellular physiology, the existence of such phenomena was first described by Ehrlich,[15] who spoke of oxidative sources and sinks in the tissue. Adjacent tissues supplied with differing respiratory enzyme systems may presumably coexist without any mutual metabolic relations, or they may exchange metabolites or some other components in a sort of symbiosis. Finally they might conceivably interact directly if the boundary between them were itself reversibly oxidizable and reducible. It is this latter form of direct interaction which, if present, might, under appropriate conditions, serve as the mechanism of secretory transport. Before inquiring into the appropriate conditions required for secretory transport, we must first decide whether the boundary in the ciliary body is reversibly oxidizable.

So far as the anomalous transport of anionic and cationic dyes is concerned, the boundary lies at or near the junction of epithelium and stroma, and coincides in effect with the boundary of differing redox potential. Unfortunately, we have found no way in which this boundary can be mechanically isolated and subjected to direct chemical study. It is quite possible, in fact, that the effective boundary may be merely a mono-

molecular layer. Consequently, it was difficult to plan an experimental approach by which the chemical characteristics of the boundary could in part be revealed. We were very lucky to find that, under conditions under which the active anomalous transport of dyes was suppressed, that is, under asphyxia or cyanide poisoning, the boundary exhibits a selective permeability, being more permeable to anionic than to cationic dyes. Moreover, this selective permeability was reversed at lower pH.
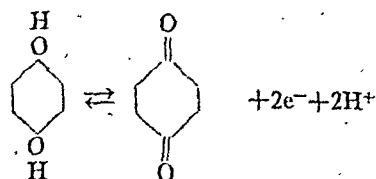
We were thus provided with a means by which the isoelectric point of the boundary could be determined, and found that the isoelectric point could be shifted reversibly on exposing the tissue to oxidizing or reducing solutions. Moreover, the level of oxidizing potential required to shift the isoelectric point partially toward its value in the oxidized state was not greater than that normally present in the epithelium under aerobic conditions, and the level of reducing potential required to shift the isoelectric point back to its value on reduction was no greater than that normally present in the stroma. The boundary, therefore, has the characteristics required to serve as a link between the redox-reactive pools of materials in the epithelium and in the stroma.

On oxidation the isoelectric point of the boundary shifts toward higher pH, and the isoelectric zone becomes broadened, indicating that strong basic groups appear on oxidation. However, even on oxidation the isoelectric point remains on the acid side of physiologic pH, consequently the overall charge on the boundary is negative in both its oxidized and its reduced states. There are many familiar substances in which strong basic groups appear on oxidation. Methylene blue is such a substance. Nicotinamide which furnishes the redox groups in coenzyme I and II has similar properties.
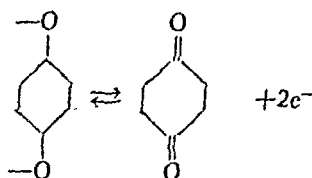
When any substance is oxidized, the primary reaction consists in the loss of one or more electrons. It is for this reason that characteristic electrical potentials are found

in relation to redox reactions. The electron loss may be associated with the loss of a hydrogen ion. In this case the overall effect of oxidation is the removal of hydrogen from the substance oxidized. Or again, the loss of electrons may be associated with the uptake of water and loss of hydrogen ions. In this case the overall effect of oxidation is the addition of oxygen to the substance oxidized. In either of the latter cases no net change in electrical charge need occur in the substance oxidized.
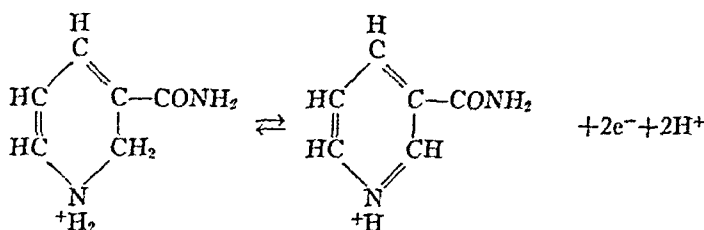
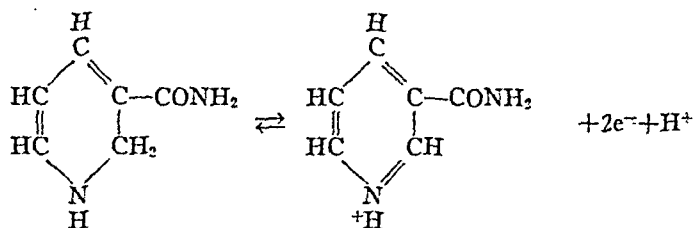A boundary composed of a substance of one of these sorts, operating between two systems of differing redox potential, would transfer a hydrogen ion from the reducing side to the oxidizing side with each electron. Electrical neutrality would thus be maintained at each step of the reaction, and nothing else need be transported in the process. Such systems would not in general act as secretory mechanisms. Incidentally a boundary composed of such substances would suffer no change in its charge, and hence no appreciable shift in its isoelectric point on oxidation and reduction.

For almost all such substances there exist pH ranges in which the electrically compensating loss of hydrogen ions is incomplete or absent. In such case the oxidized substance suffers a net loss of anionic charges or a net gain of cationic charges. Compare, for instance, the oxidation of hydroquinone at low pH:

$$+2e^- + 2H^+$$

with the same reaction at high pH:

$$+2e^-$$

or the oxidation of nicotinamide at low pH:

$$+2e^- + 2H^+$$

with the same reaction at high pH:

$$+2e^- + H^+$$

There are indeed very many substances in which the electrically compensating loss of hydrogen ions is absent or incomplete on oxidation at physiologic pH. A boundary composed of one of these latter substances, operating between two regions of differing redox potential, would not transfer a hydrogen ion from the reducing side to the oxidizing side with each electron. The maintenance of electrical neutrality in such cases could be accomplished only through a net transfer of cations from the reducing to the oxidizing side, or of anions in the opposite direction or both. Such a transfer of ions is precisely that which we have found to characterize the anomalous transport of anionic and cationic dyes in the ciliary body. Moreover, a boundary of this type would suffer a net change in its electrical charge, and con-

sequently a shift of its isoelectric point with oxidation and reduction. It is to be concluded, therefore, that an oxidative interaction of the type described would satisfactorily account for the phenomena of anomalous dye transport in the ciliary body.

The full course of one cycle of oxidative interchange between the two tissue components can be outlined as follows: The ciliary epithelium contains cytochrome oxidase, and the anomalous dye transport is inhibited by cyanide. We can assume, therefore, that the oxidative cycle begins with the oxidation of cytochrome oxidase by molecular oxygen, a process which requires the transfer of electrons from the cytochrome oxidase to oxygen.

(1) Reduced cytochrome oxidase $+\frac{1}{2}O_2\rightarrow$ oxidized cytochrome oxidase $+O^-$

(2) $O^-+H_2O\rightarrow 2\overline{OH}$

In a system buffered by bicarbonate there would follow:

(3) $\qquad 2\overline{OH}+2CO_2\rightarrow 2H\overline{CO_3}$

Regeneration of reduced from oxidized cytochrome oxidase we assume occurs in respect to the particular chain of events that we are following, at the expense of corresponding oxidation in the boundary. When this latter has been reduced by the stroma, the net effect of the reduction of one atom of oxygen so far as the epithelium is concerned is to produce in the epithelium two new anions (bicarbonate ions) not completely balanced locally by corresponding cations.

The reduction of the boundary by the stroma occurs ultimately at the expense of oxidation of a metabolite.

(4) $\qquad RH_2-2e^-\rightleftarrows R+2H^+$

Again, in the presence of bicarbonate buffer

(5) $2H^++2Na^++2H\overline{CO_3}\rightleftarrows 2Na^++2H_2O+2CO_2$

Thus the full effect of one cycle involving the reduction of one atom of oxygen in the epithelium, and the oxidation of one molecule of metabolite in the stroma, yields a net gain of two incompletely balanced anions in the epithelium and two incompletely balanced cations in the stroma. Electrical neutrality under these circumstances can be maintained only by a transfer of anions from epithelium to stroma, or of cations from stroma to epithelium. Such an ionic transfer constitutes an ionic electrical current, balancing and neutralizing the electronic transfer of the redox interaction. Which of the two phases of the ionic current will predominate, that is whether the ionic current will consist predominantly in a transfer of anions toward the stroma or of cations toward the epithelium will depend on the character of the boundary.

We have already seen that the boundary in its reduced state is isoelectric at pH 5.5. It is, therefore, an amphoteric substance containing both acidic and basic groups, the dissociation constants of which are such that at physiologic pH, the number of dissociated acid groups exceeds that of the dissociated basic groups yielding a net overall negative charge on the boundary relative to the surrounding watery medium. Elementary considerations of electrostatic forces lead to the conclusion that in the layer of fluid immediately adjacent to such a negatively charged boundary, the so-called adsorbed layer, there would be a relative excess of cations and deficit of anions as compared with the surrounding fluid.

On oxidation of the boundary, some new basic groups appear in it and the isoelectric point is shifted to pH 6.5. At physiologic pH there is, therefore, even in the oxidized boundary a net excess of dissociated acid groups, and a net overall negative electrical charge on the boundary relative to the surrounding medium. Under these circumstances there would still be a relative excess of cations and deficit of anions in the adsorbed layer compared with the surrounding fluid, although the excess of cations and deficit of anions would be less marked than

when the boundary is in its reduced state.

Bethe and Toropoff[4] have shown that the imposition of an ionic electrical current across a charged membrane in a saline environment leads to the predominant movement of those ions that are present in excess in the adsorbed layer. The application of their findings to our case would lead to the conclusion that the predominant ionic movement in the maintenance of overall electrical neutrality would be that of cations (sodium ions) from the stroma to the epithelium. Osmotic and electro-osmotic movement of water would, of course, accompany the cations. The net product of such a secretory organ as we have so far identified in the ciliary body would be a slightly hypertonic fluid whose chief electrolyte constitutent would be sodium bicarbonate. Since this does not correspond to the facts, it is evident that the analysis given so far cannot be complete.

The pattern of organization pictured so far, although incomplete, is not absurd. There are several secretory organs which do, in fact, produce a secretion consisting chiefly of a slightly hypertonic solution of sodium bicarbonate. The salivary secretion of the cud-chewing herbivora is an example of such a secretion. The coelomic fluid of the turtle has been shown by Homer Smith to contain chiefly sodium bicarbonate. The basic reaction of the secretion of the small intestine is in man no doubt the result of the predominance of bicarbonate among its anions.

In the intraocular fluid the chloride-bicarbonate ratio is approximately the same as that in the plasma. If the primary secretion product is bicarbonate solution, the conversion of this to the composition of the actual aqueous could occur as the result of an ionic exchange. Exchanges of this type are well known in many biologic processes and can be extremely rapid.

A phenomenon closely related to that which is here postulated has been extensively studied in the blood. On passing through the peripheral capillaries the red blood cell loses oxygen, some acidic groups of the hemo-globin become undissociated, and bicarbonate ions are picked up. In passing through the pulmonary capillaries the reverse process takes place. Each capillary transit requires, on the average, only a few seconds at most, and yet equilibration is effectively completed each time. No special mechanism appears to be required to account for such an exchange as is here postulated. Rather we must wonder what special mechanism impedes such an exchange in organs like the small intestine.

I have given an account of the studies into which we were led, and of the argument that we have followed in search for an explanation of the anomalous dye transport in the ciliary body. These studies have revealed a complicated arrangement of complicated substances in the tissue, some of which we have identified approximately as to their nature and their location.

If chemical reactions between these substances do, in fact, occur in accordance with the general organized pattern in which we have shown they might occur, then the anomalous dye transport would be fully accounted for and, in addition, there would be a secretory transport of electrolytes and water from stroma to epithelium.

Up to this point in the argument, evidence is lacking as to whether the tissue components do in fact interact in the way we have shown that they might interact. Even if we assume that such interaction does in fact take place, we have no quantitative measure of how much of such interaction takes place, and cannot decide whether the potential contribution of this mechanism constitutes a major or a trivial aspect of the intraocular fluid transport.

It is not easy to find an experimental approach that could be expected to allay these doubts and uncertainties. A possible road, however, becomes apparent from the following argument. The oxidative chain which we have postulated, connecting the oxidase enzymes of the epithelium to the boundary and the boundary to the dehydrogenases of the stroma, must consist of many links. If one

could identify some of these links, if one could find experimental procedures by which a given link could be removed from the system and then readministered, it might be possible to show that the set of phenomena that we have linked in theory—anomalous dye transport, redox potential of the epithelium and of the stroma, and water transport—are conjointly altered in the manner expected from the theoretical considerations outlined above.

Time does not suffice to report on this phase of our studies,[19, 21] but it may be stated in summary that adrenalin and ascorbic acid each appear to contribute a link in the intercellular redox chain. Adrenalectomized animals (protected against cortin deficiency) and animals on a vitamin-C deficient diet show marked and similar changes in the physiology of their ciliary processes. Anomalous dye transport ceases. The redox potential of the epithelium rises and that of the stroma falls, indicating a decrease in the rate of reduction in the epithelium and a decrease in the rate of oxidation in the stroma. Water transport into the eye is reduced as can be shown in experiments on the reformation of the aqueous after removal of some of the intraocular fluid. All these phenomena occur at a time when the animals show no gross signs of debility as the result of the experimental procedure, and all are back to the normal state immediately on administration of the defective substance.

The results of these experiments lend very strong support, indeed, to the interpretations we have given, and indicate that the contribution of the mechanism that we have described to the intraocular fluid transport is a very significant and not a trivial one. Moreover, the role which this interpretation assigns to ascorbic acid leads to a simple and ready explanation of the mechanism of intraocular ascorbic acid secretion.

This brings the account of our studies to a suitable resting place, but it is not to be presumed that we have reached a satisfactory and full account of the secretory mechanism.

Our knowledge of the secretory boundary is very incomplete. The apparent activation of a redox chain by adrenalin raises questions regarding the pharmacologic mechanisms of adrenergic action that are at once fascinating and difficult to approach. [23, 24, 28] No data are, as yet, available to indicate whether or not the synthesis of the ocular mucoid is linked to the secretory mechanism that we have described.

Moreover, even if we have a full knowledge of how each component of the intraocular fluid is transferred across the secretory boundary, we would still stand only on the threshold, for the secretory organ that we have so far identified can act only on the fluid and solutes in the ciliary stroma. Transfer from plasma to extravascular fluid spaces in the ciliary stroma is required in order to make fluid and solutes available to the secretory organ. Since the classical studies of Starling,[45] it has been assumed that osmotic and diffusional forces suffice to explain the transfer across the capillary wall, but the inadequacy of such assumptions is clear if we try for a moment to specify what happens to the capillary wall during inflammation, and under the operation of vasomotor and humoral controls. In respect to the ciliary body such neural and humoral vasomotor controls have, as yet, not even been explored.[20]

The findings so far present few implications with respect to the pathologic physiology or control of glaucoma. At most they raise the question as to whether more effort might not profitably be directed toward a reduction in the formation of aqueous in cases of glaucoma, in addition to the present approach which concerns largely an effort to increase the outflow of fluid from the eye.

May I add one final word. The picture that has emerged from our studies of a busy metabolic interaction at the boundary between epithelium and stroma in the ciliary body, and of the dependence of secretory activity upon this interaction was not in our minds when these studies were begun, but has forced itself upon us with increasing

emphasis as the work progressed. It may well be that tissue boundaries in other organs are sites of equally busy interactions. Recent studies on the cornea in our laboratory have shown that there exist complex metabolic exchanges and interactions between the epithelium and the stroma in that tissue. The suggestion that metabolic exchange and interaction between adjacent cells and tissues in embryonic life may play a role in the process of development and differentiation has been tentatively advanced by some embryologists. A dim but intriguing vista of integrative relations at the intercellular level is thus presented.

1212 Eutaw Place (17).

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ANIRIDIA WITH ECTOPIA LENTIS AND SECONDARY GLAUCOMA*

GENETIC, PATHOLOGIC, AND SURGICAL CONSIDERATIONS

ALSTON CALLAHAN, M.D.
Birmingham, Alabama

Aniridia or, more correctly, irideremia is the clinical absence of the iris. A rudimentary iris is usually present, but the short stump is concealed behind the corneoscleral junction. Because of its extraordinary propensities as a dominant characteristic, occasionally an irregular dominant, and because of its striking appearance which facilitates investigation, it has received extensive study by geneticists. Indeed, so interesting are its hereditary and pathologic aspects that these have received far more attention than have therapeutic measures for aniridic cases.

Moreover, the gene producing aniridia also effects different varieties of abnormalities, ectopia lentis, ectopia pupillae, abnormalities of the mesodermal and ectodermal defects of the iris, iridotasis and embryotoxon, and so forth. Thus any of these abnormalities, in either severe or mild degree, which follow no certain pattern of distribution would indicate the presence of the gene in the specific family being studied. Cases with ectopic lenses are sometimes children of parents with uncomplicated aniridia and vice versa. Those with coloboma of iris or hypoplasia of stroma occur in sibships affected with aniridia alone or with the graver condition. In Beattie's report, affected members only transmitted the disease and normal children invariably had normal offspring, which fulfills the conditions of an irregular Mendalian pattern. Falls has on record a series of dominant patterns and two pedigrees which display the abnormality inherited as a simple recessive disease. The latter is supported by the presence of consanguinity of the parents of the affected individual.

HISTORY

Barrata reported a case in 1818, and is credited as being the first to investigate this condition. Reports of aniridia then appeared with increasing frequency and, in 1898, Foster was able to collect 154 cases in the literature and added two cases of his own. Since then Collins, Waardenberg, Ida Mann, Gates, and many others have reported aniridia cases and have enlarged our knowledge of this subject. Relative papers by Beattie and by Pincus have been recently published. Of the many theories advanced for aniridia, the two most probable refer the primary fault to a failure in development of the retinal ectoderm or an aberrant development of the vascular mesoderm. Duke-Elder believes both are operative in different cases.

GENETICS AND MUTATION

The prevailing view on mutation as a direct cause of abnormality in man has been that it is an extremely rare phenomenon without practical significance. Mutation has long been recognized in lower forms of life, such as molds and yeast, and even in higher forms of life. Importance is attached to gametic mutation because it is transmitted through reproduction of the species from one generation to another; somatic mutation occurs in the body cells outside gametes and asserts itself only in one individual. In recent years the occurrence of mutation in man has been acknowledged and its form may be dominant or recessive, the later type representing 92 to 95 percent of all mutations.

Evolution is assumed to have a tendency

to establish complete dominance of the normal type in relation to the pathologic type arising from mutation which lowers the viability of the individual. It is obvious that in man, the knowledge of whom is limited to relatively few generations and on whom no cross-breeding experiments may be performed, we shall never be able with certainty to demonstrate that a recessively hereditary disease has arisen from mutation. If a disease, which is known from experience to be dominantly hereditary, suddenly appears in a previously healthy family and afterward is inherited with regular dominance, it is reasonable to assume that the disease has arisen through mutation in one of the family concerned. Although the pathologic type may become extinct to clinical recognition after several generations, it meanwhile provides an interesting study.

Not uncommonly there occurs in a human pedigree a single, solitary eye abnormality which in other pedigrees shows marked evidence of heredity. Little is known about the proportion of such single-case pedigrees to those that show heredity, and figures based on published pedigrees generally will almost certainly understate the number of single-case pedigrees, which are less likely to be published than those which show hereditary. It is difficult to explain the presence of these solitary cases in a pedigree, whether retinitis pigmentosa, albinism, blue sclerotics, or aniridia. They occur probably in all hereditary eye conditions.

Are such manifestations Mendalian recessives linked to cases which existed in generations more remote than those to which our information extends, or is their presence the result of factor mutations in the chromosomes, or do they arise independently of the germ-plasm?

Furthermore, if the presence of a solitary case as previously defined is in some instances accounted for by the heredity alone, in other instances by environment alone, and in still other instances by the combined influence of both, what is the relative importance of these causes in hereditary eye affections?

The answer to these questions is of importance in any estimation of the inheritability of an eye affection, and it must influence opinion regarding whether any of the progeny are likely to be affected or not. Also, it may materially alter our conception of the proportion of single-case pedigrees to those showing inheritance.

The disease of aniridia is generally inherited from affected members of a family in a proportion of approximately 50 percent. In this study, 3 in the first generation were affected, and 6 in the second generation, amounting to a little less than 50 percent of the first member known (fig. 1). Being a dominant characteristic the trait becomes apparent as a heterozygote. There are no cases reported of two heterozygotes for the condition marrying each other and it is therefore impossible to say what appearance a homozygote for the condition would present. It is possible that lethal genes would accompany the homozygote condition. Infertility does not seem to accompany aniridia; in fact, the pedigrees reported are relatively prolific.

It can be assumed that in some ancestor the condition arose as a gene-mutation, and thereafter, as in other alterations of the germ plasm, the defect was transmitted in accordance with Mendalian principles. Nothing is known of the cause of gene mutations in human beings or indeed of mammals generally, but in the insect world the normal production of mutations can be multiplied by means of thermal or X-ray stimulation of the germ plasm. Stevenson and others have reported cases of aniridia without known affected ancestry, and in such cases it would seem that a new mutation must be postulated.

In recent years an attempt has been made to assess the mutation rate of various human abnormal conditions. J. B. S. Haldane began this work with the calculation of a mutation rate for hemophilia. Mollenbach has esti-

Fig. 1 (Callahan). Pedigree of aniridia family. Note that Generations III and IV are not arranged chronologically, but are altered to save space. However, proper ages are given.

mated the mutation rate for aniridia, on the basis of his findings in Copenhagen, to be between 1:50,000 and 1:100,000. Falls believes this estimate to be satisfactory.

CLINICAL APPEARANCE

Since no iris is visible, the "pupil" is as large as the cornea. Photophobia is present and poor vision is usually but not always the rule. In the absence of other abnormalities the frequent occurrence of low visual acuity may be accounted for by the fact that clinical and pathologic examinations have shown that sometimes the fovea is absent. Alger proposed the theory that in cases in which the macula is anatomically present, since refraction of light both outside and inside the equator of the lens without the iris diaphragm causes poor images, this lack of precision may deprive the macula of effective stimulation in the early months of life when normal development takes place.

Additional ocular anomalies are common, and these cases have cloudy corneas and ectopic lenses, which are cataractous. All eyes have or have had secondary glaucoma which has continued for years, increasing the size of the eye, and decreasing the vision.

PATHOLOGY

The first pathologic report of an aniridic eye was that of Pagenstecher who showed that at least a rudimentary iris was nearly always present. Treacher Collins reported his findings on three aniridic eyes. Two of these were removed from individuals with double aniridia, in each of whom a corneal ulcer perforated in one eye, and the development of subsequent secondary glaucoma necessitated removal of the eye. In the first of these the ciliary body ended anteriorly in a rounded, slightly projecting nodule which, although not sufficiently large to be seen through the cornea, was present, and was pushed forward in contact with the posterior surface of the cornea and was blocking the filtration angle. In the second the iris was represented solely by a small

rounded projection on the anterior surface of the ciliary body. The filtration angle of the cornea was blocked by the intimate adhesion of this projection.

The third case was of traumatic aniridia followed by secondary glaucoma and the eye was removed 12 years after the accident. The eye had remained blind since the accident and during the last 3 years had gradually increased in size, and was staphylomatous. The anterior part of the cornea showed some round-cell infiltration and new vessels between its layers. Besides other findings it was observed that the iris had been torn away at its extreme root. The ciliary body was very atrophic and the most anterior of the anterior processes of the ciliary body was intimately adherent to the posterior surface of the cornea at its periphery in the region of the ligamentum pectinatum.

Lembeck reported a case in which the rudimentary iris was enclosed between two lamellae of Descemet's membrane and had formed an abnormal union with the cornea and sclera. One of the lamellae of Descemet's membrane passed beneath the iris to which it had grown fast and was lost in the ligamentum pectinatum, while the other passed down over the posterior surface to cover the imperfectly developed ciliary bodies. The uveal part of the iris lay stretched out on the cornea to a greater distance than the retinal part in which one could easily recognize two layers.

We were fortunate in persuading the eldest affected child to permit us to remove her blind eye for examination and Dr. T. E. Sanders has kindly furnished us with the pathologic study.

A rudimentary iris is present (fig. 2) which varies slightly in size but is about 1 mm. in length. Here the iris is inserting into the face of the ciliary body, but in most of the sections the iris is in contact with the posterior surface of the cornea, forming a dense peripheral anterior synechia.

Except for this small rounded tip, the

Fig. 2 (Callahan). A rudimentary iris is present, which varies slightly in size but is about 1 mm. in length. Here the iris is inserting into the face of the ciliary body, but in most of the sections the iris is in contact with the posterior surface of the cornea, forming a dense peripheral anterior synechia. Except for this small rounded tip, the iris stroma is so atrophic that it can hardly be recognized. The area of stroma not in contact with the endothelium is extremely fibrotic and there is no evidence of differentiated muscle groups although muscle fibers are present. Both the greater and lesser circular anastomoses of the anterior ciliary vessels are present.

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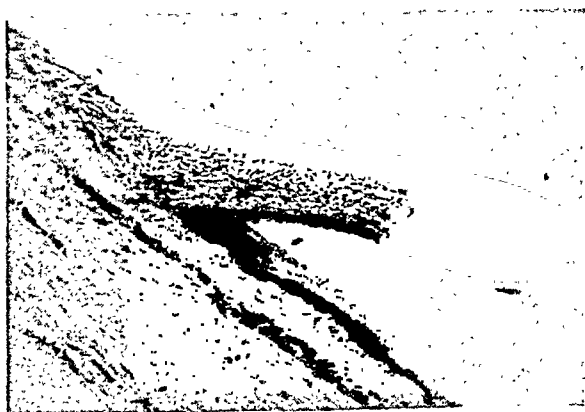

Fig. 3 (Callahan). Another section of the iris root. There is no evidence of the canal of Schlemm or spaces of Fontana. It is impossible to determine the condition of the filtration angle structures because this area is almost completely atrophic.

and lesser circular anastomoses of the anterior ciliary vessels are present.

On the opposite side of the same section, the iris root looks somewhat different (fig. 3). There is no evidence of the canal of Schlemm or spaces of Fontana. It is impossible to determine the condition of the filtration angle structures because this area is almost completely atrophic.

A section taken longitudinally through the optic nerve (fig. 4) shows the deep cupping resulting from increased ocular pressure and nerve fiber atrophy. A transverse section through the optic nerve well back from the globe (fig. 5) shows complete atrophy of nerve fibers with columnar
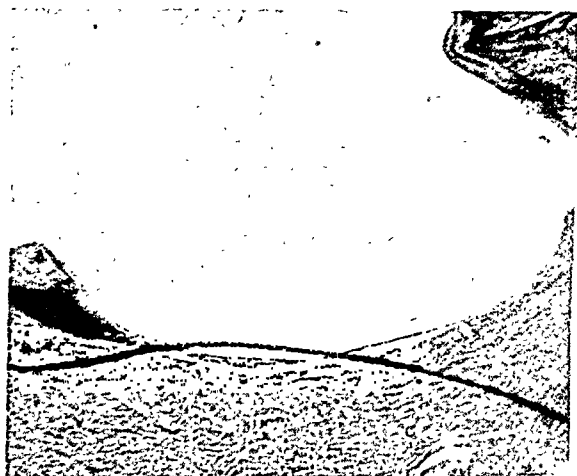

Fig. 4 (Callahan). Section taken longitudinally through the optic nerve showing the deep cupping resulting from increased ocular pressure and nerve-fiber atrophy.

replacement gliosis. There is moderate passive congestion of all vessels present. The sheath of pia-arachnoid surrounding the central vessels is well outlined and one corpus amylaceum is present.

Dr. Sanders has allowed us to include in this report a pathologic specimen of an aniridia from his collection (WU-2928). This is a case of true aniridia (fig. 6). There is complete absence of the iris. The ciliary body is atrophic but the longitudinal fibers of the muscle may be seen. The secretory epithelium is present but the cells are flatter than

Fig. 5 (Callahan). Transverse section through the optic nerve well back from the globe showing complete atrophy of nerve fibers with columnar replacement gliosis. There is moderate passive congestion of all vessels present. The sheath of pia-arachnoid surrounding the central vessels is well outlined and one corpus amylaceum is present.

are usually seen. The canal of Schlemm is well outlined and contains a few red blood cells. The ciliary body attaches to the scleral spur in a normal fashion. On the other side of the eye, the cuboidal secretory cells show more activity (fig. 7). The ciliary processes are normal in outline. The scleral spur is not readily identified nor are the structures at the iris angle normal.

PHYSIOLOGY

Why the presence of an ectopic lens greatly increases the tendency to glaucoma is not certain. In congenital ectopia lentis without aniridia the incidence of glaucoma is low. It seems to us that in aniridia with ectopia lentis the condition is more severe, and the adhesion of the rudimentary iris to

Fig. 6 (Callahan). (Case WU-2928). True aniridia, complete absence of the iris. The ciliary body is atrophic but the longitudinal fibers of the muscle may be seen. The secretory epithelium is present but the cells are flatter than are usually seen. The canal of Schlemm is well outlined and contains a few red blood cells. The ciliary body attaches to the scleral spur in a normal fashion.

Fig. 7 (Callahan). (Case WU-2928) (Second section). The ciliary processes are normal in outline. The cuboidal secretory cells show more activity than in Figure 6. The scleral spur is not readily identified nor are the structures present at the iris angle normal. This figure contrasted with Figure 6 shows how variable the ocular structures are in this case.
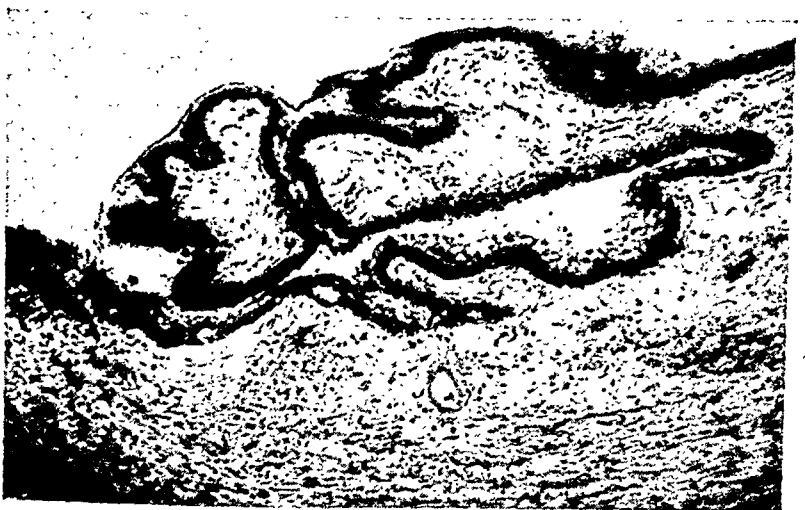
the cornea may be more complete in such cases. In our series, glaucoma has occurred in cases without ruptured zonules similarly to those cases with ruptured zonules. The lens may be responsible for exerting pressure against the ciliary processes and rudimentary iris in some cases. In the one case in which the lens was removed, most of the lens material was extruded upon completion of the limbal section. A severe postoperative reaction with ocular hypertension developed and required several paracenteses. The remainder of the lens absorbed, but the inflammatory reaction continued for three months.

The iris normally has some function in the interchange of fluids in the eye, and its absence may have a deleterious effect. The ciliary processes are atrophic and it is probable that less aqueous than normal is formed. If so, perhaps aniridic eyes have a metabolic rate lower than normal. Observations on the appearance of fluorescein in the aqueous after its intravenous injection were inconclusive. In one instance it appeared one minute after intravenous injection, but in another it did not become apparent even after observation for a period of one hour and a half. Possibly the absence of the constant contraction and dilatation of the iris may remove a normal stimulus and be responsible for a more sluggish circulation of the aqueous.

CASE REPORTS

A mother and 5 of her 10 children have double aniridia, hazy corneas, and cataractous lenses. All of the affected 5 children have ectopic lenses and glaucoma, 3 have external strabismus of about 45°, and 4 of the 5 have nystagmus. The defect has occurred without regard to sex or chronology.

There are other affected sibships living, which are being verified. The genealogy of the family is shown in Figure 1. The ectopic lenses follow an interesting pattern of position; all of them are partly cataractous, some advanced. The gene producing aniridia has

been fairly constant in that all forms have been about the same, and no mild forms, such as coloboma of the iris, have been observed.

The optic nerve and gross fundus details can be seen in several eyes with external illumination, because only aqueous and vitreous intervene between the cornea and the retina. All corneas have generalized opacities with haze, and this has prevented successful gonioscopic examination.

Photophobia has not been a problem in this study for, although the children replied to questioning that they were sensitive to light, they have preferred not to wear shaded lenses which were repeatedly supplied. Tattooing of the cornea has been reported but in our cases the glaucoma and the haziness of the corneas prevented such considerations. The nystagmus ruled out the use of contact lenses with painted irides.

Prior to our first observation of the family in June, 1946, no ocular surgery had been performed. In all eyes, the operative site was recorded in detail to prevent a secondary or a tertiary operation from occurring at the site of the primary operation.

All eyes have shown a complete lack of response to pilocarpine, eserine, and similar drugs. The clinical examination and course of each individual are presented in the following case reports.

Case 1. Cora, the mother, aged 48 years, has vision of: R.E., 20/200; L.E., hand movements at 3 feet. She has had poor vision since birth. Seventeen years ago, the left eye was struck by a stick, which further diminished vision, and it has deteriorated still more in last two years. Both corneas show deep vascularization at the periphery. The right lens has a posterior cortical cataract; the left, a mature cataract. The zonular system cannot be seen in either eye. Nystagmus is present. The tension is: R.E., 30 mm. Hg; L.E., 22 mm. Hg. This patient has been unwilling to undergo surgery.

Case 2. Loreen, aged 24 years, has vision of: R.E., 9/200; L.E., blind. Poor vision

has been present since birth; the left eye has been blind for several years. There was no injury of either eye. The right cornea shows diffuse opacities more numerous at the epithelium, with central superficial bullous keratitis. The lens shows an anterior and posterior cortical cataract, with more opacities in the axial region. The zonular system is intact inferiorly. The periphery of the fundus, as seen through the aphakic area,

tension, and the patient consented to the enucleation to provide material for microscopic study.

Case 3. Emma Kate, aged 17 years, has vision of: O.U., 10/200. She has had poor vision since birth, but it has diminished in the past few years. The patient's coöperation has been difficult to maintain, and she would not attend the clinic even for observation in 1947. Both corneas show generalized
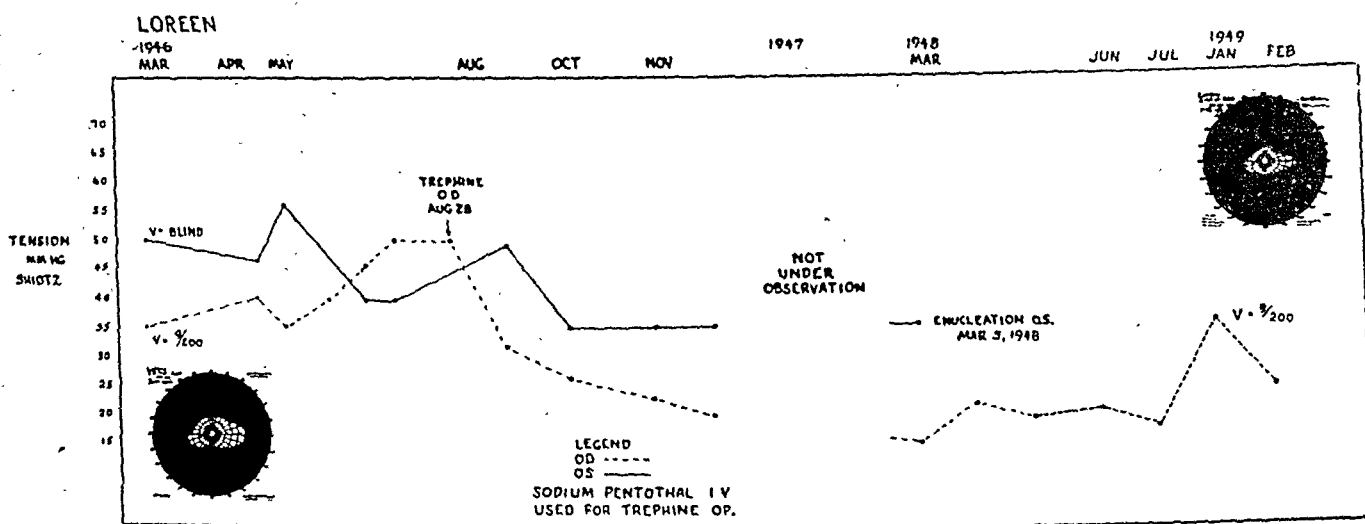

Fig. 8 (Callahan). Clinical course of Loreen. The tension became lower after trephination of the right eye in August, 1946. In late 1948 it increased, and the reduction in January, 1949, may or may not be due to the intravenous administration of sodium pentothal anesthesia for 20 minutes, no surgery being performed. The visual acuity has not decreased, but the visual field has contracted moderately. She consented to removal of the left eye to provide material for pathologic study.

seems normal. The corneal opacities obscure details. The left eye exhibits the same findings and, in addition, the optic nerve shows advanced atrophy with deep cupping.

Clinical course (fig. 8). A trephination was performed on the right eye in August, 1946, and this has been followed by a satisfactory lowering of tension. In late 1948 the tension increased, the stimulus being unknown. The reduction in January, 1949, may or may not be due to the administration of sodium pentothal anesthesia intravenously for 20 minutes, no surgery being performed. During the course of observation, the visual acuity has remained 9/200, and the visual field has contracted slightly. The left eye was not painful despite the greatly elevated

opacities. The lenses are ectopic, and in each eye the lower margin of the lens extends from about the 9-o'clock position on the limbal margin to about the 1-o'clock position. Generalized capsular opacities occur in both lenses. The fundi, observed through the aphakic area, appear normal.

Clinical course (fig. 9). Following a trephination of each eye and a cyclodiathermy of the left eye during mid-1946, the tension became elevated toward the end of the year, and probably remained so during 1947. In March, 1948, a cyclodialysis was performed on the right eye, but it was not successful in lowering the tension. Several paracenteses were done, and in April, 1948, the cataract was removed through an ab externo incision.
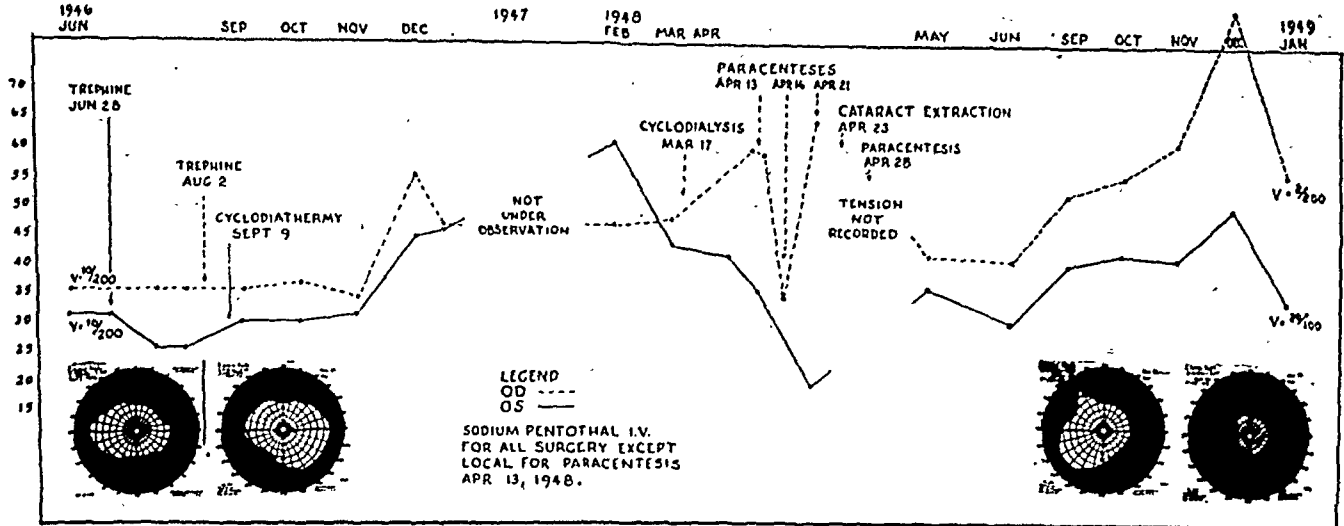
Fig. 9 (Callahan). Clinical course of Emma Kate. Following a trephination of each eye and a cyclo-diathermy of the left eye in mid-1946, the tension increased and probably remained so throughout 1947. A cyclodialysis of the right eye in March, 1948, increased the tension in the right eye and at the same time the tension in the left eye decreased. In April, 1948, the cataract of the right eye was removed through an ab externo incision, and about two thirds of the lens material was immediately extruded. Prolonged ocular reaction followed for several months. The tension has remained abnormally elevated since the operation, and has fluctuated widely without apparent cause. The vision has decreased from 10/200 to 2/200 and no lens correction improves the acuity. In the left eye the tension has varied con-siderably and has remained elevated despite two surgical procedures. It has retained acuity of 10/200 and about the same visual field.

About two thirds of the lens was immedi-ately extruded. No vitreous was lost, and irrigation of the retained lens material was then considered unwise. The remainder of the cortical material slowly absorbed, an aqueous flare remaining for 6 weeks after surgery. The ocular reaction continued for 3 months. The tension has fluctuated widely, the cause being unknown. The acuity has decreased from 10/200 to 2/200. The tension
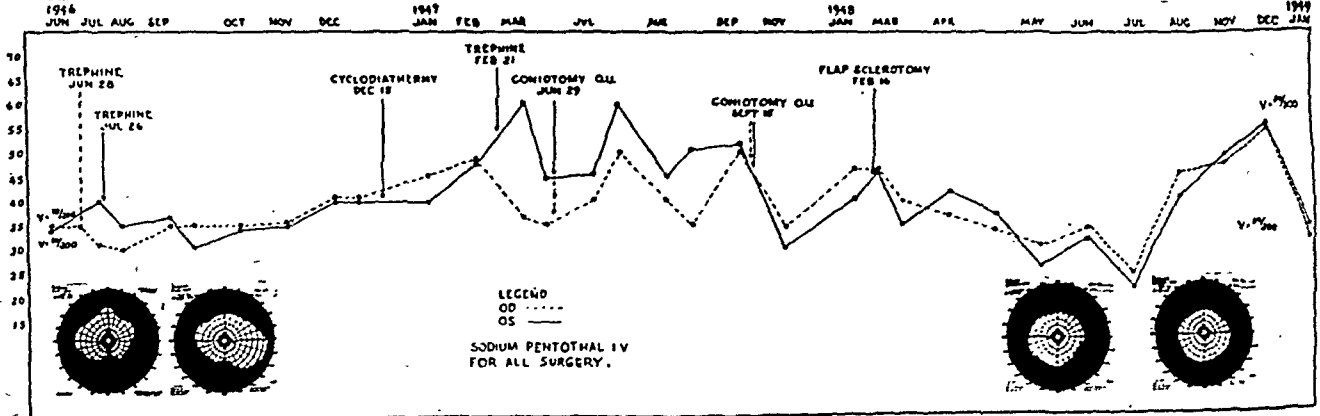

Fig. 10 (Callahan). Clinical course of Seaborn. The inadequacy of all glaucoma surgical procedures is apparent. In this case, also, a rise in tension followed the cyclodiathermy. The flap sclerotomy of the left eye in February, 1948, has been followed by a gradual lowering of tension and, as is true in many instances in this series, surgery of one eye has been followed by lowering of tension of both eyes. The cause of the elevation of tension in late 1948 is unknown, and the reduction may or may not be due to the intravenous administration of sodium pentothal for 20 minutes, no surgery being performed. The visual acuity has remained about the same, and the visual fields have contracted slightly.

in the left eye has varied considerably, and has remained elevated despite two surgical procedures. The eye has retained an acuity of 10/200 and about the same visual field area.

Case 4. Seaborn, aged 14 years, has vision of: O.U., 10/200. Poor vision has been present since birth, and he has complained some of photophobia and painful eyes. Both corneas show generalized opacities, involving all layers. The lenses are ectopic and, in each eye, the zonular system is ruptured

the elevation in late 1948 is unknown, and the reduction may or may not be due to the intravenous administration of sodium pentothal for 20 minutes, no surgery being performed. The visual acuity has remained about the same, and the visual fields have contracted slightly.

Case 5. Sara Mae, aged 13 years, has vision of: O.U., 10/200. Although she has had poor vision since birth, she has noticed no recent diminution of vision. Mild photo-
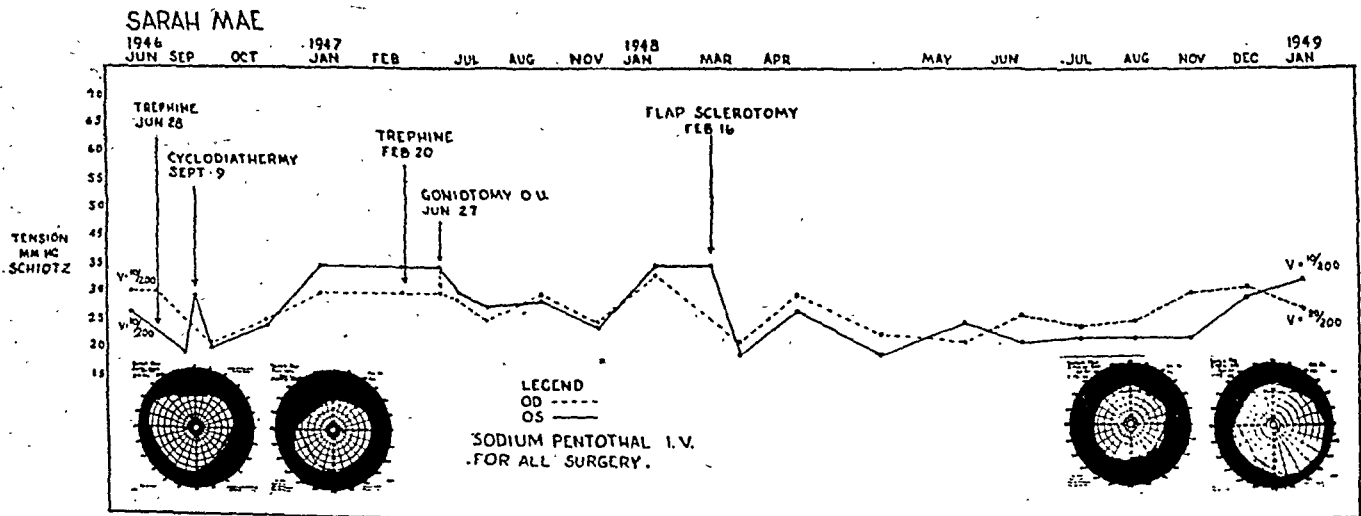

Fig. 11 (Callahan). Clinical course of Sara Mae. The trephinations and cyclodiathermy in late 1946 and early 1947 did not control the tension. Goniotomies in June, 1947, also failed to control the tension. A flap sclerotomy of the left eye in February, 1948, has been followed by a fairly satisfactory tension level. The vision has remained about the same and the fields have not diminished.

from about the 8-o'clock position on the limbal margin to the 4-o'clock position. Vitreous seemed to be almost in contact with the posterior surface of the cornea. The details of the fundi which could be seen were apparently normal, but no foveal reflex could be observed. Nystagmus is present.

Clinical course (fig. 10). The general inadequacy of all surgical measures is apparent, and in this, as in the preceding case, a rise in tension followed the cyclodiathermy. The flap sclerotomy of the left eye done in February, 1948, has been followed by a gradual lowering of tension. In this graph may be noted the general tendency of both eyes to follow the same curve, even though only one eye is operated upon. The cause of

phobia and lacrimation are present. Both corneas show relatively infrequent corneal opacities, generalized in distribution. The lenses are ectopic, the lower edge of the equator showing opposite the limbus from about the 9-o'clock to the 3-o'clock positions in the right eye, and from the 9-o'clock to the 1-o'clock positions in the left eye. Lens opacities are moderately advanced in the right eye, and more marked in the left; they are located chiefly in and near the posterior capsule. Vitreous does not present toward the cornea, perhaps because the zonular system is intact in both eyes. At the lower portion of each optic nervehead there is an inferior crescent. Nystagmus is present. There is external strabismus of 45°,

with tendency to fix with the right eye.

Clinical course (fig. 11). The trephinations and cyclodiathermy in late 1946 and early 1947 did not control the tension. Goniotomies were performed in mid-1948, but were not successful in controlling the tension. Because of the corneal haziness, it is difficult to see the rudimentary iris and to locate the chamber angle. A more basic reason for the failure of all goniotomies may be that at the age these children have reached, in all probability the constantly increased intraocular tension has caused

position. Vitreous seems to be almost in contact with the posterior surface of the cornea. The fundal details appeared normal, but the foveal reflex could not be seen. Nystagmus is present. There is alternating external strabismus of 45°.

Clinical course (fig. 12). In the youngest affected child the tension has followed a fairly satisfactory course, and only three surgical procedures have been performed. The visual acuity has decreased slightly, and the visual fields have remained approximately the same.
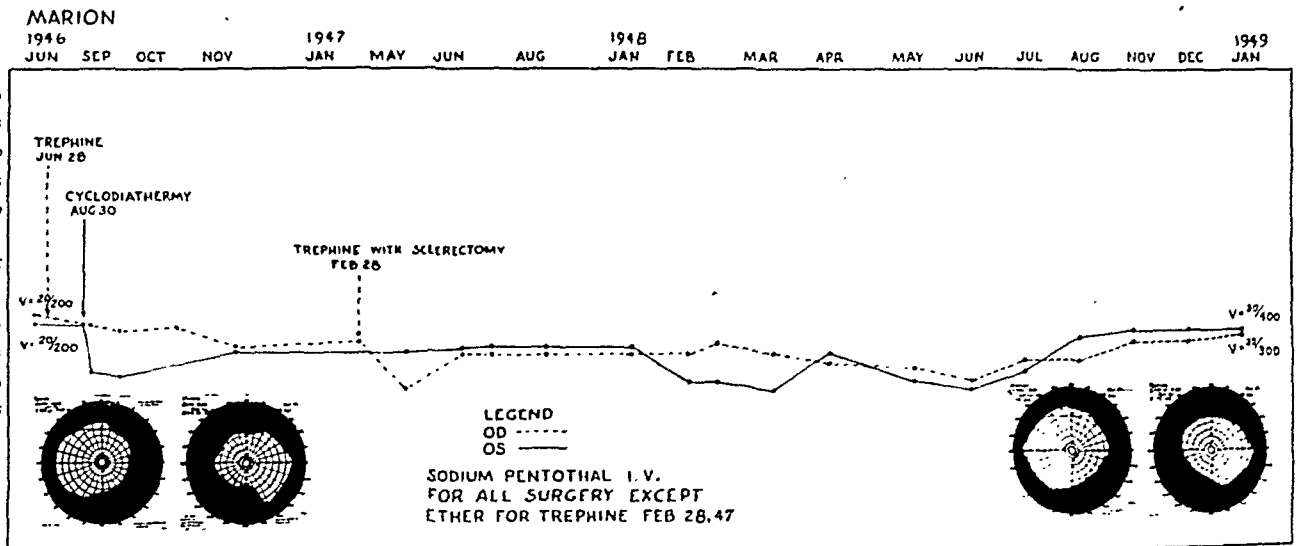

Fig. 12 (Callahan). Clinical course of Marion. In the youngest child, the tension has remained lower and more constant. Three surgical procedures were performed. The visual acuity has decreased slightly and the visual fields have remained approximately the same.

obliteration of any semblance of Schlemm's canal that may have been present. A flap sclerotomy on the left eye in February, 1948, has been followed by a fairly satisfactory tension level. The vision has remained about the same, and the visual fields have not diminished.

Case 6. Marion, aged 11 years, has vision of: O.U., 20/300. He has had poor vision since birth, but has noticed no diminution. Both corneas show generalized opacities, involving all layers. The lenses are ectopic, and in each eye the zonular system is ruptured from about the 7-o'clock position on the limbal margin to about the 5-o'clock

DISCUSSION

Most of this family attend the State Blind School and it is planned to follow all individuals for a decade. Another report is planned after several years, and at that time it is likely that there will be more members of the family. Some of these may be affected.

The disordered physiology of the formation of aqueous and its elimination is not at all clear. In the eye subjected to pathologic examination, the canal of Schlemm and the spaces of Fontana are entirely absent. In the other eyes it can be reasonably

assumed that the rudimentary iris is adherent to the cornea, obstructing the angle. In both pathologic specimens, the ciliary processes are atrophic, and it would seem likely that aqueous is formed slowly, thereby conducting the metabolism of the eye at a lower rate than normal. Meller and others have proposed the theory that much of the absorption of the aqueous is performed by the crypts of the iris, and the lack of this absorptive surface may be another factor in the production of glaucoma.

Few surgical experiences in controlling the glaucoma in aphakia have been reported, but a few investigators have noted their results in operating upon cataractous ectopic lenses in aphakia. Treacher Collins removed such a lens, and the patient regained 20/100 acuity with a plus-16 lens. Discissions have been performed in young children, and Beattie suggested an intracapsular extraction to avoid the lens protein reaction. This was our plan in the one cataract extraction performed, but upon completion of the ab externo incision over the ectopic lens, the lens material was immediately extruded, and, to avoid vitreous loss, the McLean sutures were pulled taut and tied. This is the only eye in which considerable vision has been lost.

Few conclusions can be made after following these cases for two and a half years, but a few observations are advanced.

1. The general inadequacy of the various types of glaucoma surgery is apparent. Cyclodiathermy is particularly contraindicated, since in three instances the tension increased and in one it did not change. Goniotomies are also contraindicated, probably because the canal of Schlemm, if present at birth, has become obliterated by the long-continued increased pressure.

2. The similarity of tension curves of both eyes in the same patient, regardless of which eye is operated upon, is noteworthy. They show that in several instances in which the tension became elevated, the unoperated eye has a similar or even greater lowering than the operated eye. This raised the question that perhaps factors other than surgery might be responsible. It might be the factor of relaxation provided by the general anesthetic, or the action of the sodium pentothal on the ciliary body. Several times on three of the patients, sodium pentothal has been administered intravenously for 20 minutes, no surgery being performed. The results are inconclusive, because the pressure dropped in some instances immediately and later in others. However, a general trend downward over the course of a month occurred in all three cases. Our present plan for the future management of these cases is to give sodium pentothal intravenously for 20 minutes, and not to operate.

3. These eyes seem to withstand the elevated pressure better than glaucomatous eyes usually do, as shown by the relatively small loss of visual fields despite the greatly increased intraocular pressure.

Medical College of Alabama (5).

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DISCUSSION

DR. DAVID G. COGAN (Boston, Massachusetts) : To start the discussion, I would like to ask Dr. Callahan if he has any suggestions as to why glaucoma should develop late in these cases of aniridia, when presumably it is based on a congenital defect? Is there any evidence in the specimen of a progressive lesion which has occurred postnatally?

DR. K. W. ASCHER (Cincinnati, Ohio) : I wonder whether aqueous veins were found in the eyes of the members of this interesting family? In eyes like these, observation of the aqueous veins and of the aqueous-humor elimination might yield interesting results.

A second question: on eyes with a desperate prognosis like this, could one try one of the toxic depressants of intraocular pressure, erythrophleine or nervocidine? Besides an inflammatory reaction, they produce corneal anesthesia and a long-lasting hypotony. In eyes responding to miotics, I would not use these drugs but in eyes which are doomed to become blind, it might be justified to use one of these powerful drugs.

DR. CONRAD BERENS (New York City) :

I should like to ask Dr. Callahan if he has had any great difficulty with bullous keratitis in these cases?

I have had two patients on whom I have tried to perform superficial keratectomy. In both cases, I have had great vascular reactions and I have had no success in maintaining transparency of the cornea. One case is under observation now and I would appreciate help.

DR. CALLAHAN (closing) : It seems likely that glaucoma is present at birth or develops soon afterward, and the condition gradually becomes more severe. There is no evidence in the specimen of a progressive lesion except that continued tension has thinned out all layers and obliterated Schlemm's canal. So severe is the corneal haze that aqueous veins, if present, were not visible. The chamber angle could not be seen with the gonioscope. The suggestion for the use of a toxic depressant of intraocular pressure is appreciated, and will be used with the indications as suggested by Dr. Ascher.

Bullous keratitis has not been present in our cases of aniridia.

A GENE PRODUCING VARIOUS DEFECTS OF THE ANTERIOR SEGMENT OF THE EYE*

WITH A PEDIGREE OF A FAMILY

HAROLD F. FALLS, M.D.†

Ann Arbor, Michigan

Genes producing developmental anomalies are well known for their diversified effects upon different individuals within a family. This appears to be particularly true of those genes causing structural defects in the anterior segment of the eyes.[1-8] Seldom, however, does one see such a wide variety of pathologic changes as was demonstrated by the single family reported herein. In this kindred, the inheritance is due to a single dominant gene which has resulted in varying combinations of the following abnormalities: congenital corneal opacity, embryotoxon, corectopia, pseudopolycoria, slit-pupil, iridotasis, dyscoria, ectopia pupillae, ectopia lentis, anterior polar cataract, and hydrophthalmos. An increased intraocular pressure was observed in the majority of the affected individuals, and, in cases where gonioscopy was performed, abnormal tissue (? mesodermal) was found to occupy the anterior-chamber angle. There is, in addition, some evidence that the gene also may produce a defect in the hearing sense.

METHOD OF STUDY

The investigation of this family was initiated by the appearance at the University of Michigan ophthalmological clinic of a brother (G-5) and sister (G-9) on November 27, 1940. Both of these patients had previously visited the clinic on separate occasions and a careful review of their histories indicated the presence of similar ocular pathologic changes in their antecedents and collateral relatives. Subsequently a careful pedigree was obtained from A-2.

With the pedigree serving as a work sheet all living members were examined with the exception of A-4 who refused examination. The greater number of the examinations had to be carried out in the homes of the patients under rather difficult conditions. Many medical prejudices as well as general apathy had to be overcome before even an interview could be obtained in certain branches of the family.

The examinations performed consisted of a complete ocular examination and a series of genetic test factors. The latter included serologic tests of blood and saliva, determination of the taste reaction to phenyl-thio-carbamide, tests of color vision and ocular dominance. The blood samples were tested with respect to the blood groups O, A, A_1, A_2, and B, and the M and N types. The "secretor factor" was determined on the saliva by means of human A and B serum and anti-O ox serum. Data on these known hereditary characters are of interest primarily in regard to their genetic linkage. No evidence of linkage between these test factors and the gene studied in this family was uncovered.

PEDIGREE

This pedigree chart (fig. 1) follows that of conventional diagrams by arranging the children of a single union horizontally and

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● ANTERIOR SEGMENT OCULAR
   DEVELOPMENTAL ANOMALIES
◐ REPORTED AFFECTED
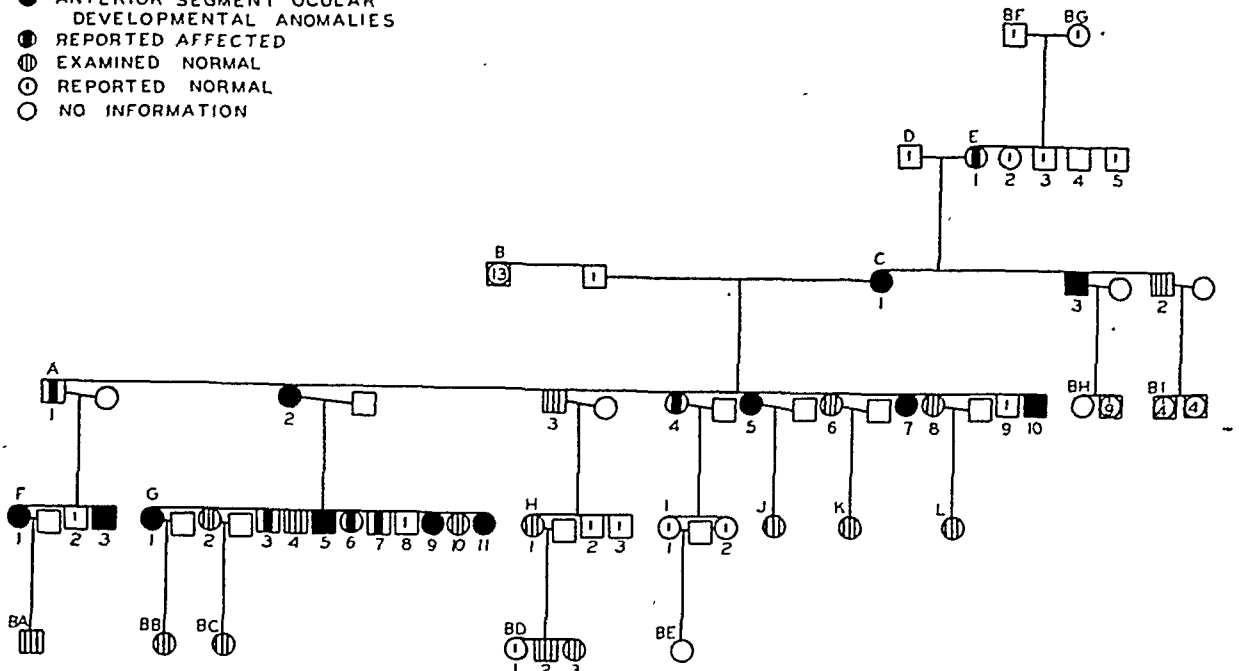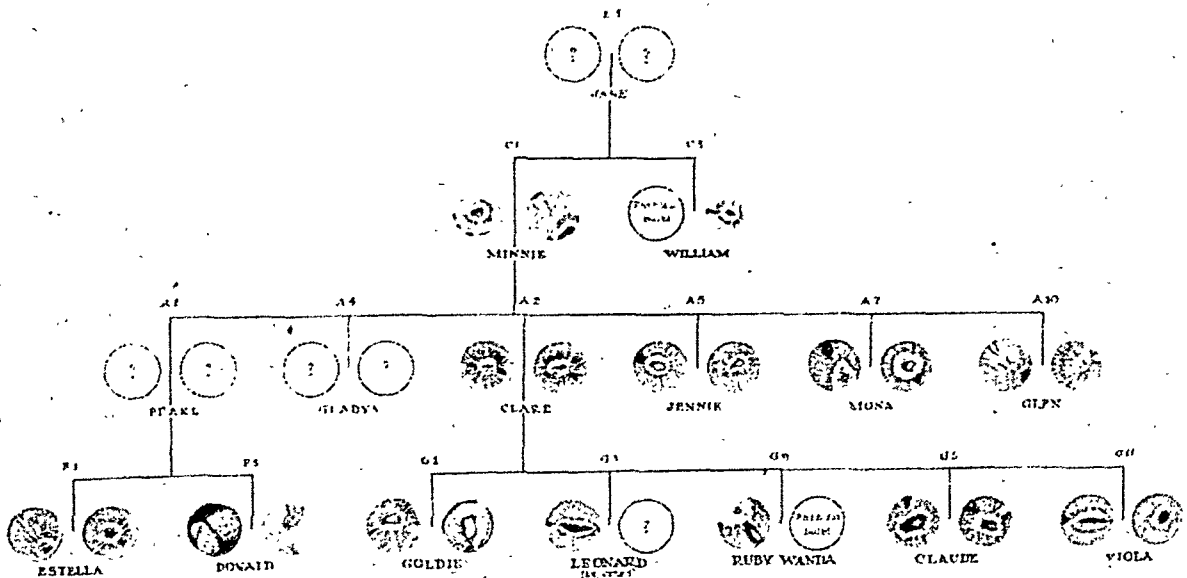◍ EXAMINED NORMAL
◉ REPORTED NORMAL
○ NO INFORMATION

Fig. 1 (Falls). Pedigree chart showing occurrence of ocular defects in four generations of a family.

ANTERIOR SEGMENT DEVELOPMENTAL ANOMALIES

Fig. 2 (Falls). Chart showing pathologic changes in various members of the family.

in order of their birth. Information is available concerning four affected generations, the first being known only through historical evidence provided by the living descendants. Genealogic evidence concerning the spouses was only incompletely obtained and it is therefore not definitely known if the respective unions are free from consanguinity. At least it was denied in most instances.

The ocular anomalies in this family are transmitted in a characteristic dominant Mendelian pattern. A dominant gene will be transmitted by an affected parent to an anticipated 50 percent of his or her offspring. It is also to be expected, in turn, that an affected person will have one affected parent. The normal siblings of involved individuals, as well as normal offspring of the latter, will have children normal in respect to the trait in question. This pedigree indicates that the gene being studied in this family fulfills all of the specified prerequisites of a dominant inheritance pattern.

PATHOLOGIC CHANGES

E-1

Family reports, substantiated by a very incomplete hospital record, indicate that this woman was very probably affected and that she was responsible for the transmission of the defect to all cases subsequently described. She was reported to have had large eyes which "bulged out" like those of her daughter, C-1, and the corneas were said to be "milky-white" in color.

Vision had always been poor and for many years the patient experienced severe ocular and head pains associated with blurred and distorted vision. She was finally forced to consult an ophthalmologist. Dr. Walter Parker initiated surgery in both eyes for relief of her glaucoma, a diagnosis of "buphthalmos" having been made. Total blindness ensued several years before her death at the age of 74 years. She also suffered in later years with a rather marked loss of hearing. The patient was described as short and stocky, of dark complexion and with "dark chocolate brown" iris color.

C-1

This obese, 70-year-old woman insisted that she had had no difficulty with her eyes until she was nearly 14 years of age. Short periodic attacks of blurred vision were then experienced in combination with rather severe frontal head pains. Many pairs of glasses were worn but failed to relieve her symptoms or materially improve her visual acuity. All useful vision had been lost 20 years prior to our examination. The woman was short in stature and rather darkly pigmented. No signs of von Recklinghausen's disease could be observed. Her blood pressure was 165/85 mm. Hg. The patient was hard of hearing, otosclerosis having been previously diagnosed and a hearing aid prescribed by a local otologist.

Ocular findings. The vision was nil in both eyes, and there was marked divergence of the visual axes. Ocular movements could not be obtained due to loss of fixation. The corneal diameter in the right eye was 13.5 mm. horizontally and 13.0 mm. vertically; and in the left eye, 13.0 mm. horizontally and 12.5 mm. vertically. A rather pronounced scleral over-riding was evident in both eyes.

The corneal surfaces presented an opalescent color in which was interspersed small dark-gray, calciumlike deposits, the latter being more conspicuous in the palpebral fissure area. The entire anterior segment was grossly enlarged in both eyes. The sclera anterior to the equator was so thin as to have a distinct bluish cast. The exophthalmometer reading (Hertel) was 18.5 mm., O.D., and 22 mm., O.S.

Right eye. Transillumination revealed an irregular but nearly centrally placed pupil, with marked prominence of the sphincter. The iris stroma was extremely atrophic. Inferiorly and temporally the iris seemed adhered to the corneal surface despite the presence of an abnormally deep anterior chamber. The lens appeared cataractous. The tonometer tension was 36 mm. Hg (new Schiøtz).

Left eye. Visualization of the inferior portion of the anterior chamber was possible through the macular and nebulous scarring of the cornea. The anterior chamber was deep and large. A portion of the sphincter could be seen at the 5-o'clock position, at which point it seemed adhered to the cornea and angle. An iris dehiscence or small iridotasis was observed near the periphery at the 11-o'clock position. The iris stroma was attenuated and nearly absent except for the pigment layer. The tonometer tension was 36 mm. Hg (new Schiøtz).

C-3

This dark-complexioned, well-developed, 72-year-old woodsman was examined in his bed to which he had been recently confined by a heart attack. The patient stated that his right eye had been injured in a logging accident at the age of 18 years and that vision in this eye failed completely within one month. During the last five years there had also been a gradual loss of vision in the left eye, and the patient recalled occasional colored halos and blurred vision associated with mild ocular discomfort. The blood pressure was 155/85. mm. Hg.

Right eye. The corneal horizontal diameter was 7.5 mm. The entire cornea was leukomatous and vascularized, and its surface was flattened. The entire eye was small and the globe was cuboidal

in outline. The tonometer tension was 8 mm. Hg (new Schiøtz).

Left eye. The uncorrected visual acuity was 6/12—2. The corneal diameter was 12.5 mm. horizontally and 12.0 mm. vertically. The corneal stroma was clear except for nearly complete arcus senilis, and the anterior chamber was of normal depth. The iris color was hazel; the stroma was moderately well developed but presented a certain degree of atrophy which permitted visualization of the pigment layer. The lesser arterial circle of the iris was incomplete, but the iris sphincter was abnormally well seen through the attenuated stroma. The pupil was oval and irregular. Pupillary reflexes were prompt. The lens was clear except for cuneiform opacities at the inferior nasal periphery. A few strandlike vitreous opacities were present.

The optic nervehead was pale and moderately cupped with a fair preservation of the nasal tissue. The retinal vessels were arteriosclerotic. The macular area and retinal periphery were normal except for prominence of the choroidal vasculature and choroidal verrucae. No unusual degree of choroidal arteriosclerosis was noted. The tonometer tension was 32 mm. Hg (new Schiøtz). The confrontation field suggested a moderate concentric peripheral contraction.

A-1

This man died as a result of a cerebrovascular accident several years before the initiation of this investigation. Bilateral iridectomy had been performed by a Chicago physician in 1923, but no records are available, except that a diagnosis of glaucoma had been made. This man's eyes were described as very large, with prominent opalescent corneas and chocolate-brown irides, and the pupils were eccentrically placed. Severe ocular pain had been experienced most of this man's life, and this was not relieved by surgery. No nystagmus was known to have been present. His visual acuity was very poor both before and after the operation. Auditory acuity was "good."

A-2

This 51-year-old woman had been gradually losing her visual acuity for several years, but seemed strangely euphoric about it. Only mild remorse was expressed over the fact that so many of her children were blind or nearly so. This woman was well developed, slightly obese, and not as darkly complexioned as her other affected brothers and sisters. She reported that she had rarely encountered any ocular discomfort but had noted some blurring of vision of her right eye.

Ocular findings. The uncorrected visual acuity was: R.E., 6/15—1; L.E., 6/30; with correction, it was: R.E., 6/9—2; L.E., 6/15—2. The eyes were straight in the primary position, with marked lateral deviation under cover. The extraocular movements were normal except for a marked overaction of the right inferior oblique muscle when looking up and to the left. The pupillary reflexes

were prompt and equal bilaterally.

The glasses worn were: +1.0D. sph. ◯ +0.37D. cyl. ax. 65° = +2.25; +0.75D. sph. ◯ +0.25D. cyl. ax. 180° = +2.25.

Right eye. The corneal horizontal diameter was 12.5 mm. The corneal stroma was clear and the anterior chamber was of normal depth. The pupil was irregular and oval horizontally. The anterior iris leaf was very scant and atrophic. There was no lesser arterial circle or collarette. Thin scattered radial gray strands ran from the iris base directly to the pupillary border. The pupillary sphincter was easily seen and existed as a broad band superimposed on a background of light chocolate brown. The latter was easily visualized through the nebulous or absent stroma.

Extensive anterior peripheral synechias were grossly noted between the 7- and 10-o'clock positions. The lens and central media were clear. The disc was oval horizontally, very pale in color, and showed deep glaucomatous cupping. The retinal vasculature showed signs of arteriosclerosis. The macular area, retinal periphery, and choroid were devoid of pathologic conditions. The tonometer tension was 30 mm. Hg (new Schiøtz). The confrontation visual field presented superior and nasal contracture. The exophthalmometer reading was 16 mm. (Hertel).

Left eye. The corneal horizontal diameter was slightly over 12 mm. The corneal stroma was clear, except for a gray linear deposit on the peripheral endothelial surface extending from the 2- to 4-o'clock positions. The anterior surface of the iris was adhered to this embryotoxon. The anterior chamber seemed large and deep. The pupil was triangular in outline, with the base directed temporally. The sphincter followed the outlines of the pupil and was quite broad. The anterior iris stroma was attenuated and lacking in many areas.

The pigmented iris surface was easily visualized and appeared atrophic and moth-eaten to transillumination. The fundus was similar to that of the right eye, except that the glaucomatous atrophy of the nervehead was less advanced. The tonometer tension was 20 mm. Hg (new Schiøtz). The confrontation field was normal. The exophthalmometer reading was 16 mm.

A-4

This short, stocky, 42-year-old woman refused examination. She considered her very poor vision to be the result of her medical contacts and was strongly prejudiced. During the course of a rather long argumentative conversation, the following observations were possible. There were at least 15 to 20 degrees of left divergent strabismus—early phthisis bulbi of the left eye.

A large cornea was present in the right eye with a corneal horizontal diameter of at least 13 mm. The cornea was partially leukomatous with band keratitis in the palpebral fissure. Pendular nystagmus of irregular amplitude was noted. The pupil was displaced superiorly and nasally and was cu-

boidal in shape. The iris sphincter was conspicuous. The iris was dark-brown in color. A thin gray posterior peripheral corneal deposit extended from the 4- to 7-o'clock positions.

The patient's ophthalmologist has advised that a cataract extraction had been attempted many years ago and that fluid vitreous was lost at the time of incision. It was observed that the cataract was anterior polar in type. No specific details were recalled as the patient's record had been lost.

The patient was moderately hard of hearing and wore a hearing aid.

A-5

This 39-year-old, well-developed woman was darkly pigmented. For many years she had had frequent and severe occipital and frontal headaches, which were occasionally associated with blurred vision and colored halos about lights. This woman had been attended by many physicians, but had obtained no relief, and had finally resorted to naturopathy.

Ocular findings. The uncorrected visual acuity was 5/21 bilaterally; with correction 5/6—1 in the right eye and 5/4.5—3 in the left eye. The eyes varied from straight in the primary position to several degrees of alternating divergent strabismus. The extraocular movements were normal except for overaction of the right inferior oblique muscle when looking up to the left. A moderate lagophthalmos was present bilaterally due to the extensive exophthalmos which measured 24 mm. in the right eye and 21 mm. in the left eye (Hertel).[10]

Right eye. The corneal horizontal diameter was 13 mm. and 12.5 mm. vertically. The corneal stroma was clear except for a thin gray linear arcuate posterior surface deposit in the extreme periphery. This extended from the 4:30- to 7:30-o'clock positions. Despite the presence of a large, and very deep anterior chamber, there were numerous adhesions of the iris to the embryotoxon. The iris was a dark cocoa brown.

The pupil was large, oval horizontally, and displaced temporally. Ectropion uveae was noted about the entire circumference of the pupil. The sphincter was broad and easily observed. A small dehiscence existed in the iris running from the sphincter to the base at the 9:30-o'clock position. Other than for an occasional thin radial strand the iris stroma was absent. Transillumination indicated the atrophic character and moth-eaten appearance of the pigment layer. Although moderate iridodonesis was noted, there was no definite subluxation of the lens.

The lens and central media were normal. The optic-nerve disc was oval vertically, of pale color, and exhibited definite glaucomatous cupping. The retinal vessels, macular area, and periphery were normal. The intraocular pressure measured 15 mm. Hg (new Schiøtz). The confrontation field was markedly contracted in a concentric manner.

Left eye. The corneal diameter was 12.5 mm. horizontally and 13 mm. vertically. The corneal stroma was clear except for a gray linear streak

extending from the 12- to 5:30-o'clock positions in the extreme periphery.

The anterior chamber was large and deep. The pupil was displaced temporally and was flattened above and below. The iris sphincter was broad and prominent. The iris stroma was almost completely absent. Two minute dehiscences, each about 1 mm. in diameter, were located about 2 mm. apart at the 9-o'clock position. Numerous anterior synechias ran to the embryotoxon area.

The fundus appeared as in the right eye, except that there was only slight evidence of glaucomatous cupping of the optic nervehead. The tonometer tension was 14 mm. Hg (new Schiøtz). The confrontation field showed superior nasal contracture.

A-7

This asthenic, darkly-pigmented, 34-year-old woman presented nil vision in her right eye and was able to count fingers at one foot with her left eye. Her ophthalmologist reported that he had attempted to perform a visual iridectomy in the right eye but had been defeated when it became apparent that the corneal leukoma was adhered to the lens and iris. Poor vision and a pendular horizontal nystagmus had been present since birth. A diagnosis of bilateral otosclerosis had been made within the past four years. This woman was of good intellect and was a rather talented musician.

Ocular findings. There were 14 to 16 degrees of right divergent strabismus. The ocular mobility could not be studied because of lack of ocular fixation. A constant horizontal nystagmus of varying amplitude existed. No gross muscle paralysis was noted.

Right eye. The horizontal corneal diameter was 11.5 mm. and the vertical diameter was 11.8 mm. The central cornea exhibited a dense leukoma and the anterior corneal surface was quite flat. The peripheral or limbal cornea was opalescent.

The anterior-chamber details and a few iris details were demonstrated by transillumination. The anterior chamber was shallow but its depth varied greatly in the peripheral areas. The anterior ocular segment was large.

The pupil was placed at the 5-o'clock position, and a large peripheral iris dehiscence was present at the 10-o'clock position. The sclera over the anterior ciliary body was thin and revealed the underlying blue-black pigment of the latter.

The tonometer reading was 40 mm. Hg on first examination, but varied on subsequent readings from 25 to 45 mm. Hg (new Schiøtz).

Left eye. The corneal diameter was 11.5 mm. horizontally, and 11.2 mm. vertically. A large, irregular, dense central leukoma, measuring 3 by 4 mm., was present; the surface was flat and the substance of the scar showed conspicuous vascularity. Transillumination suggested an anterior capsular opacity upon which a pyramidal extension was superimposed. The latter did not seem to contact the cornea. The anterior chamber was moderately deep.

Gray linear posterior corneal surface deposits were noted, but no details could be obtained. The pupil was displaced temporally and appeared oval horizontally. An iris dehiscence was evident at the 5-o'clock position. The tonometer reading was 35 mm. Hg (new Schiøtz). The confrontation visual field was markedly contracted in a concentric manner.

A-10

This rather well-developed, light-complexioned young man, aged 27 years, declared that he was born with his corneal scars. He stated that he had had sufficient visual acuity to enable him to get about quite satisfactorily until the age of 18 years. The left eye was then injured in a gymnasium accident following which all vision was lost. This young man was quite talented and he was a piano tuner by trade.

Ocular findings. The visual acuity was nil bilaterally at the time of examination. There was eccentric bilateral wandering of the eyes associated with a coarse, irregular, but pendular, nystagmus. The eyes were divergent. No anomaly of the lids or conjunctivas was noted.

Right eye. The horizontal corneal diameter was difficult to measure due to scleral over-riding, but was 12 mm. or slightly less. A large irregular central leukoma was present. The surface of the cornea was flattened and quite vascular. The peripheral cornea was opalescent to transparent. The anterior chamber depth varied greatly but was quite shallow centrally and deeper at the periphery. Several gray linear deposits of embryotoxon were seen in the peripheral posterior corneal stroma. Anterior synechias were attached to the latter.

The pupil was displaced down and in at the 4:30-o'clock position. The sphincter could be easily observed. The lens seemed maturely cataractous. No iridodonesis could be exhibited. The anterior segment of the eye was large. The ciliary scleral area presented a light blue appearance. No staphyloma was present. The tonometer reading was 40 mm. Hg (new Schiøtz).

Left eye. The corneal diameter was 12 mm. horizontally and slightly less than 12 mm. vertically. There was scleral over-riding. The central cornea was densely leukomatous and was moderately vascularized. Transillumination indicated that the pupil was centrally placed. Many peripheral anterior synechias were present and accounted for the varying depth of the anterior chamber.

The anterior iris stroma was almost completely absent in certain areas and markedly attenuated elsewhere. Several small iris dehiscences existed; one at the 2-o'clock, another at the 2:30-o'clock, and a third at the 7-o'clock position. Embryotoxon extended from the 8- to 11-o'clock positions. Iridodonesis was present. The lens was maturely cataractous as viewed through the dehiscences of the iris. The tonometer reading was 28 mm. Hg (new Schiøtz).

F-1

This attractive, well-developed, dark-brown-haired, 29-year-old woman seemed surprised when informed that she was afflicted. Symptoms of increased intraocular pressure in either eye were stoutly denied. There was no evidence of von Recklinghausen's disease.

Ocular findings. The eyes were straight in the primary position, and the ocular movements were normal. The pupillary reflexes were present and equal in both eyes, but there was a sluggish reaction to direct light.

Right eye. The uncorrected visual acuity was 6/6—3. The corneal diameter was 12.5 mm. horizontally and 12 mm. vertically. The corneal stroma was clear except for a thin grayish strand on the posterior peripheral endothelial surface extending from the 2- to 7:30-o'clock positions. The anterior chamber was of moderate depth except inferiorly and temporally where it was shallow.

The pupil was displaced nasally and inferiorly. It was irregular and oval in shape and the pupil was adhered to the posterior corneal surface at the 5-o'clock position. Ectropion uveae was present at this point. The pupillary sphincter was markedly prominent due to the absence of overlying stroma. The pigmented layer of the iris stood out in bold relief. Two small holes in the iris were present at the periphery in the 11-o'clock meridian. Iridodonesis was evident, but the position of the lens, if displaced, could not be determined.

The lens, central media, and optic-nerve disc were normal. The macular area, retinal vessels, and retinal periphery were devoid of pathologic changes. The confrontation visual field was normal. The tonometer reading was 12 mm. Hg (new Schiøtz).

Left eye. The uncorrected visual acuity was 6/15—1. The horizontal corneal diameter was 13 mm. The vertical diameter was 12.5 mm. The corneal stroma was clear except for a thin band of gray tissue on the posterior surface inferiorly and nasally. The anterior chamber was deep. The pupil was irregular and angular in outline and displaced nasally. The sphincter muscle was broad and prominent.

The iris stroma was nearly absent except for five delicate radial strands running from the base to the pupillary margin. No lesser arterial collarette could be seen. The pigment layer of the iris was intact but very atrophic as demonstrated by transillumination. The fundus appeared as in the right eye. The confrontation field was normal. The tonometer reading was 12 mm. Hg (new Schiøtz).

F-3

This well-developed, dark-brown-haired, alert young man, aged 24 years, reported that he had enjoyed a fair degree of visual acuity until 10 years of age. His relatives tell of a bilateral operation performed to relieve glaucoma at the age of three years. His vision had gradually deteriorated during the last decade until he became totally blind four years ago.

Right eye. The visual acuity was nil. The corneal horizontal diameter was 16 mm. The corneal stroma was clear. There was no evidence of rupture of Descemet's membrane. The anterior chamber was extraordinarily deep. The iris color was slate-black. The iris remnants were tremulous and were so atrophic that they seemingly lacked structure. There was no evidence of stroma and it appeared that only pigment remained.

A small band of iris extended across the visual axis and suggested a possible sphincter remnant. An extremely large iris dehiscence existed both above and below this strand. The superior coloboma probably represented the site of a former iridectomy.

The lens was maturely cataractous and was freely movable except for persistent zonular fibers inferiorly and nasally. The vitreous contained a large number of large and small strandlike opacities. The disc was very pale, very atrophic, and very deeply cupped.

The macular retinal area was mottled with pigment clumps and seemed moth-eaten. The entire retina was atrophic. The retinal vasculature was attenuated. The choroidal circulation was vividly seen. The tonometer reading was 46 mm. Hg (new Schiøtz).

Left eye. The horizontal corneal diameter was 14.8 mm. and the vertical diameter was slightly over 14 mm. A broad stripe of band keratitis extended across the cornea in the pupillary fissure area. *Clear* cornea was scant. The anterior chamber was very deep. There was considerable scleral over-riding. The sclera over the ciliary body had a light bluish tinge. The iris was very atrophic and the pigment appeared moth-eaten upon transillumination. A large iris dehiscence above represented presumably the area of surgical coloboma. The pupillary position could not be determined. The lens seemed cataractous and there was iridodonesis. The tonometer reading was 38 mm. Hg (new Schiøtz).

G-1

This well-developed, light-brown-haired, 30-year-old woman had had very large and prominent eyes since birth. She resembled A-2 in a great number of physical attributes. Since six years of age this individual had been totally deaf and an examination had revealed bilateral total nerve deafness. During the past five years recurrent severe ocular pain had been experienced in the left eye associated with marked loss of vision.

Ocular findings. The uncorrected visual acuity was 6/6—1 in the right eye and nil in the left eye. There were 20 degrees of right divergent strabismus (Priestly-Smith).

Right eye. The direct light and accommodation pupillary reflexes were prompt. The corneal horizontal and vertical diameter was 13 mm. The corneal stroma was clear except for a thin grayish-white posterior peripheral strand extending from the 6- to 10-o'clock positions. The anterior chamber

was deep. The pupil was displaced up and in. The sphincter muscle band was broad.

The iris stroma was thin and very attenuated, consisting of an occasional thin radial strand running to the pupillary margin. Ectropion uveae was present inferiorly and nasally. Numerous anterior synechias were present in the vicinity of the embryotoxon. The iris color was a soft golden brown. No iridodonesis was seen. The lens, central media, disc, vessels, periphery, and macular area were devoid of pathologic changes. The tonometer reading was 18 mm. Hg (new Schiøtz). The confrontation field was normal.

Left eye. The corneal horizontal diameter was 13.5 mm. and the vertical diameter was 13 mm. A moderate degree of scleral over-riding existed superiorly. The cornea was edematous. The anterior chamber was very deep. The pupil was dilated, oval vertically, and was fixed to all stimuli. The sphincter muscle band was broad and conspicuous. Ectropion of the uveal pigment existed inferiorly at the 6-o'clock position, the pigment being adhered to the endothelial surface of the iris.

Two minute iris dehiscences were present in the periphery at the 6-o'clock position, and several small holes were also present at the 10-o'clock position. The iris stroma was nearly absent and even the pigmented leaf appeared moth-eaten to transillumination.

After instilling glycerin, the funduscopic examination revealed that the lens and central media were normal. The optic-nerve disc was pale and very deeply cupped. There was extensive peripapillary retinal atrophy. The macular area was atrophic and the pigment mottled and finely clumped. The retinal vessels were small. The choroidal vasculature was prominent. The tonometer reading was 40 mm. Hg (new Schiøtz).

G-3

Very little definite information could be obtained in respect to this boy. He died early of a congenital heart lesion. It is known that he was afflicted, having had the large prominent eyes which are typical of this family. The late Dr. Kniskern of Muskegon, Michigan, could recall that the right eye possessed a horizontal slitlike pupil. The diagram was made up from this physician's description. A small dehiscence existed in the periphery in the 3-o'clock meridian, extending to the base. The visual acuity was less than 6/30 in the right eye and better than 6/9 in the left eye. The tonometer reading was not recalled. The iris sphincter was conspicuous and broad. The iris was of a dark brown color.

G-4

This child died of diphtherial complications at a very early age. The mother states that her eyes were involved. The eyes were large and prominent. The iris color was dark chocolate brown. No iris details were recalled.

G-5

This tall, thin, asthenic, blond young man was first seen at the university ophthalmic clinic, November 27, 1940. The history suggested that the patient had never experienced any ocular pain but that a gradual loss of visual acuity had been noted bilaterally for the past 4 years. During the last year the right eye had started to diverge and colored halos about lights had been encountered on occasion. Prior to his hospital visit he had desired no medical attention.

Ocular findings. There were 20 degrees of right divergent strabismus (Priestly-Smith). The ocular mobility was normal.

Right eye. The horizontal corneal diameter was 13 mm. and the vertical diameter was 12.5 mm. The corneal stroma was clear. The anterior chamber was deep. The pupil was dilated 8 mm. and was oval horizontally. The pupil reacted sluggishly to direct light and accommodation, but promptly to consensual light from the left eye. The pupillary sphincter was raised and broad.

The iris stroma was very attenuated but a sufficient amount was present to give the iris a blue color. No iridodonesis was present. The lens and central media were normal. The optic-nerve disc was pale and presented extreme cupping. Rather extensive circumpapillary retinal atrophy was present.

The macular area was stippled with minute clumps of pigment. The retinal vessels were normal. The retinal periphery was negative. The tonometer reading was 36 mm. Hg (new Schiøtz). A light field disclosed marked concentric field contracture.

Left eye. The corneal horizontal diameter was 13 mm. The corneal stroma was clear. The anterior chamber was deep. The pupillary sphincter was easily seen due to the atrophic character of the iris stroma. The pupil was oval horizontally and dilated 4 mm. It reacted promptly to all stimuli. No lesser arterial collarette was seen. The iris color was blue. The lens and central media were normal. The pulsation of the vessels on the disc surface and the cupping of the latter suggested increased intraocular pressure. The remainder of the fundus was devoid of pathologic changes. The tonometer reading was 60 mm. Hg (new Schiøtz).

Interval history (November 27, 1940, through May 13, 1941). Intensive miotics seemed to influence the intraocular pressure but very little. An Elliot trephination was performed once in the right eye and three times in the left eye. Cyclodialysis was also employed in the left eye. When discharged on May 13, 1941, the visual acuity was light perception in the right eye, and 6/6—2 in the left eye with the following correction: —0.50D. sph. ⊃ +1.25D. cyl. ax. 167° = 6/6—2.

The visual field was contracted centrally to 20 degrees. The tonometer reading was 22 mm. Hg (new Schiøtz). The patient was not contacted again until 1944 when the following findings were noted:

Right eye. Visual acuity tests showed light perception inferiorly and temporally. The old trephination area above presented no bleb. The anterior chamber was deep. The pupil was very widely dilated and oval horizontally. The sphincter was broad and prominent. No essential change had occurred in the iris stroma. The iris was tremulous. A peripheral surgical iris coloboma was present at the 12-o'clock position. Anterior synechias were noted at the 9- to 11-o'clock positions. No changes were apparent in the fundus. The tonometer reading was 30 mm. Hg (new Schiøtz).

Left eye. The corneal scleral junction showed the three trephination bleb areas all quite flat and scarred down. The cornea was clear. The anterior chamber was deep. The pupil was displaced down and out and was slightly dilated. Three peripheral surgical colobomas were seen at the 11-, 12:30-, and 2-o'clock positions. The iris stroma was less blue than on the original examination, as the brown ectodermal pigment was now more conspicuous. Anterior synechias were seen from the 2- to 5-o'clock positions, but no embryotoxon was apparent.

Funduscopically the lens was clear and the central media were negative except for vitreous opacities. The disc was markedly atrophic and cupped, and the retina showed no change. The tonometer reading was 16 mm. Hg (new Schiøtz).

G-9

This 20-year-old young woman of asthenic build was first seen at the university ophthalmic clinic, November 8, 1932, her chief complaint being severe frontal headaches.

Ocular findings. The eyes varied from straight to several degrees of left divergent strabismus. The ocular movements were normal.

Right eye. The corneal diameter was 14 mm. horizontally, and 15 mm. vertically. The corneal stroma was clear except for embryotoxon extending from the 9- to 12:30-o'clock positions. The anterior chamber was deep. The pupil was displaced up and in toward the 11-o'clock position but reacted to direct light, consensual light, and accommodation stimuli. The pupillary opening was irregular in shape, being somewhat cuboidal. Ectropion uveae was present at the 11-o'clock position. The iris was very atrophic in the lower inner two thirds. A large vertical dehiscence extended from the sphincter border to the iris base at the 5-o'clock position. The sphincter pupillae was prominently seen.

The slitlamp revealed some vascularization of the iris surface. A persistent embryotoxon membrane strand extended from the 5- to 2-o'clock positions. The corneal radius was 9.1 mm. The lens was dislocated slightly up and out. A small Mittendorfer was present nasally. The central media were normal. The disc was small and presented moderate, but early, atrophy and cupping. A large cilioretinal vessel was seen at the 11-o'clock position. The remainder of the fundus was negative.

Left eye. The corneal diameter was 13 mm.

horizontally and 14 mm. vertically. The radius of curvature was not determined because of irregular astigmatism. The cornea was irregular in outline as a result of scleral over-riding. A large moderately well-vascularized leukoma occupied the central zone of the cornea. The entire cornea showed deep or interstitial vascularization. The anterior chamber was deep.

A large triangular dehiscence was present in the iris, the apex being at the 1-o'clock position and the base extending from the 5- to 7-o'clock positions. Through this large dehiscence the ciliary body and attenuated zonular fibers could be easily seen with the slitlamp. A small anterior capsular opacity was present just above the anterior lens pole. A distinct bluish-white posterior corneal deposit ran around the nearly complete peripheral circumference. The lens was displaced slightly up and in. Otherwise, the lens, central media, and fundus appeared as in the right eye. The tonometer reading was 65 mm. Hg (new Schiøtz).

Interval history (November 18, 1932, to September 26, 1945). During this interval two Elliot trephining operations were performed in the right eye and three in the left, combined with a Lagrange sclerectomy in order to control the intraocular pressure. The left eye finally became phthisical. The visual acuity in the right eye remained 6/20—1 up to the above date. The tonometer reading on November 26, 1945, was 40 mm. Hg in the right eye. Iridencleisis was advised but refused by the patient.

Last examination (February 25, 1946). The patient had observed complete loss of vision three days prior to consultation, but vision gradually returned to the point where she could count fingers on February 25, 1946. The corneal horizontal diameter was 14 mm. There was moderate scleral over-riding superiorly. The corneal stroma was clear except for embryotoxon superiorly and temporally. In this region the iris and sphincter muscles were included in a broad anterior synechia.

There was no evidence of previous trephinations except for a small iridectomy at the 2-o'clock position. The dehiscence below was larger than when previously seen. The iris was tremulous and the lens was dislocated down and in. A small coloboma or notch of the lens was present at the 11:30-o'clock position.

Right eye. The lens showed nearly complete opacification superiorly, but was fairly clear inferiorly. No other fundus changes were seen. The tension was 45 mm. Hg. An iridencleisis was advised and performed by a local ophthalmologist, but the operative result has not yet been ascertained.

Gonioscopy (February 25, 1946). The angle was well seen and seemed completely filled with a grayish-golden trabecular tissue, which was decidedly more dense in certain areas, especially superiorly and temporally. The ciliary processes were seen through the small iridectomy at the 12-o'clock position. The iris surface was adhered to the cornea from the 11:30- to 12-o'clock positions, at which place the sphincter was included in the embryotoxon. Some fairly well-dilated vessels were seen in among the abnormal meshwork. Schwabe's line could not be visualized, and, indeed, no normal anatomic details of the angle were noted.

G-11

This well-developed, intelligent and coöperative little 4-year-old girl presented the most unusual ocular changes seen in her sibship. Her eyes had not changed since birth and she had never had previous ophthalmologic examination.

Ocular findings. The eyes were straight in the primary position, with considerable divergence noted under cover.

Right eye. The uncorrected visual acuity on the E chart was 6/15+. The corneal horizontal diameter was 12.5 mm. and the vertical diameter was 13 mm. The cornea was clear except for an embryotoxon present from the 11- to 7-o'clock positions. The anterior chamber was very deep.

The pupillary opening was a horizontal slit, 5 to 6 mm. in length, running obliquely from the 10- to 3:30-o'clock positions. The nasal portion of the pupillary opening was adhered to the embryotoxon. A dense band of ectropion uveae was also adhered to the latter. The sphincter muscle was broad and very conspicuous due to the attenuated character of the iris stroma. The latter was represented by thin incomplete grayish radial strands. No iris collarette was seen. The pupil showed normal direct, consensual, and accommodative reflexes.

The iris color was a grayish brown. A small dehiscence, 1.5 mm. in length, was present in the atrophic iris at the 10-o'clock position near the iris base. Some vascularization was evident on the iris surface. The iris was tremulous. No ectopia lentis was noted.

The lens and central media were clear. The disc was oval vertically, of excellent color. A moderate-sized physiologic depression was present. The vessels, macular area, and retinal periphery were devoid of pathologic changes. The fundus was easily seen with a plus-one sphere. The tonometer reading was 21 mm. Hg (new Schiøtz).

Left eye. The visual acuity was 6/15+1 as determined by the E chart. The corneal horizontal and vertical diameter was 12.5 mm. The corneal stroma was clear. A small thin grayish band of tissue was present on the posterior corneal surface in the extreme periphery and extended from the 11- to 2-o'clock positions. The anterior chamber was quite deep.

The iris was grayish brown in color. The superficial stroma was nearly absent except for attenuated radial strands, as noted in the right iris. The sphincter band faded out into the substance of the pigmented leaf of the iris. The pupil was irregular and somewhat triangular, with the base situated inferiorly and nasally. The pupil was displaced up and out. Minimal ectropion uveae was noted at the 6-o'clock position. The iris was tremulous. Funduscopically, the left eye presented normal findings as in the right eye. The tonometer reading was 23 mm. Hg (new Schiøtz).

ETIOLOGY

It is rather obvious that the ocular defects in this family are germinal in origin and are inherited in a dominant pattern. It is possible, therefore, to avoid a discussion of maternal influences and environmental noxious agents of unknown character and effect. The factor to be discussed is that of the mechanism at work, and, if possible, to implicate the ocular tissue primarily involved. The diversity of ocular pathologic changes is so varied and extensive that the discussion cannot be limited to one anomaly but must be inclusive of influences affecting the entire anterior ocular segment.

There are available in the literature numerous explanations or theories attempting to explain similar developmental or congenital anomalies of the anterior ocular chamber, cornea, and iris. Most writers seem to look with favor on the following two hypotheses:

I. A failure of development of the neural ectoderm especially with reference to a primary failure of the development of the rim of the optic vesicle.[9]

II. A mechanical obstruction to the development of the iris and anterior-chamber angle by persisting remnants of the tunica vasculosa lentis (capsulopupillary fibers) and its anastomoses with the extraocular mesoderm.[10]

Theory I anticipates an association of other ectodermal defects such as congenital amblyopia, retinal anomalies, nystagmus, lens-ciliary processes, and zonular defects. In this family A-7 and A-10 presented nystagmus, and F-3, G-9, and G-11 disclosed moderate ectopia lentis in association with extensive iris and corneal changes. No demonstrable posterior-segment ectodermal changes were recorded.

Theory II suggests that there is an abnormal prolonged persistence of the vascular network around the margin of the optic cup. In the anterior segment, this would offer an obstacle to the subsequent development of the iris and ciliary processes. When

such exists early and in extensive degree, aniridia may result; if only a partial obstruction exists, a coloboma of the iris may develop; or if very mild in extent and quite late, an ectopic pupil may ensue. It would be entirely possible to explain the majority of the pathologic changes of the affected eyes in this pedigree by postulating variations of this second theory.

A third and somewhat related theory is suggested by the findings of Hagedoorn (1928) who reported evidence that the anterior chamber is formed by the laying down of a scaffolding in the anterior vitreous (ectodermal) of a primitive cornea, anteriorly, and a primitive membrane, posteriorly, both of which are later permeated by invading mesoderm. Anomaly in this primary ectodermal scaffold could explain the later mesodermal defects effecting congenital corneal leukomas (A-7, A-10); embryotoxon and peripheral anterior synechias (C-1, A-2, A-7, A-10, F-1, G-1, G-9, and G-11); and the persistent embryonic tissue in the filtration angle in G-9 and G-5.

In this family and in those reported in the medical literature it is possible to select individuals whose defects could be explained by either theory. When such is the case, one anticipates that many influences are playing a role or that some entirely unsuspected and unknown mechanism is at work.

The embryologist is prone to stress the time relationship and sequence of events occurring in the development of the organism. He is aware that certain features of development occur only at and during a specific limited period of time.

It is also important to note that developmental phenomena occur in direct and quite meticulous sequence to preceding events. Much has been learned in respect to the influence of noxious chemical agents on the embryo with reference to the aforementioned time relationships.

It has been observed that the chemical action of certain agents will affect most of

those structures that are changing (growth) extensively and rapidly at the time of influence.

The same agent working at a different time will produce totally different effects depending again on which structure or tissue is undergoing the most energetic metabolism at the moment. Thus the cells exhibiting the greatest metabolic activity at the specific time that a noxious agent is present will demonstrate the most marked changes.

It is interesting to note that the geneticist emphasizes that genes are merely chemical agents and thus certain mutant genes can be expected to exert a relatively abnormal chemical or noxious effect on the developing embryo. In this light the tissue most active in its metabolism at the time that the gene exerts its effect would suffer according to the extent and duration of that influence.

In this family one could postulate an early and prolonged effect in A-7 and A-10 starting at the 6- to 9-mm. stage, thus effecting the extensive corneal and anterior chamber changes. The surface ectoderm and primary vitreous are most actively changing at this stage. The nystagmus present in both individuals could also suggest a deleterious influence on the neuro-ectoderm present as the primary optic vesicle at that stage.

In summary, one is forced to say that the specific mechanism producing the reported ocular anomalies is unknown. That a germinal influence is present cannot be denied in that the trait is transmitted in a very definite dominant pattern of inheritance.

TREATMENT

The glaucoma which accompanies the anterior-chamber anomalies described in this report has proved to be most difficult to manage either medically or surgically. Miotic therapy has had little, if any, influence upon the intraocular pressure in those individuals studied at the university ophthalmic clinic (E-1, A-7, G-5, and G-9).

Surgery, consisting of iridencleisis, iridectomy, trephine sclerotomy, and cyclodi-

alysis, has failed completely in those cases so treated. Extensive scar-tissue reaction has been a constant finding in those eyes which were reoperated and such connective-tissue proliferation could account for the failure of most of the surgical procedures employed. Iridencleisis is apparently controlling the tension in the right eye of G-9, but the period of observation has been very short.

Goniotomy has been suggested by its advocates for use in such cases as are encountered in this kindred. We have not utilized this procedure in this family but do anticipate doing so if granted the opportunity.

While not intending to discourage the quest for better methods of repairing such abnormalities, we would urge that the control of such defects should preferably be prophylactic. We have advised the affected members of these families of the genetic pattern of transmission and have strongly impressed them with the consequences of further propagation.

ECONOMIC CONSIDERATIONS

In general, the level of intelligence of the members of this family was moderate to good with no outstanding variation in any sibship. The occupation of most wage earners was clerkship and unskilled labor. The homes of most were modest but in a few the conditions were poor. The personalities of most individuals were affable to pleasant once a rapport was established.

An interesting and gratifying observation was the degree of independence and self-reliance exhibited by those individuals educated at the Lansing School for Blind (A-7, A-10, F-3, and A-4) all of whom were capable of earning their own living or managing their own household. F-3 and A-10 drew good salaries during the war as factory workers.

The marriage of A-7 to a classmate from the school for blind is disquieting. They do not intended to have children but no reliable

steps to prevent this likelihood have been taken to date.

Despite the position of the families, a considerable financial burden has been imposed on the county and state welfare by this family. The expense of support of the totally blind C-1, G-5, and F-3 has not been insignificant. The cost of special education has been high. The affected members have also been, in a few specific cases, a burden financially and in personal care to their siblings and parents. A-4, A-7, F-3, A-1, G-9, and G-5 have been frequent visitors to ophthalmologists and semiprofessionals. Such attention has resulted in the expenditure of many thousands of dollars in surgical and medical fees. If only C-1 had been prevailed upon not to have had children!

Conclusions*

1. A pedigree presenting the dominant inheritance of a trait effecting a wide variety of anterior ocular segment anomalies has been reported.

2. The ocular anomalies adversely affect the physical and mental well being, as well as the economic and educational achievements of the majority of the affected.

3. The associated glaucoma is most difficult to manage either medically or surgically.

4. Primary importance has been attached to giving eugenic advice to all members of this kindred.

University Hospital.

* For discussion, please see page 58.

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THREE CASES OF MARCUS GUNN PHENOMENON IN TWO GENERATIONS*

Harold F. Falls,[†] M.D., William T. Kruse,[‡] M.D., and
Charles W. Cotterman,[§] Ph.D.
Ann Arbor, Michigan

Hereditary Marcus Gunn phenomenon

The hereditary aspect of the Marcus Gunn phenomenon has received but scant attention from medical observers. The medical literature in this respect is indeed quite sterile. It is the purpose of the authors to present herein a family in which the Marcus Gunn anomaly occurs in three individuals in two consecutive generations.

I. General literature

The ill-termed "jaw-winking" phenomenon, in which there is an associated involuntary movement of one or both upper eyelids with movements of the lower jaw, was first described in 1883 by Marcus Gunn.[1] The association of extraocular muscle palsy with the phenomenon was emphasized by Lutz,[2] in 1919. Other observers have included such associations as: movements of the eye lids upon blowing out the cheeks, swallowing, singing, speaking, chewing, sucking, and thrusting out the tongue.

Several very excellent reviews are available for study and include reports by W. W. Sinclair,[3] in 1895; A. Lutz, in 1919; H. Villard,[4] in 1925; and F. C. Grant,[5] in 1936. The latter summarized 101 cases up to 1935. Among Grant's observations were: (1) Males are more frequently affected; (2) the left eyelid is the more commonly implicated; (3) the absence of ptosis of both eyelids has occurred only seven times;

and (4) bilateral ptosis has been noted in only three cases.

W. W. Sinclair summarized 32 cases and divided them into four variations (Series I) of the phenomenon as follows:

I. (13 cases) of unilateral congenital ptosis in which the drooping eyelid is raised both when the mouth is opened (? digastric muscle) and also when the jaw is directed to the opposite side (external pterygoid muscle).

II. (13 cases) of unilateral congenital ptosis in which the drooping eyelid is raised when the jaw is depressed but is not raised on lateral movements of the jaw.

III. (3 cases) of unilateral congenital ptosis in which the drooping eyelid is raised with lateral movement of the jaw (action of the external pterygoid muscle) but not with simple opening of the mouth.

IV. (4 cases) in which similar associated movement of one upper eyelid with movements of the lower jaw occurs but in which there is no ptosis.

W. W. Sinclair's classification included two other series: (1) Acquired pseudo-Graefe phenomenon and (2) Duane's retraction syndrome. These have been disregarded since attention is being confined wholly to the congenital type in our studies.

Etiology

The etiology of the syndrome has stimulated much literature as well as research, but unfortunately a satisfactory explanation is yet lacking. Helfreich and Bernhard[6] emphasized neuronal intercommunications between the nuclei of the facial, trigeminal, and oculomotor nerves. Bing[7] suggested a cortical or subcortical pattern analogous with the Bell's phenomenon.

Lewy, Grant, and Groff[8] believed that the

Marcus Gunn phenomenon could be explained by the presence of a proprioceptive arc, the afferent limb (in part) being the sensory division of the mandibular division of the trigeminal nerve. The efferent limb to the eyelid they assumed to be by the autonomic fibers questionably via the ophthalmic division of the trigeminal nerve.

Spaeth[9] wonders "if the Marcus Gunn syndrome cannot be caused by congenital misdirection of developing peripheral nerve fibers; the source of the fibers arising properly in the proper nuclei, the faulty distribution, however, occurring in the posterior longitudinal bundle or even more peripherally within the brain stem, excluding wholly any relationship of the autonomic nervous system."

The incidence is rather rare, there being now available in the literature only about 110 to 115 cases. Spaeth estimates that when properly observed 2 percent of all cases of ptosis would demonstrate the Marcus Gunn phenomenon. We feel this to be a little high but do agree that, if looked for, the incidence will be rather higher than heretofore anticipated.

II. DISCUSSION OF HEREDITARY CASES REPORTED IN THE LITERATURE

There have been several instances of familial occurrence of the Marcus Gunn anomaly reported in the literature. Leri and Weill[10] reported bilateral Marcus Gunn phenomenon in a woman, aged 63 years, and congenital unilateral Marcus Gunn anomaly in her son, aged 49 years. There were no other similarly affected individuals in the family.

Volmer[11] reported a family in which there were six members (hearsay evidence) with the jaw-winking anomaly, three females and three males in four generations, one generation being skipped, the defect being transmitted through two supposedly normal males to the succeeding generation. Volmer only examined one of the affected individuals, an

8-year-old girl with unilateral left-lid involvement.

Meyer[12] reported the phenomenon in a father and his 3-year-old daughter. In the latter it was congenital, left sided, and produced by eating and drinking. Blok[13] observed the phenomenon in two brothers. Phillips[14] also reported the Marcus Gunn phenomenon in two brothers, aged 3 years and 7 years.

There are also several papers in which the Marcus Gunn anomaly was known or thought to be present in other members of the family. E. C. Fischer[15] reported a case involving the right eyelid of a male child and stated that the right eyelid of the child's grandfather had had a similar appearance.

Jean S. Charamis[16] wrote that the brother and father of his patient (male) had had a similar ptosis but that he was unable to see or examine either. Vossius[17] mentioned the association of external ophthalmoplegia with his case of jaw winking and emphasized that a brother of his patient also had external ophthalmoplegia but no Marcus Gunn effect. E. Cooper[18] quoted family remarks in his case to the effect that an aunt had had a "similar eyelid."

PEDIGREE

The study of the family described here (fig. 1) was first undertaken because of the interest stimulated by the occurrence of this rather rare human anomaly in several members within two generations. The family is largely of farmer stock residing in southeastern Michigan. The propositus and his mother were referred for consultation to one of us (H. F. F.) through the courtesy of Dr. Thomas McEachern of Ann Arbor, Michigan. The pedigree chart is of the conventional type. Siblings are arranged horizontally and in order of their birth. Each generation is indicated by a Roman numeral and each member of the family proper by an Arabic numeral. Combination of these numbers are used to identify persons in the text.

PATHOLOGIC NOTES

(III-1). The propositus, a boy aged 7 years, exhibited the Marcus Gunn phenomenon in the left eye only. This jaw winking was first observed in the child as a nursling and was described by the mother as having been more conspicuous then than it was when first examined by us.

The visual acuity (uncorrected) was: O.D., 6/9+2; O.S., 6/6−2, E chart. Muscle measurements were 2-degrees esophoria for distance and orthophoric in accommodation.

in both eyes. The funduscopic examination was negative in both eyes.

There was a definite retraction of the upper eyelid, O.S., associated with chewing movement of the jaw. This was accentuated when the jaw opened and when it was protruded. Applying forceful resistance against the jaw accenuated the degree of elevation of the lid which was at the most only moderate, measuring 2 to 2.5 mm. Down-
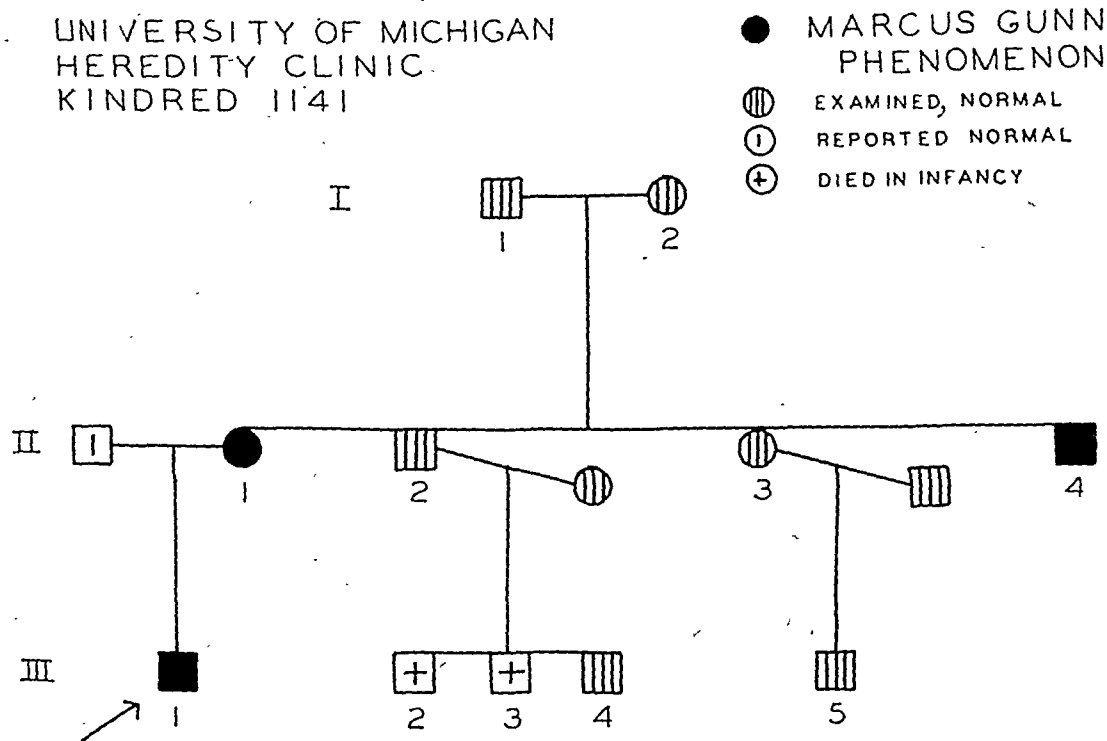
Fig. 1 (Falls, Kruse, and Cotterman). Pedigree chart showing occurrence of Marcus Gunn phenomenon in two generations of a family.

measurements were 2-degrees esophoria for distance and orthophoric in accommodation.

The eyes were straight in the primary position with minimal lateral deviation under cover. The external ocular movements were normal. The p.c.b. was 60 mm. The upper eyelids were normal and presented a good lid fold bilaterally. There was a very slight ptosis in the left eye, the palpebral fissure measuring 8 mm. O.D., and 7.5 to 7 mm., O.S. The pupils were normal. The pupillary reflexes were likewise normal. Conjunctiva, cornea, and anterior chamber were normal

ward gaze made the lid retraction more evident. The lids could be elevated voluntarily. Very minimal or no upward movement of the lid was produced by deviating the jaw to the right. No other associated cranial nerve action produced the retraction of the lids.

(II-1). This 31-year-old, well-developed woman accompanied her son for examination. Like her child her anomaly had been first noted when she was a baby and especially when she was nursing. Her facial appearance was pleasing and a right ptosis

could be noted only on careful observation. Chewing and talking produced observable retraction of the right upper lid.

The visual acuity was: O.D. 6/6−1; O.S., 6/6−3. The near point of accommoda-

position with minimal lateral deviation under cover. The extraocular movements were normal. The conjunctiva, cornea, anterior chamber, and iris were negative. The pupils were equal and round. The palpebral fissure,
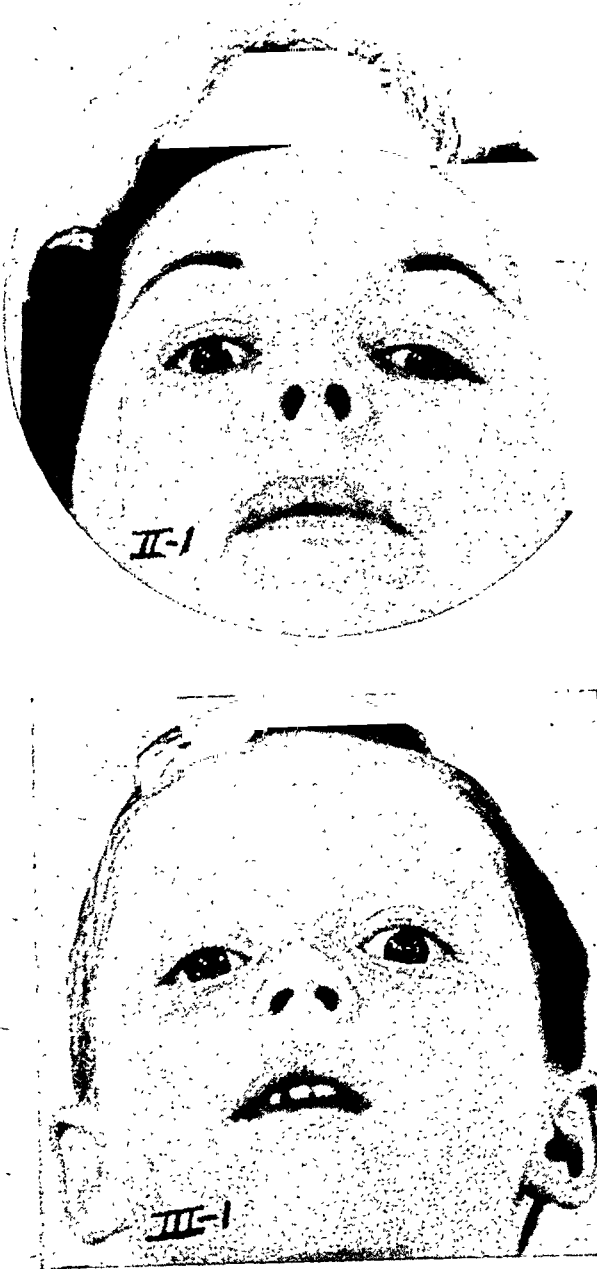

Fig. 2 (Falls, Kruse, and Cotterman). Three individuals in two generations exhibiting the Marcus Gunn phenomenon. (Kindred 1141, Heredity Clinic, University of Michigan.)

tion was J0 at 18 cm., O.D., and J0 at 17 cm., O.S. Muscle measurements revealed orthophoria in distance and 3 degrees of exophoria in accommodation. The p.c.b. was 75 mm.

The eyes were straight in the primary

O.D., measured vertically 8 mm. and O.S., 8.5 mm. The funduscopic examination was normal in both eyes. There was a definite retraction of 2 to 2.5 mm. of the right upper eyelid, more marked with protrusion of the lower jaw. Little or no elevation of the

upper right eyelid could be noted with lateral movements of the jaw to either side. Downward gaze of the eyes accentuated the retraction movement. No other cranial nerve association could be demonstrated.

(II-4). This well-developed, muscular 28-year-old man was not conscious of his Marcus Gunn phenomenon until our examination revealed its presence. The visual acuity was: O.D., 6/6; O.S., 6/9—2.

The external examination disclosed that the eyes were straight in the primary position with moderate lateral deviation under cover. The lids were normal with a good lid fold of both upper eyelids. A barely perceptible ptosis, O.D., was noted. Palpebral fissure vertical height was 8.5 mm., O.D., and 9 to 9.5 mm., O.S. There was gross nystagmoid jerking in the extremes of lateral gaze in both eyes. The conjunctiva, cornea, anterior chamber, and iris were normal in both eyes. The p.c.b. was 105 mm. The funduscopic examination was normal in both eyes.

On protruding the mandible, the upper right eyelid elevated approximately 2 to 3 mm. and remained elevated until the jaw was retracted. The eyelid moved synchronously with the back and forth action of the jaw. Slight retraction of the upper right eyelid was noted on ordinary chewing. Neither lid was seen to move on lateral movement of the mandible. There were no other cranial nerve associations demonstrable.

No other member of the family displayed any suggestion of the phenomenon.

HEREDITY OF THE PHENOMENON

All of the available evidence including the family herein reported and a second now being studied suggests that the trait is most probably inherited as an irregular dominant. In such a pattern many deviations may occur from the anticipated ratios. Usually when a trait is dominantly inherited one may expect certain rather clear-cut patterns of events, such as:

1. An affected individual will have an affected parent.

2. Fifty percent of the affected individuals' children may be anticipated to be likewise affected.

3. The trait does not skip a generation, but is dramatically constant from generation to generation.

In an irregular dominant pattern of inheritance certain unknown factors (modifying genes) may exert an influence on the presence or absence of the anomaly. The gene may be present in the germ-plasm of an individual (genotype) but may not be evident physically (phenotype). This latter individual may, however, transmit the trait to his or her children who can present the typical phenotypic appearance of the phenomenon. The degree of severity of the manifestation may vary greatly within the same family, from unilateral severe ptosis to very mild bilateral Marcus Gunn phenomenon without ptosis (variable expressivity), or no observable abnormality at all. Studies now in progress will be presented soon to support the latter observation.

COMMENT

The necessity for a careful and meticulous observation of every available member of families having the Marcus Gunn phenomenon cannot be too thoroughly emphasized. II-4 did not know he had the phenomenon, nor did his relatives, and certainly we would have missed him if we had relied merely on hearsay evidence.

SUMMARY

1. A family demonstrating a possible irregular dominant inheritance pattern of the Marcus Gunn phenomenon is presented.

2. Literature is presented to support the hereditary aspect of the Marcus Gunn phenomenon.

3. A plea is made for meticulous study of all members of Marcus Gunn families.

University Hospital.

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DISCUSSION

A GENE PRODUCING EYE DEFECTS AND MARCUS GUNN PHENOMENON

DR. CLEMENT MCCULLOCH (Toronto, Canada): Dr. Falls has presented theories in his first paper to explain multiple anomalies on the basis of one characteristic in one chromosome. I am wondering if there is any evidence in the distribution of cases in the family to suggest the presence of multiple characteristics in one chromosome?

Secondly, in discussing the family presented in the first paper he mentioned horizontally oblique discs in at least one case. I was wondering if he noticed oblique discs aside from the glaucoma change in any great number of that family and if they followed the anomaly of the anterior segment of the eye?

DR. K. W. ASCHER (Cincinnati, Ohio): Dr. Fall's contribution is certainly important and stimulating. The following approach might help to explain the congenital Marcus Gunn phenomena as well as those which appear during the adult life. Connections between the oculomotor and other nuclei are an atavistic inheritance, and associated movements occur in animals and in children like the forced opening of the mouth associated with opening of the lids.

While these connections always are pres-

ent their utilization is inhibited during normal adult life. This inhibition may be missing either congenitally, as in the great majority of the Marcus Gunn phenomena, or it may disappear temporarily as in a case described by me in 1937 (Med. Klin., 33:1259).

A Marcus Gunn phenomenon appeared in a 44-year-old man during the recovery from a unilateral third-nerve paralysis. After intensive antiluetic treatment, the patient noticed that his upper lid, paralyzed for months previously, opened involuntarily as often as he performed chewing movements. This associated movement was observed for about a week and disappeared when the patient became able to open his eye voluntarily.

This is a single observation only but together with phylogenetic and ontogenetic analogies it seems to indicate that the Marcus Gunn phenomenon might be due to disinhibition of a normally inhibited, preformed, associated innervational mechanism.

DR. DAVID G. COGAN (Boston, Massachusetts): A point of interest, although I don't know whether it has any significance, is that this lid retraction occurs only during the opening act of the jaw. If the jaw is held open, the lid does not stay retracted. I have no explanation for it. Maybe Dr. Falls has made a similar observation or may have some explanation.

DR. FALLS (closing): First, in respect to Dr. McCulloch's question—that is, "Is there any evidence of the fact that the multiple characteristics in this family may be due to multiple genes?"—I should like to say that it is very difficult to study multiple gene effects in human genetics, but because the pedigree in this family presents such a definite inheritance pattern, mainly that of dominant inheritance, and because the gene effect is so limited to the anterior chamber, we felt that we were dealing with a uni-gene factor.

In respect to multiple changes in the body due to one gene a rather interesting study by Dr. Cotterman, at our clinic, indicates a single gene will produce a specific defect in the developing embryo and in turn produce tremendous changes in the entire body due to the influence of migrating blebs of cerebral spinal fluid.

I am not too sure, Dr. McCulloch, whether you meant slit pupils or oblique discs.

DR. McCULLOCH: Oblique discs.

DR. FALLS: There were no frequent abnormalities of the optic nervehead in this family. It is my opinion that the oblique disc mentioned was only a chance association.

I should like to answer Dr. Ascher and thank him for his contribution. I cannot add anything to his statement. I do want to emphasize, however, that we limited our study entirely to the jaw-winking phenomenon of congenital origin. It is my opinion that your case report comes largely under the role of pseudo-von Graefe phenomenon.

In respect to Dr. Cogan's contribution I wish to mention that I have a more interesting family which will soon be published in which there are two specifically different types of Marcus Gunn phenomenon present. One member of the family presents no ptosis whatsoever, but when this man opens his jaw and turns it to the right and then to the left he has an elevation of the opposite lid. His sister has a unilateral ptosis and again there is lid elevation upon lateral movements of the jaw. It is true that the lid retraction does gradually relax with continuation of the jaw protrusion. I do not believe that I can explain this phenomenon.

In closing I should like to urge that the families in which Marcus Gunn phenomenon occur be more thoroughly studied, particularly from the viewpoint of the inheritance of the anomaly.

ELECTROCOAGULATION OF THE SCLERA*

REDUCTION IN OCULAR VOLUME AND PATHOLOGIC CHANGES PRODUCED

HAROLD G. SCHEIE, M.D., AND BOURNE JEROME,† M.D.

Philadelphia, Pennsylvania

I. INTRODUCTION

Although the value of sealing retinal holes in the cure of retinal detachment, pointed out by Gonin,[1-5] (1921-1930), has been confirmed by most subsequent workers in the field of retinal detachment surgery, a significant percentage of surgical failures continues to occur. Numerous techniques and almost every conceivable type of instrument have been employed to seal retinal holes. It therefore seems reasonable to investigate further any supplementary aids which are available to help reduce the number of failures. One of these aids is scleral resection or scleral shortening.

Reduction in volume of the scleral coat by resection was introduced in 1903 by Leopold Müller.[6] Müller mentioned its use in 7 instances all with satisfactory results. His stated aim was to reduce the volume of the sclera to that of its contents. Various reports have since appeared in the literature regarding the use of scleral resection. Müller,[7] 1930, reported results in 19 patients.

In 1934, Lindner[8] reported its use in retinal detachments carrying poor prognoses such as those associated with aphakic eyes, nystagmus, proliferating retinitis, and funnel-shaped detachments with bands following previous retinal detachment surgery. Lindner described his technique in detail.

He was very conservative in estimating his results and advocated doing the procedure only after electrocoagulation had previously been done. Pischel,[9] Borley,[10] Vail,[11] and Bogart[12] have written recently on the subject in our own country. Vail pointed out its value in retinal detachment with equatorial staphyloma.

Shortening of the eyeball or reduction in volume of the sclera has been accomplished by excising a piece of sclera. This can be a technically difficult procedure. There is reason to believe that some reduction in ocular volume can also be produced by electrocoagulation. Albaugh and Dunphy,[13] 1942, first commented upon the marked initial rise in pressure associated with the cyclodiathermy operation. Stocker,[14] 1943, made the same observation. Meyer and Sternberg[15] claimed that the volume of the eyeball is decreased in cyclodiathermy operations because of shrinkage of the sclera. Berens, Pischel, and Thorpe, in discussing a paper by Pischel,[9] stated that electrocoagulation consistently produced rather marked shrinkage of the sclera during retinal detachment operations. One of us (H. G. S.) made similar observations independently which led to the work presented in this paper.

Little is known about the actual changes in volume associated with either electrocoagulation of the sclera or scleral resection. Such knowledge and a comparison of the changes in volume produced by either technique might be of some value. If reduction in ocular volume could be safely produced by electrocoagulation which was comparable in amount to that resulting from scleral resection, a much simpler method of approach might be made available for clinical use. The duration of such changes should also be as-

certained. The following experimental work was therefore performed.

II. PURPOSE OF EXPERIMENT

The object of the experiments about to be described was:

A. To measure the volume changes occurring in the eye as a result of electrocoagulation of the sclera.

B. To establish the duration of such changes in volume.

C. To compare the changes in volume resulting from electrocoagulation with those of experimental scleral resection.
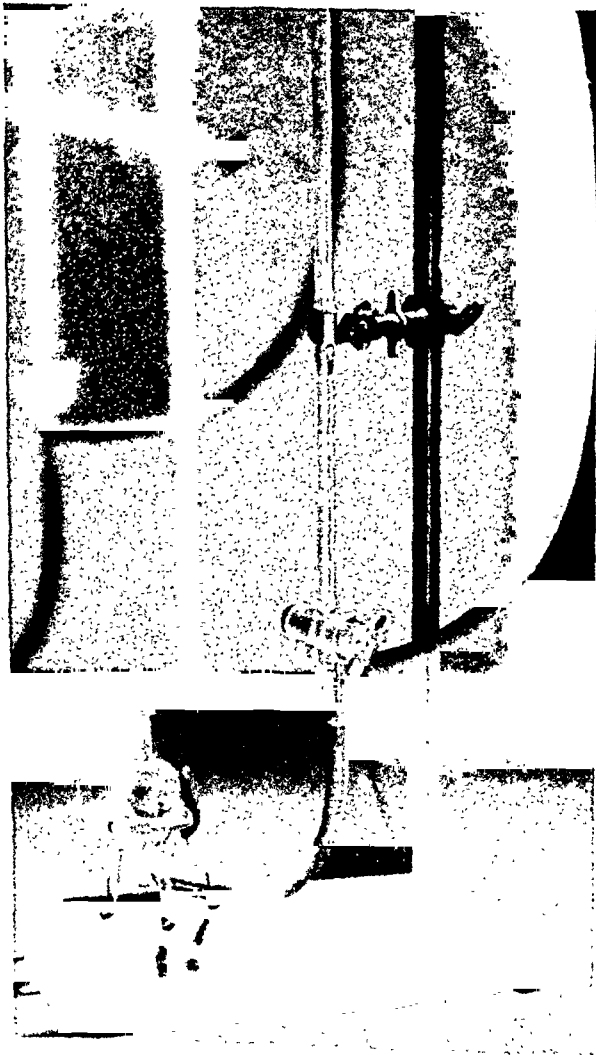
D. To observe the pathologic changes occurring in eyes so coagulated.

Fig. 1 (Scheie and Jerome). Apparatus for volume measurement, assembled.

III. TECHNIQUES AND APPARATUS

Several methods for measuring the volume of an eyeball and subsequent volume changes suggested themselves. After some trial, a fluid displacement method was decided upon and suitable apparatus devised (figs. 1 and 2). This consisted of a bell-
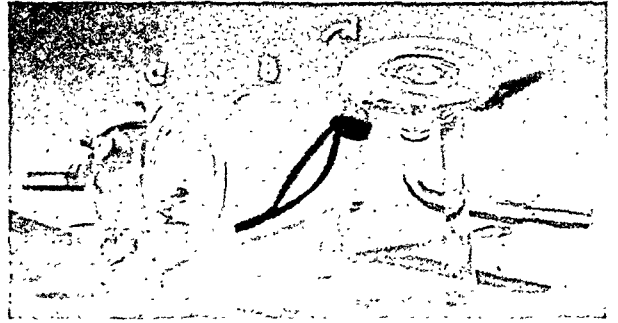
Fig. 2 (Scheie and Jerome). Device for volume measurement. (A) Etched mark indicating level to which device is filled. (B) Ground-glass surfaces on "bell" and base, lightly oiled. (C) Hooks, on which rubber banks from base are fastened. (D) Glass tube to fill device, with etched mark at zero level.

shaped chamber of 15-cc. capacity. The bell, which was open at the bottom, rested upon a base with a flat surface. Their approximating surfaces were of ground glass.

The dome of the bell was surmounted by a cannula that was etched at the level corresponding to 15 cc. when the apparatus was filled. At the center of the base was a small opening communicating with a small cannula which connected through a short piece of heavy rubber tubing to a 10-cc. analytical certified burette calibrated in 0.02-cc. divisions.

A fine film of oil applied to the ground glass surfaces achieved a water-tight union between the base and the bell. This union was given support by the traction of elastic bands.

The eye was debrided of its muscles and all adherent connective tissues and was placed on the center of the base and covered by the bell. Fluid was then allowed to enter the chamber filling it to the mark on the can-
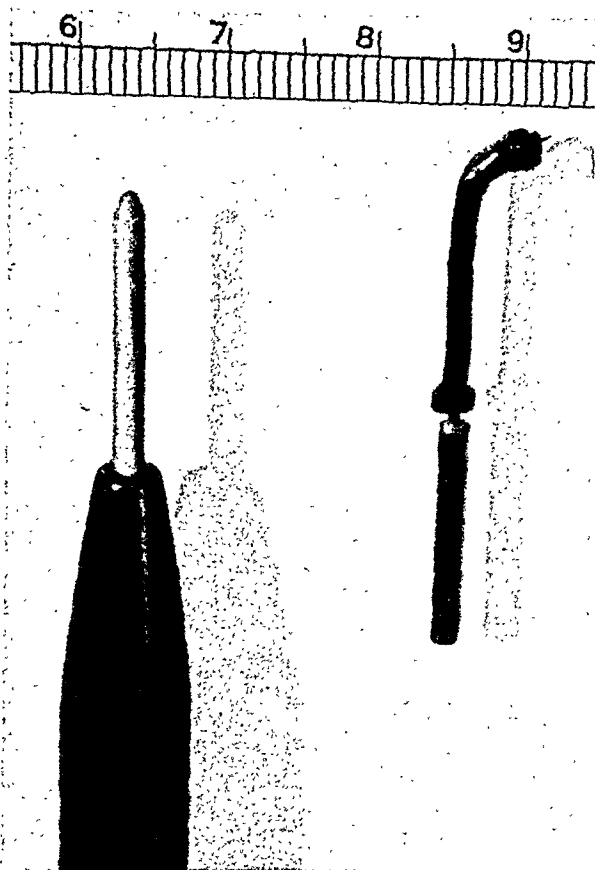
Fig. 3 (Scheie and Jerome). Surface and penetrating electrode employed in experiments.

nula surmounting the bell. The difference between the volume of fluid required to fill the apparatus containing the eye and the volume when empty gave the amount of fluid displaced by the eye, or its volume. Various control measurements were made.

Measurements repeated on the same eye could be duplicated with an average error of

0.01 cc. (Table 1). The eyes were kept at a constant intraocular pressure, for obviously an eye displaces less fluid when soft than when hard. To evaluate this relationship, measurements of five eyes were made with pressures varying from an eye too soft to measure with a Schiøtz tonometer* to 50 mm. Hg (Schiøtz) (Table 2).

The average difference between these two extremes of pressure was 0.48 cc. The difference between 10 mm. Hg and 25 mm. Hg was only 0.02 cc. while that between 25 mm. Hg and 50 mm. Hg (Schiøtz) was 0.1 cc. All volume measurements were subsequently done in these experiments on eyes in which the intraocular pressure was maintained between 15 and 25 mm. Hg because of the small error at that level.

The apparatus used for electrocoagulation was the standard Walker retinal detachment unit. The 1.1-mm. penetrating electrode from the Liebel-Flarsheim retinal detachment kit was used. The surface electrode was made of aluminum and designed to give a contact surface of one square mm. in area (fig. 3).

The technique of electrocoagulation in both enucleated eyes and on living animals was that employed at the hospital of the University of Pennsylvania in clinical retinal detachment surgery both in regard to intensity of current and time of application. A current of approximately 90 ma. was applied for

* All intraocular pressures in these experiments were recorded with a Schiøtz tonometer.

TABLE 1

ACCURACY OF VOLUMETRIC APPARATUS DETERMINED BY REPEATED MEASUREMENTS OF THE SAME DOG EYE
(Intraocular Pressure Constant, Schiøtz)

Eye 1	Eye 2	Eye 3	Eye 4	Eye 5	Eye 6	Eye 7	Eye 8
5.32 cc.	5.26 cc.	5.44 cc.	6.10 cc.	6.06 cc.	5.34 cc.	5.71 cc.	5.68 cc.
5.34	5.25	5.42	6.10	6.08	5.34	5.70	5.68
5.32	5.25	5.40	6.08	6.08			
5.31	5.24	5.40	6.08	6.07			
5.35	5.24	5.39	6.08	6.05			Average Error Between Successive Measurements = .01 cc.

TABLE 2

VOLUME OF DOG EYES AT VARIOUS INTRAOCULAR PRESSURES, DEMONSTRATING MINIMAL VARIATIONS
BETWEEN 10 AND 25 MM. HG (SCHIØTZ)

Eye No.	Too Soft to Register	Vol. Diff.	10 mm. Hg	Vol. Diff.	25 mm. Hg	Vol. Diff.	50 mm. Hg
1	5.57 cc.	.23 cc.	5.80 cc.	.01 cc.	5.79 cc.	.13 cc.	5.92 cc.
2	5.19	.57	5.76	.04	5.80	.07	5.87
3	5.04	.59	5.63	.06	5.69	.09	5.78
4	5.44	.24	5.68	.03	5.71	.06	5.77
5	5.54	.14	5.68	.02	5.70	.14	5.84
	Average Difference	.35		.03		.10	

about two seconds. The factor most variable and difficult to control in applying coagulation was the degree of wetness of the sclera.

Klein[16] has pointed out the importance of keeping the sclera moist because the electrical resistance of dry sclera is so unpredictable that control of the process is impossible and the degree of coagulation is uncertain. Pischel,[9] in discussion following his paper, implies that shrinkage of the sclera is much greater in degree when coagulation is applied to a wet field, but he believes that much of this shrinkage is temporary. Thorpe,[9] in the same discussion, warns that puncture coagulation must be carried out in a dry field or an "hour glass" eyeball will be produced by excessive shrinkage.

In our experience, a dry field would be difficult to maintain because of capillary oozing, even if it were desirable. To obtain uniform results an arbitrary number of applications of the electrodes was used for the purpose of our measurements. Fourteen surface applications were employed because dog eyes seemed to tolerate this number well. Thirty punctures were used in the experiments with penetrating electrocoagulation, a number which we felt did not exceed that used in some retinal detachment operations.

IV. EXPERIMENTAL DATA

A. SELECTION OF SPECIES

The earlier experiments were attempted upon rabbit eyes, but these were found to be entirely unsatisfactory because of the thinness of the sclera. The eyes tolerated electrocoagulation poorly, and the sclera necrosed. Measurements were also difficult because of the constant escape of intraocular fluid through openings in the thin sclera with lowering of intraocular pressure. Dog eyes were then used and found to be quite satisfactory.

TABLE 3

COMPARISON OF VOLUME OF THE RIGHT AND LEFT NORMAL DOG EYES

Intraocular Pressure Right Eye	Intraocular Pressure Left Eye	Volume Right Eye	Volume Left Eye	Difference in Volume between Eyes
10 mm. Hg	10 mm. Hg	5.94 cc.	5.98 cc.	.04 cc.
16	15	5.44	5.43	.01
13	11	5.14	4.89	.25
22	19	4.69	4.65	.04
25	25	5.26	5.26	.00
19	19	4.17	4.19	.02
17	15	4.97	4.97	.00
17	17	5.73	5.72	.01
17	17	5.54	5.53	.01
25	22	5.79	5.80	.01
25	25	5.69	5.71	.02

Average Difference .037 cc.

TABLE 4

CONTRACTURE OF ISOLATED STRIPS OF SCLERA FROM FRESHLY ENUCLEATED HUMAN EYE FOLLOWING ELECTROCOAGULATION OF ENTIRE EXTERNAL SURFACE

Measurements of Strips Before Electrocoagulation	Measurements of Strips After Electrocoagulation	Percent Shrinkage in Length
19 = 5 mm.	13×3 mm.	32
43×6	24×3.5	44
21×6	13×3	38
19×6	12×4	37
44×6	24×3	45
25×6	15×3.5	40
25×6	14×3	44
28×5	18×3	36
27×6	19×3	30
		Average 38.4%

The thickness of the sclera lies between that of the rabbit and the human eye.

Experiments upon the living animal required that one eye of each pair be used as a control. Equality of volume of the two eyes had to be determined. The volume of 11 pairs of eyes was measured and compared. The difference in volume between the eyes of 10 of these pairs ranged only from zero to 0.04 of a cc. (Table 3). The 11th pair differed in

Fig. 4 (Scheie and Jerome). Flattening and puckering of sclera produced by surface coagulation. (Freshly enucleated dog eyes.) (A) Rear view. (B) Side view.

size by 0.25 cc. The average difference between the two eyes of 11 pairs therefore was only 0.037 cc.

B. EFFECT OF SURFACE COAGULATION ON EXCISED STRIPS OF SCLERA

Before proceeding to experiments upon an intact eye, coagulation was performed on isolated strips of sclera from freshly enucleated human eyes. These strips contracted approximately 38 percent in length (Table 4).

C. EFFECT OF ELECTROCOAGULATION UPON INTRAOCULAR PRESSURE OF ENUCLEATED DOG EYES

Before utilizing the living animal, coagulation was carried out upon enucleated dog

Fig. 5 (Scheie and Jerome). Effect of increasing amounts of surface coagulation upon the intraocular pressure. (Freshly enucleated dog eyes.)

eyes. Penetrating electrocoagulation was unsatisfactory in these experiments because vitreous flowed from the punctures and the eye became so soft as to render volume measurements impossible. Experiments were therefore carried out using surface electrocoagulation.

Marked shrinkage of the sclera with puckering and flattening at the site of application of the surface electrode was seen (fig. 4). The intraocular pressure rose rapidly (fig. 5). After only 4 to 6 applications of the surface electrode, the average intraocular

pressure rose from a level too low to record on a tonometer to 40 mm. Hg. After 9 or 10 applications, the intraocular pressure approached 70 mm. Hg beyond which further increase was impossible because ruptures occurred in the sclera.

These experiments confirmed previous observations regarding contracture of sclera and increase in intraocular pressure following surface coagulation. These observations also demonstrated the necessity of reducing the volume of the ocular contents during electrocoagulation to permit the sclera to contract without the resistance of increasing intraocular pressure. Therefore, in succeeding experiments, in order to maintain the intraocular pressure as nearly as possible between 15 and 25 mm. Hg, aqueous was aspirated by paracentesis with a No. 27 needle inserted through the limbus obliquely.

D. Effect of surface coagulation in reducing the volume of enucleated dog eyes

Reduction in volume following surface electrocoagulation was studied in 11 dog eyes. The usual 14 applications of the surface electrode were used (Table 5). All of the measurements were taken with the tension within the limits noted above. If the eye

TABLE 5
EFFECT OF SURFACE COAGULATION IN REDUCING THE VOLUME OF ENUCLEATED DOG EYES
(14 Applications of Electrode)

Volume Before Coagulation	Volume After Coagulation	Reduction in Volume
4.70 cc.	3.89 cc.	.81 cc.
5.28	4.42	.86
5.32	4.52	.80
5.94	4.72	1.22
5.98	4.77	1.21
5.44	4.42	1.02
5.43	4.40	1.03
5.14	3.91	1.23
5.89	3.86	1.03
4.69	4.09	.60
4.65	3.85	.80

Average Reduction in Volume .96 = 18.5%

was too soft following coagulation, as a result of excessive paracentesis, saline solution was injected through the same fine needle to elevate the intraocular pressure to a dependable level. The smallest reduction in volume was 0.6 cc., the largest 1.23 cc. An average reduc-

TABLE 6
EFFECT OF SCLERAL RESECTION (4×22 MM. ELLIPSE) IN REDUCING THE VOLUME OF ENUCLEATED DOG EYES

Volume of Eye Before Resection	Volume of Eye After Resection	Reduction in Volume
4.96 cc.	4.46 cc.	.50 cc.
4.88	3.90	.98
5.11	4.39	.72
4.70	3.66	1.04
5.17	4.44	.73
6.23	5.58	.65
4.86	4.21	.65
6.04	5.55	.49
5.26	4.68	.58
4.97	4.35	.62

Average Reduction in Volume .7 cc. = 13.3%

tion in volume of 0.96 cc. or 18.5 percent of the volume of the eye resulted.

E. Effect of scleral resection in reducing the volume of enucleated dog eyes

Scleral resections, consisting of the removal of an ellipse of 4 by 22 mm., were performed on 10 enucleated dog eyes. The technique was the standard one for scleral resection described in some detail by Lindner.[8] The average reduction in volume was 0.7 cc. or 13.3 percent (Table 6) which was less than that occurring with the surface coagulation of enucleated eyes.

F. Immediate effect of surface coagulation in reducing the volume of the dog eye in the living animal

One eye of each of 5 animals was prepared by incision of the conjunctiva and tenotomy of the external rectus muscle to expose the sclera. Cautery was then carried out in a

manner similar to that in the experiments on the previously enucleated eyes. Care was taken to avoid electrocoagulation of the ciliary body. Fourteen applications of the surface electrode were made. Paracentesis had to be
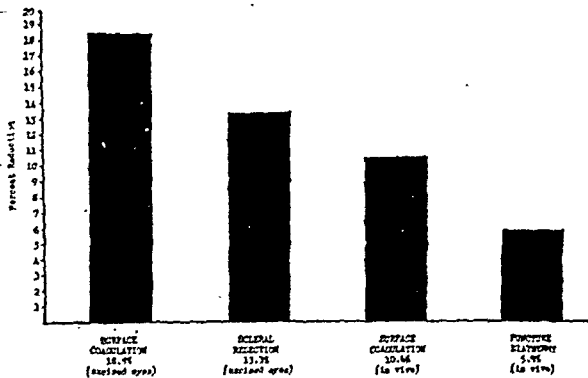

Fig. 6 (Scheie and Jerome). Comparison of reduction in volume in dog eyes produced by various operative procedures.

electrode were made. Paracentesis had to be performed to prevent the rise of intraocular pressure to an extremely high level and to permit reduction in volume. Immediately following the coagulation procedures both eyes were enucleated. The unoperated eye was used as a control for the determination of volume changes.

The average reduction in volume was found to be 0.64 cc. (12.7 percent) which

was closely comparable to that obtained by scleral resection. As shown in the table, a rather marked discrepancy in results exists between the operation performed upon eyes previously enucleated and the operations done in the living animal (fig. 6). This can best be explained as due to variations in effectiveness of the electrode.

The eyes already enucleated were coagulated after moistening the area of contact with saline solution which is an excellent conductor. The amount of current delivered and the effect of each application was therefore quite uniform. In the living animal such application is more difficult because of constant oozing of blood into the field of operation and inevitable variation in the delivery of current.

G. Persistence of Reduction in Volume Produced by Surface Coagulation

Having determined the fact that electrocoagulation of the sclera produced a reduction in volume of the eye in the living animal comparable with that of a scleral resection of a size used clinically, it seemed important to establish the duration of such changes.

To determine this, animals were operated
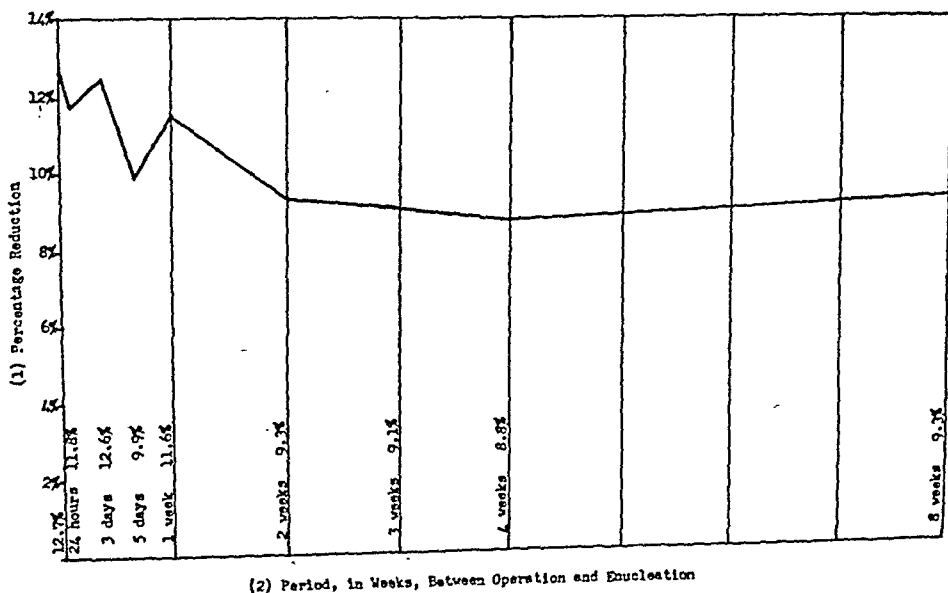
Fig. 7 (Scheie and Jerome). Relationship between (1) volume reduction of dog eyes resulting from surface coagulation and (2) period between coagulation and enucleation.

in the manner just described and the eyes of 5 dogs, were removed and measured at each of the following periods: 24 hours, 3 days, 5 days, 1 week, 2 weeks, 3 weeks, 4 weeks, and 8 weeks (fig. 7).

The reduction in volume fell slowly during the first two weeks when a reduction of approximately 0.5 cc. or 9 percent was reached. Subsequent to the second week the reduction remained unchanged and the operated eye remained smaller than the unoperated eye throughout the period of observation of two months. This was true even though both eyes appeared normal to external examination. The intraocular pressure was normal in each, except in animals subjected to short-term experiments.

H. THE EFFECT OF PENETRATING ELECTRO-COAGULATION IN REDUCING THE VOLUME OF THE DOG EYE IN THE LIVING ANIMAL

Control measurements on enucleated eyes using penetrating diathermy were unsuccessful because of the low intraocular pressure resulting from vitreous loss through the punctures. It was not possible by injecting fluid into the eye to raise the tension to a dependable level (15 to 25 mm. Hg). The fluid escaped as fast as it was injected. The same was true in experiments in the living animal where the eyes were enucleated shortly after operation. The difficulties, however, were obviated by postponing enucleation of the eyes until one week after operation. By this time the punctures had sealed and the eye could be injected so that the intraocular pressure was within the limits satisfactory for volume measurements.

Thirty applications of the penetrating electrode distributed over almost half of the scleral surface behind the ciliary body were made. The average reduction in volume by this technique was 0.26 cc. or 4.9 percent. Eyes of another group of 5 animals were enucleated 4 weeks following operation. A reduction in volume of 0.36 cc. or 6.9 percent was found.

The discrepancy between volume changes of the eyes of these two groups of animals cannot be explained. The essential fact remains that although reduction in volume with this number of applications did occur, the amount was only approximately half that produced by the technique of surface coagulation used in our experiments (fig. 6). This was undoubtedly due to the fact that a smaller area of the sclera was affected by the penetrating technique than by the surface application.

V. PATHOLOGY

Previous experimental studies on eyes treated by various perforating techniques—actual cautery (Herzfeld,[17] 1930, Luntz,[18] 1939) perforating diathermy (v. Szily and Machemer,[19] 1933, Cordero,[20] 1934), electrolysis, trephining with application of caustic to the choroid (v. Szily and Machemer[19]), and perforation with a sharp instrument (Weekers[21, 22]) have shown a general agreement as to nature and sequence of pathologic changes in the eyes so treated. Weekers especially emphasizes that the histopathologic picture is essentially the same regardless of the nature of the perforating agent. He conclusively shows that the origin of the fibrous tissue band that holds the retina so firmly in place after perforating wounds is in the episclera, and that this fibrous tissue invades the wound toward the retina in a remarkably short time after the injury.

The first stage in the sequence of the pathologic change referred to is characterized by mechanical adherence of retina to choroid at the operative site (Herzfeld[17]), edema and vascular engorgement of the sclera, choroid, and retina, outpouring of fibrin or blood into the wound, and mild inflammatory changes of the acute type, with polymorphonuclear leukocytes predominating.

These changes are followed in from 1 to 2 weeks by a second phase consisting of subacute inflammation, in which mononuclear cells predominate. The sclera loses its nuclei and begins to look necrotic, but it does not

disintegrate. Active connective-tissue proliferation starting from the episclera is seen. The choroid and retina lose their vascular engorgement and pigment rearrangement occurs.

The third stage is characterized by completion of a firm fibrous tissue bridge which extends between episclera and choroid, frequently reaching to or invading the retina. Localized atrophy and thinning of sclera, choroid, and retina are seen. The retina at this stage is very firmly attached to the scar beneath it.

Following surface coagulation, basic histopathologic changes show essentially the same nature and sequence, according to most observers, with the exception that the invasion of the necrotized sclera by scar tissue from the episclera is much slower and is not mentioned by several authors as occurring at all.

Weekers[21, 23] emphasizes that broad, fairly firm adhesions form between retina and choroid after surface coagulation, but he does not mention or illustrate fibrocytic invasion of the sclera as occurring with this technique, despite the fact that some of the eyes in his series remained in vivo for 5 weeks after operation.

Pischel[24] obtained less firm but broader retinochoroidal adhesions using surface coagulation than he did with the penetrating technique. He emphasized that changes in sclera, choroid, and retina spread farther from the operative site with surface coagulation. The longest period between operation and enucleation in his series is two weeks; sections of eyes coagulated with the penetrating electrode show marked fibrosis into the scleral wound, but no such change is seen in surface-coagulated eyes.

Cordero's[20] studies of eyes enucleated in periods ranging from 3 to 70 days after surface and penetrating diathermy did not disclose instances of fibrous tissue invasion of the sclera after the former method, but confirmed the similarity of other pathologic changes occurring with each method. He

found that the reaction of the uveal tract and retina is more severe to surface coagulation. He based this conclusion on ophthalmoscopic and microscopic evidence.

Bucallosi[25] was able to demonstrate in rabbit eyes that a bridge of fibrous connective tissue connecting episclera to retina is present one month after surface coagulation with caustics or diathermy. He was possibly the only investigator to describe this reaction.

Occasional or frequent concomitant changes with both perforating and surface technique listed by these investigators are: vitreous opacities, corneal edema, cellular deposits within the eye, retinal hemorrhages, retinal folds, detachments, retinal tears, and degeneration of retina and choroid extending well beyond the operative sites. The frequency and intensity of these reactions seems to be directly related to the amount of operative trauma.

A. PATHOLOGIC CHANGES OCCURRING IN EYES COAGULATED WITH SURFACE ELECTRODES (TABLE 7)

Slides for microscopic study were prepared from most of the eyes operated during the conduct of the volume studies. The specimens were fixed in formalin, after which they were embedded in nitrocellulose. Sections were 14 to 20 microns in thickness. They were stained with hematoxylin and eosin and mounted in Canada balsam. We were thus able to follow the histologic changes resulting from electrocoagulation at the same periods of time used for studying the volume changes. The sequence followed, therefore, involved eyes of periods ranging from those enucleated immediately after coagulation to those followed for as long as 8 weeks.

In general, the changes seen confirmed those of previous observers. The histologic changes seen in the episclera were somewhat modified because the episcleral connective-tissue mantle had to be dissected away as completely as possible to permit accuracy of volume measurements. Following removal of

Tenon's capsule and this connective-tissue mantle, the sclera appeared somewhat darkened and thinned at each site where the electrode had been applied. This was true for eyes treated with perforating as well as surface diathermy.

1. Changes in eyes removed immediately after coagulation (fig. 8). Ophthalmoscopic examination revealed white exudative areas

coagulation revealed the same white areas of retinal exudate at the site of each coagulation point. The fifth eye had a hyphemia preventing a view of the fundus. Two of the eyes had retinal detachment. A large retinal hemorrhage could be seen in one eye in the area of coagulation.

The microscopic changes were much more marked than those which had occurred in the

TABLE 7

SUMMARY OF PATHOLOGIC CHANGES RESULTING FROM SURFACE COAGULATION

Length of time Observed	Ophthalmoscopic	Histopathologic Findings			
		Coagulated Area			Associated Findings
		Sclera	*Choroid*	*Retina*	
Acute to 5 days	White retinal exudates; spotty or confluent, site of coagulation.	Edema moderate. Coagulation necrosis.	Vascular engorgement. Edema increasing.	Edema. Degeneration with irregularity of layers.	Deposits of granulocytes and pigment on corneal endothelium.
	Retinal hemorrhages in coagulated area.	Pmns, fibrin, fibroblasts on surface.	Pmns maximum at 3 days.	Vascular engorgement.	Vitreous: clumps of rbc occasional.
	Retinal detachment frequent.	New vessels occasionally.	Occasional hemorrhages.	Detachments frequent. Hemorrhages occasional.	Papilledema occasional.
1 week to 2 weeks	Retinal exudates absorbing. Retinal hemorrhages. Occasional localized retinal detachment. Vitreous opacities occasional.	Coagulation necrosis. Fibrocytes cover surface. Wbc decreasing. New vessels occasionally.	Vascularity decreasing. Edema subsiding. Pigment dispersed. Hemorrhage occasional.	Atrophy increasing. Detachment frequent. Hemorrhage occasional.	Deposits of wbc plasm cells and pigment. Same type cells in cilioscleral sinus frequently. Vitreous hemorrhage occasional.
3 weeks to 4 weeks	Retinal exudates nearly absorbed. Hemorrhages persist. Occasional retinal detachment. Beginning retinal atrophy coagulated area.	Coagulation necrosis. Fibrocytes invading necrotic region. A few new vessels.	Vascularity decreasing further. Pigment dispersal increasing. Thickening frequent. Thinning occasional.	Atrophy severe. Detachment occasional. Hemorrhage occasional.	Retina: Irregularity of layers near coagulated area occasional Ciliary Body: Plasma cells occasional.
8 weeks	Atrophy coagulated area. Pigment disturbance frequent. Hemorrhage occasionally. Vitreous opacities occasionally.	Coagulation necrosis same as at 4 weeks. Fibrocytes cover surface and invade necrotic region. Pigmentation occasionally seen.	Vascularity same as at 4 weeks. Thinning inconstant.	Atrophy severe. Detachment occasional. Firm adherence between retina and choroid frequent.	Retina: atrophy frequently extends beyond operative site.

at the site of each application of the surface electrode. The media appeared clear.

Only one eye was studied microscopically. The sclera was thickened by edema, severe engorgement of the choroidal vessels was present. Hemorrhagic foci were seen in the choroid. Retinal edema and degeneration with irregularity of the various retinal layers was present. No other pathologic changes were seen.

2. Changes in eyes removed 24 hours after coagulation. Ophthalmoscopic examination of 4 of the 5 eyes removed 24 hours after

eyes removed immediately. Coagulation necrosis had occurred; edema of the sclera was present; fibrin could be seen on the surface of the sclera; some infiltration with polymorphonuclear cells had occurred. The choroid showed marked vascular engorgement. Many polymorphonuclears were also seen, as well as a few monocytes. Edema of the choroid was present. The retina was edematous. Detachment of the retina had occurred over the coagulated site in 2 of the eyes. Pigment disturbance was present in 1 eye. The retinal vessels were engorged. A few cellular

Fig. 8 (Scheie and Jerome). Photomicrograph of section (×160) from an eye removed directly after operation showing edema and density of staining reaction at the scleral operative site, as well as edema, folding, and architectural distortion of the retina.

deposits could be seen on the corneal endothelium of 2 eyes; the iris vessels were engorged; the ciliary body was edematous in 2 of the eyes studied.

3. Changes in eyes removed 72 hours after coagulation. Ophthalmoscopic examination revealed little change from that in the eyes enucleated immediately and at 24 hours. Retinal hemorrhages were more common.

Microscopically, the sclera revealed little change from that in eyes removed at 24 hours. The mantle of connective tissue and cellular infiltrate over the coagulated area was probably more marked. The sclera at the operative sites now appeared slightly necrotic. The choroid was engorged and edematous. The same type of cellular infiltrate was present as at 24 hours. The retina was edematous in all eyes over the coagulated area and the various cellular layers were

irregular, as is shown in Figure 9.

One of the 4 eyes examined revealed some cellular deposits on the corneal endothelium. The iris vessels were engorged in 2 of the eyes. The ciliary body was edematous in 3 of the eyes. The choroid was diffusely edematous in 1 eye. Clumps of cells were found in the vitreous of 2 eyes.

4. Changes in eyes removed 5 days after coagulation. White retinal exudate and retinal hemorrhages over the coagulated areas were characteristic by ophthalmoscopic examination.

Three eyes were examined microscopically. The sclera over the coagulated area was edematous and showed necrosis. The fibroblastic mantle could be seen over the coagulated area. This contained many white blood cells and fibroblasts. The choroid in the coagulated area was edematous and hemor-

rhagic. Rather marked vascular engorgement was present.

The retina over the coagulated area was folded and edematous. Its layers again were irregular. Cellular deposits could be seen in the anterior chamber. The ciliary body was edematous and the iris showed some engorgement. The nervehead of one eye was edematous.

5. *Changes in eyes removed one week after coagulation.* Ophthalmoscopic examination revealed less retinal exudation than was present in eyes previously described. The retinal hemorrhages remained.

The sclera showed evidence of coagulation necrosis. The fibroblastic mantle was thick and completely covered the operative site. Vascularity of the choroid was decreasing. The retina showed beginning atrophy in all

cases. Retinal detachment was present in two of the four eyes examined. The changes elsewhere in the eyes were little different from those recorded in the preceding groups except that one cornea showed what appeared to be an interstitial keratitis near the limbus.

6. *Changes in eyes removed 2 weeks after coagulation.* Ophthalmoscopic examination revealed absorbing retinal exudates and hemorrhages. Both phenomena were less marked than at one week.

Three eyes of those removed at the end of 2 weeks were examined microscopically. The sclera again showed coagulation necrosis and a connective-tissue mantle more heavily developed. Fibrocytes were beginning to invade the sclera in one eye. The choroid showed dispersion of pigment with dimin-

Fig. 9 (Scheie and Jerome). Photomicrograph of section (×160) from an eye removed 72 hours after operation showing coagulation necrosis of the sclera at the operative site; edema, vessel engorgement, and moderate inflammatory reaction in the choroid; fluid retinal detachment and edema and architectural distortion of the retina.

·ishing vascular engorgement.

The retina was atrophic over the coagulated area with detachment present in all 3 eyes. One eye was normal outside the coagulated area; 1 showed degenerative change

eyes connective tissue was seen invading the coagulated sclera. The choroid showed less vascular engorgement with some pigment disturbance at the site of the coagulation. The retina was detached in 2 of the eyes at
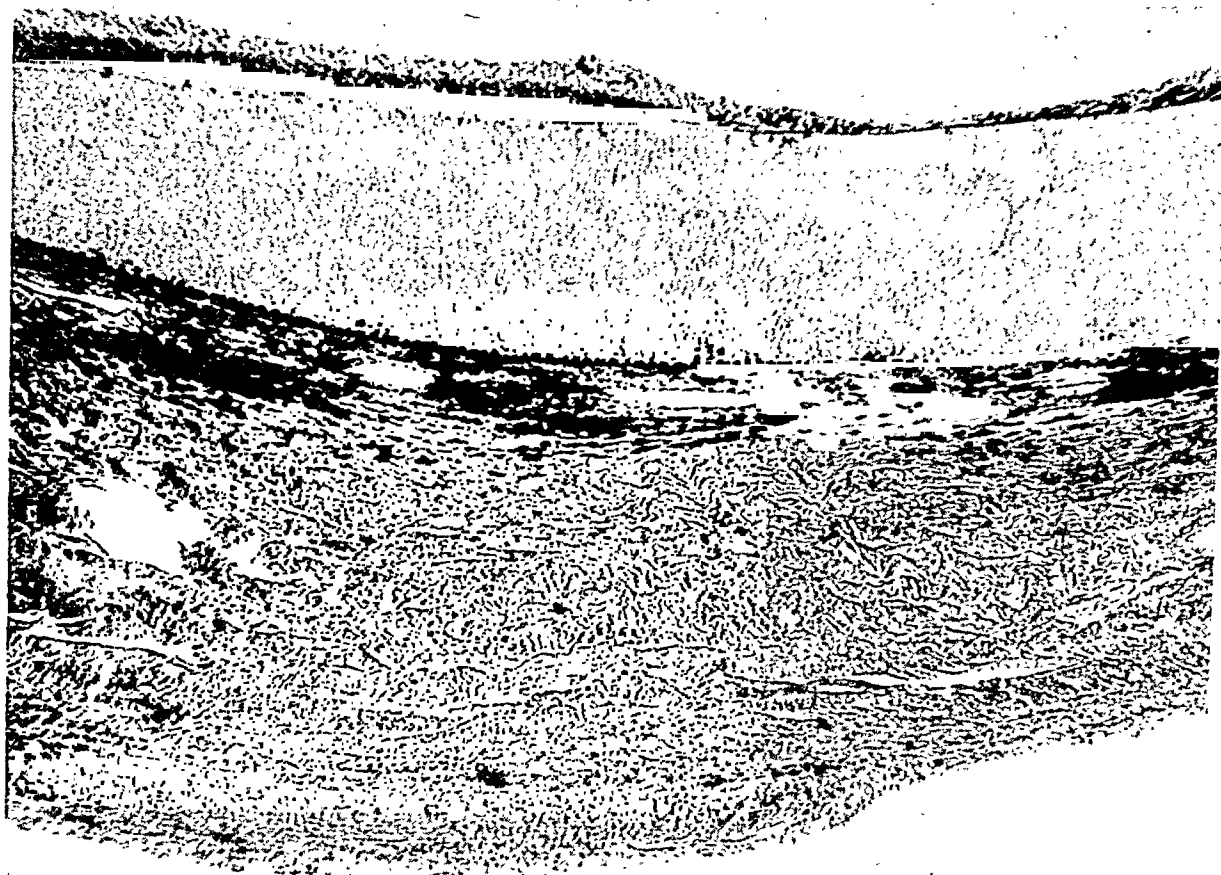
Fig. 10 (Scheie and Jerome). Photomicrograph of section (×80) from an eye removed three weeks after operation showing necrotic scleral operative site; hemorrhagic retinal detachment; and "band type" retinal atrophy immediately under the operative site.

of the ciliary body near the operative site. Apparently a portion of the ciliary body had been coagulated.

7. *Changes in eyes removed 3 weeks after coagulation* (fig. 10). Ophthalmoscopic examination revealed that the white retinal exudates had nearly absorbed. Retinal hemorrhages were still present. Localized pigment disturbance was common. Localized retinal atrophy over the coagulated area could be seen in 2 of the 6 eyes.

The sclera in all of the eyes still demonstrated coagulation necrosis and formation of a connective-tissue mantle. In 2 of the

the site of coagulation. Hemorrhagic exudate was present beneath the detachment in each of these eyes.

Retinal atrophy was marked over the coagulated area in 5 of the eyes. The ciliary body showed pigment disturbance and some atrophy in 2 eyes in which the coagulation was near this region. The other eyes were normal elsewhere than at the site of coagulation.

8. *Changes in eyes removed 4 weeks after coagulation.* Ophthalmoscopically the hemorrhages were less marked and retinal atrophy was much more obvious.

The sclera in all 3 of the eyes examined microscopically showed coagulation necrosis and again the connective-tissue mantle. Fibrous tissue now extended deeply into the necrotic sclera in all 3 eyes. The choroid and retina both showed irregular atrophy over the coagulated area. The eyes were essentially normal otherwise, although the ciliary body adjacent to the site of the coagulation

B. PATHOLOGIC CHANGES OCCURRING IN EYES COAGULATED WITH PENETRATING ELECTRODES (TABLE 8)

A study of these eyes was made in an attempt to prove or disprove the observation of Weekers that fibroblastic tissue from the episclera migrated inward toward the choroid and retina through the puncture holes. From our observations described

Fig. 11 (Scheie and Jerome). Photomicrograph of section (×160) from an eye removed eight weeks after operation showing advanced cicatrization about the scleral operative site and confluence of the margins of the sclera, sclerotic choroid, and atrophic retina. Note dense episcleral "mantle" of fibrous tissue over necrotic zone of sclera.

showed some pigment disturbance and probably atrophy.

9. *Changes in eyes removed 8 weeks after coagulation* (fig. 11). Retinal hemorrhages were seen in but 1 eye ophthalmoscopically. These were small and deep. Retinal atrophy was present.

Microscopically, necrosis of the sclera was still visible. The area of necrosis was covered and deeply invaded by fibrous tissue. The choroid showed diminished vascularity and atrophy over the coagulated sites. The retina was similar. Retinal detachment with subretinal hemorrhagic exudate was seen in 2 of the eyes. A vitreous hemorrhage was found microscopically in 1 of the eyes.

above, we could well predict that Weekers's observations would be confirmed because one of the earliest phenomena following electrocoagulation of the sclera is the formation of the fibroblastic connective-tissue mantle.

This fibroblastic mantle in the early stages involved only the surface of the sclera. In 1 of 6 eyes at the end of 3 weeks and in all eyes at 4 weeks, it was shown that these fibroblastic cells invaded the necrotic sclera itself. Presumably this invasion would have occurred much more promptly and earlier had openings been provided into which fibroblasts might grow.

In the microscopic study of the eyes coagulated with penetrating diathermy, the

same intervals were used as for volumetric measurements; namely, 1 and 4 weeks.

1. Changes in eyes removed one week after penetrating coagulation (fig. 12). Ophthalmoscopic examination. Vitreous opacities were seen in 1 eye of 4 examined. All eyes had soft white retinal exudates surrounding each puncture. Two eyes showed depigmentation near the puncture sites. In 1 eye a small hemorrhage was seen.

Three eyes were examined microscopi-

moscopic examination: Two of 5 eyes had nonfloating vitreous striae over and attached to the coagulated area. In all 5, chorioretinal atrophy was seen around each puncture. In one case the atrophic areas were partially confluent, while, in another, a soft white exudative appearance was superimposed on the atrophy.

All 5 eyes were examined microscopically. All showed scleral coagulation necrosis at the operative site; 3 had a substantial core

TABLE 8

SUMMARY OF PATHOLOGIC CHANGES RESULTING FROM PENETRATING COAGULATION

Length of time Observed	Ophthalmoscopic	Histopathologic Findings			
		Coagulated Area			Associated Findings
		Sclera	*Choroid*	*Retina*	
1 week	White retinal exudates sites of coagulation; occasionally confluent. Pigment disturbance at coagulated site occasionally.	Coagulation necrosis at operative sites traversed by core of fibrocytes extending from fibrous mantle on surface deep into sclera. Monocytes in necrotic area.	Moderate pigment choroid dispersal. Necrosis occasionally. Fibrosis occasionally.	Moderate necrosis or degeneration with irregularity of layers. Occasional hemorrhage. Occasional small detachments.	Essentially normal.
4 weeks	Chorioretinal atrophy at each coagulated site; occasionally confluent. Striated vitreous opacities occasionally. Occasional retinal hemorrhage or persisting exudate.	Coagulation necrosis at operative sites traversed by core of fibrocytes extending down from episcleral fibrous mantle, reaching to choroid or even retina.	Degeneration or atrophy localized to operative sites. Decreased vascularity. Pigment disturbance occasionally.	Localized atrophy. Close adherence to choroid at operative sites.	Ciliary body: Pigment disturbance, irregularity of structure occasionally.

cally. All showed scleral coagulation necrosis at the operative site traversed by a core of fibrous connective tissue which appeared to arise from an episcleral fibrous-tissue mantle and extended almost to the choroid or invaded its substance. Pigment dispersion at the operative site was uniformly present in 1 eye.

The retina under the puncture site in 1 eye was normal; in another it was necrosed and had a small hemorrhage; in a 3rd, fibrosis had extended into its substance from the episclera and through the choroid; small hemorrhagic detachments were present near the operative site in this eye. There were no abnormal findings in the other structures of these eyes.

2. Changes in eyes removed 4 weeks after penetrating coagulation (fig. 13). Ophthal-

of fibrous connective tissue reaching from a fibrous episcleral mantle down to choroid or retina. In the 4th eye the sclera at the operative site was thinned, the episcleral fibrous tissue was vascularized and there were only a few fibrocytes in the depth of the sclera. In the 5th eye the episcleral tissue was itself necrotic.

The choroid at the operative site was degenerating or atrophic in all eyes, with decreased vascularity and pigment disturbance the rule. In 1 eye, a small inward proliferation of pigmented tissue from the choroid was seen. In all 5 eyes the retina showed a bandlike atrophy confined to the operative site. In all cases it was in firm apposition with the choroid at these points.

Findings in the other structures of these eyes included pigment disturbance and mild

degeneration of the ciliary body when a coagulation was placed near its pars plana. Hyalinosis of the ciliary processes was present in another eye. One eye showed corneal bleb formation, mild degeneration of the ciliary body, and pigment deposits in the anterior chamber. One eye showed keratitis of the anterior third of the corneal stroma. Inexplicably, a small vascularized central corneal staphyloma was seen grossly in another eye.

Fig. 13 (Scheie and Jerome), Photomicrograph of section (×160) removed one month after operation showing marked episcleral fibrosis and healed penetrating diathermy wound. There is underlying choroidal and retinal fibrosis and retinal atrophy. Note close adhesion of chorioretinal tissue to scleral scar at the operative site.

Fig. 12 (Scheie and Jerome). Photomicrograph of section (×160) removed one week after operation showing well-marked episcleral "mantle" of fibrous tissue and an intermediate stage of healing with penetration of connective tissue core through necrotic sclera to underlying chorioretinal mass which itself shows atrophy and fibrous tissue formation. Note edema and early necrosis of surrounding retinal tissue.

VI. Discussion

The work reported herein was undertaken to determine the amount of scleral shrinking which could be produced by electrocoagulation of the sclera and to compare these results with those obtained by experimental scleral resection. A method for measuring the volume of an eye through a fluid-displacement technique was devised and found to be reasonably accurate. The work was done upon the dog eye because the sclera was thicker and more like that of man than was that of the rabbit.

Surface and puncture diathermy were used in different experiments. Surface diathermy produced marked shrinkage and puckering of the sclera at the site of application with rapid rise of intraocular pressure signifying reduction in volume. In enucleated eyes, the tension could be elevated to 70 mm. Hg, beyond which scleral ruptures would occur and the tension would rise no higher. These experiments confirmed the observations of several workers who had

noticed a similar rise in intraocular pressure during cyclodiathermy.

To ascertain the amount of volume change which could be produced, paracentesis of the anterior chamber had to be done permitting the sclera to shrink. Fourteen applications of a surface electrode which had a contact surface of one square mm. were used in all surface coagulation experiments. An average reduction of 0.96 cc. or 18.5 percent of the volume resulted in experiments on 10 enucleated dog eyes. This was approximately 0.25 cc. more than that produced by scleral resections of 4 by 22 mm. also performed on enucleated dog eyes. The same amount of coagulation on the living animal was somewhat less effective, the average reduction in volume being 0.64 cc. Subsequent experiments demonstrated that this volume change fell during the first 2 weeks to about 0.5 cc. or 9 percent, after which, during our observation period of 2 months, the volume remained unchanged.

The effect of electrocoagulation with the penetrating electrode was then studied. Thirty applications were used, which was felt to be within the range of at least some operations for the clinical treatment of retinal detachment. These eyes were studied and a reduction of about 6 percent in volume was found, about two thirds that of the reduction obtained by surface coagulation. Because a smaller total area of sclera was coagulated, the reduction in volume by penetrating diathermy was less than that produced by surface diathermy. Even so the amount was not insignificant.

An objection to these observations can immediately be raised, for it is certainly not a common observation that the refraction of an eye operated upon for retinal detachment undergoes a marked change in refraction toward the hyperopic side, as one might expect. This we are unable to rationalize, unless the change in volume results from a flattening of one side of the eye, rather than a shortening of the anteroposterior diameter. It does seem certain, however, that at least some degree of scleral shrinking is produced with every electrocoagulation operation for retinal detachment and suggests that further study ought to be done to devise more effective means of shortening by electrocoagulation. The present experiments tend to explain the advantages claimed for surface coagulation and possibly also serve as an argument for Langdon's[26] thermophore technique.

The pathologic studies carried out, in general, confirm those of previous observers. The sclera, choroid, and retina became edematous and engorged shortly after coagulation. The sclera had a coagulated appearance. Changes of acute inflammation presented, which in from 1 to 2 weeks transformed to a subacute appearance with mononuclear cells. Finally, fibroblasts proliferated throughout the area, and the sclera, choroid, and retina underwent atrophy in varying degrees.

Weekers's[22] work demonstrating a fibroblastic plug growing toward the choroid and retina through the opening in the sclera made by the penetrating electrode was confirmed. This seems of great importance since it causes the retina to adhere firmly to the choroid following such operations. Similar changes tend to occur following surface diathermy but the fibroblasts grow through necrotic sclera and hence the process takes place much more slowly, requiring 1 or 2 months. After using the penetrating technique, the plug can be seen as early as 1 week postoperatively.

The changes which occurred following surface diathermy, where the coagulation was more extensive and intense, were more severe than those following the penetrating technique. The engorgement of the retinal vessels, particularly in the nerve-fiber layer, was more marked. The appearance of these engorged vessels might well explain the common occurrence of preretinal and vitreous hemorrhage, seen clinically, following too heavy coagulation of the sclera.

The changes ensuing after surface dia-

thermy, where the volume changes were marked, were such that one would be hesitant to use this degree of coagulation clinically. Not only was the engorgement of vessels pronounced, but the final retinal atrophy was considerable, and, although the eyes were negative externally, their histologic appearance would counsel caution.

In conclusion, it can be stated that electrocoagulation is capable of producing a high degree of scleral shrinkage manifest by reduction in volume of the eye. This undoubtedly occurs to some degree in every operation for retinal detachment by the electrocoagulation technique.

Experimentally, surface diathermy produces more scleral shrinkage than penetrating diathermy, no doubt because a greater area of the sclera is affected. However, the pathologic changes resulting from surface coagulation are of such a severe nature that clinical application to the same extent would probably be inadvisable.

Further work should be done to devise a technique which would produce scleral shrinkage yet be less destructive to the underlying choroid and retina because there seems sufficient evidence to believe that reduction in volume of the scleral shell is of at least supplementary value in retinal detachment surgery.

VII. Summary

1. The value of scleral resection is discussed.

2. Surface electrocoagulation was found to produce a reduction in ocular volume in enucleated eyes and eyes in the living animal comparable to scleral resections of 4 by 22 mm. Penetrating electrocoagulation produced a smaller reduction in volume.

3. The reduction in ocular volume resulting from electrocoagulation persisted during the period of observation of 2 months

4. Electrocoagulation of the amount used in these experiments produced pathologic changes of such a nature as to suggest caution in its clinical use.

313 South 17th Street (3).

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DISCUSSION

DR. JONAS S. FRIEDENWALD (Baltimore, Maryland) : I think we are all familiar with the fact that, after successful detachment operations, the area of the fundus that has been cauterized is often visible with a higher plus lens than corresponding areas in other parts of the periphery, but in general the axial refraction is not significantly changed. I would like to ask Dr. Scheie, therefore, whether the contraction that he gets is not rather a flattening of the sclera at the point of cauterization than the general reduction in radius of the eyeball that one gets with the scleral resection.

DR. CONRAD BERENS (New York, New York) : I should like to ask Dr. Scheie whether he tried the Walker bident using the back part of it, not the points? We have thought that we got better shrinkage of the sclera by using the back of the Walker bident than by using the individual electrodes or the two points in contact with the sclera. It certainly seems to work out in practice that way, although scientifically I cannot say why shrinkage is greater than with two points introduced separately.

DR. DAVID G. COGAN (Boston, Massachusetts) : It is of interest to note that the white opacification of the retina from surface diathermy of the sclera is much more extensive during the diathermy than immediately following it. This suggests that the retinal opacification is not, as generally assumed, one of coagulation. With the diathermy applied to the sclera of an excised and bisected eye, it can be shown that the opacification is due, in some measure at least, to the formation of numerous bubbles in the retina, bubbles which, when massaged out, leave the retina transparent.

DR. SCHEIE (closing) : The question which Dr. Friedenwald raised occurred to us. We certainly haven't seen a marked degree of hyperopia occurring in our patients with operations for retinal detachment, and the only way to explain it is just as Dr. Friedenwald has. Marked flattening of one side rather than of the anteroposterior diameter of the eye can be seen in the slides of animal eyes.

In reply to Dr. Berens, we have not used the Walker bident.

INTRAOCULAR HEMORRHAGES IN YOUNG RATS ON CHOLINE-DEFICIENT DIETS[*]

J. LLOYD BURNS,[†] M.D., AND W. STANLEY HARTROFT,[‡] M.D.

Toronto, Ontario

Best and Huntsman (1932) demonstrated that choline or a precursor was essential in the diet of rats to prevent the accumulation of excess amounts of fat in the liver. Later, Griffith and Wade (1939) reported hemorrhagic degeneration of the kidneys of weanling rats deprived of dietary choline. The renal lesion was usually responsible for the animal's death within two weeks. These authors also noted intraocular hemorrhage in the animals whose kidneys were most severely affected.

Christensen (1940) stated that this intraocular hemorrhage occurred mainly from the blood vessels of the ciliary body and iris. Engel and Salmon (1941) reported that the hemorrhage "appeared to originate in the ciliary vessels and spread into the posterior chamber." They also demonstrated the presence of uremia in the rats by determinations of the levels of the nonprotein nitrogen in the blood, and by the xanthydrol reaction applied to sections of brain. All the foregoing investigators were interested primarily in the renal, rather than the ocular, lesions.

The first investigations concerned mainly with the ocular changes were those of Bellows and Chinn (1943). They found that 10 to 33 percent of their animals showed some type of ocular hemorrhage, usually within the 48 hours preceding death. The most frequent form was a column of blood in Cloquet's canal; the next, was a "hemorrhage apparently arising in the region of the ciliary body, and shortly spreading beyond the crystalline lens." Less commonly, hemorrhages visible to the naked eye appeared as hyphemia.

Microscopically, they noted that the vessels of the eyeball were generally engorged, and that the ciliary processes were swollen and frequently hemorrhagic. They found free blood most often between the anterior limiting membrane of the vitreous and the crystalline lens, and not uncommonly in the anterior chamber. Puppies on the same diet developed fatty livers, but hemorrhagic degeneration of the kidneys, eyes, and other organs did not occur.[§]

The present paper will deal with further observations regarding the intraocular hemorrhages occurring in weanling rats on diets low in choline, and after nephrectomy. The results are based on observations involving more than 350 albino rats of the Wistar strain.

METHODS

DIETS

Two diets were used. Diet A (Lucas; 1948) is extremely low in choline and its precursors, but is believed to be adequate in all other respects. Diet B (Lucas; 1948) is somewhat less deficient in lipotropic agents, but is believed to be adequate in all other respects except possibly in certain amino acids. This diet takes 1 to 2 days longer to produce its results in weanling rats than does diet A. The animals were fed these diets at pleasure in each instance.

EXAMINATIONS OF LIVING ANIMALS

A small percentage of the hemorrhages were visible to the naked eye in the form

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[§] Since this paper was prepared, these findings of Bellows and Chinn have been confirmed by Brückner, R., and Viollier, G.: Helvet. physiol. acta, 6:3, 1948.
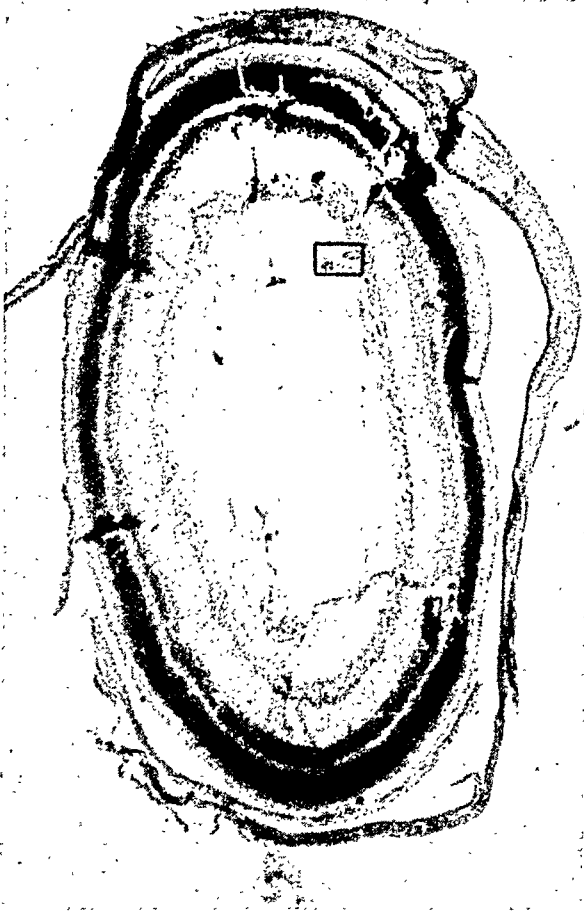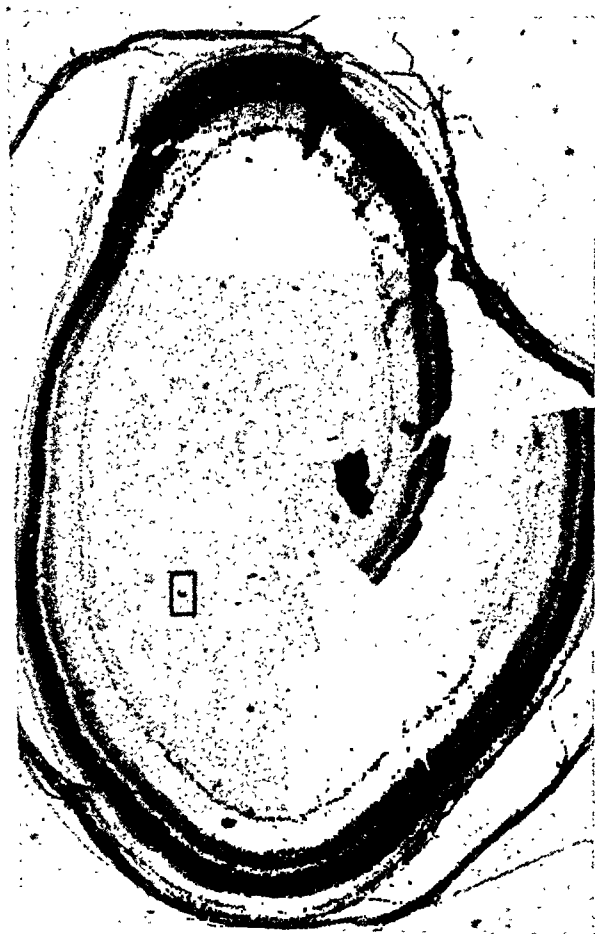
Fig. 1 (Burns and Hartroft). Section of one eye of a choline-deficient weanling rat, cut in plane No. 1 indicated in Figure 10. Masson trichrome stain (×35).

of hyphemia. A few additional ones could be seen with the aid of transillumination. However, the majority could be visualized only by means of the ophthalmoscope.

For this purpose, mydriasis was obtained by the instillation of 1 drop of 2-percent homatropine in each eye. When examinations were to be made at very frequent intervals, in an attempt to obtain greater duration of mydriasis and to reduce the number of instillations required, 1-percent atropine sulfate was substituted. This was not particularly successful as the rat possesses relatively enormous reserves of "atropinase." The mydriasis following instillation of 1 drop of 1-percent atropine rarely lasted for 2 hours.

At first, it was found necessary to anesthetize the animals in order to keep them suf-

ficiently still for satisfactory examination. Later, with increasing experience, it was possible to dispense with anesthesia in the young animals, especially those which were ill. For rats of 35 to 45 gm., 0.5 cc. of an 0.44-percent solution of sodium pentothal in saline was used.

POSTMORTEM EXAMINATIONS

a. Microsections

The whole eye was subjected to preliminary fixation in Bouin solution for approximately 4 to 6 hours. A small calotte was then removed from the equatorial region of the sclera, and fixation in Bouin solution continued for another 12 to 24 hours. The

Fig. 2 (Burns and Hartroft). High-power view of the marked square in Figure 1. This shows the main stem of the hyaloid system (upper left) and one of the main retinal arteries (lower right) at a point just anterior to their common origin from the central artery of the optic nerve.

tissues were dehydrated and cleared in ascending strengths of dioxane and embedded in paraffin.

In a preliminary experiment only random sections in the coronal or sagittal planes were prepared, but it was apparent from these that more information would be obtained from serial sections cut in the frontal plane.

Accordingly, such were prepared in subsequent experiments and over 10,000 individual sections of this type were studied. Masson's trichrome stain was used routinely, as this facilitates rapid detection of collections of red blood cells. Selected sections were also stained with hematoxylin and eosin. Additional eyes were sectioned with the freezing microtome following formalin-fixation, and stained with Sudan IV.

Fig. 4 (Burns and Hartroft). High-power view of marked square in Figure 3. This includes four branches of the hyaloid artery just distal to their origin. Note the small size and thin wall of the lowermost branch.

b. Whole mounts

1. Benzidine and benzyl benzoate. As a supplement to the study of cytologic detail by the above methods, the architectural patterns were established using whole mounts. For this purpose, the eyes were enucleated and as much as possible of the extrascleral tissue was removed. Fixation was in 5-percent formol-saline for 24 to 48 hours, a small equatorial calotte being removed. after the first·4 hours to aid penetration. This was followed by 6 to 12 hours' washing in tap water. The eyes were then treated with a modification of Ziegler's (1945) benzidine process for staining red blood cells. Clearing of the tissue was subsequently performed by a method already described by one of us (Hartroft; 1941).

Fig. 3 (Burns and Hartroft). Low-power view of one eye of a choline-deficient weanling rat, cut in plane No. 3 indicated in Figure 10.
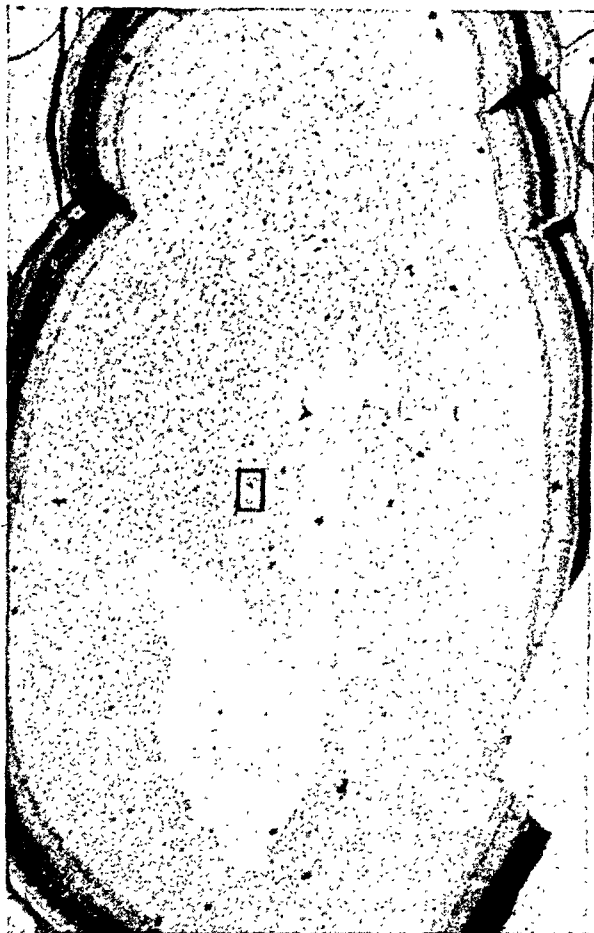
Fig. 5 (Burns and Hartroft). This illustrates an accumulation of fibrin and platelets (without red blood cells) surrounding a hyaloid vessel. (Plane No. 5 in Figure 10.)

The modifications of Ziegler's method were: (a) Shorter fixation period, (b) weaker formalin solution, (c) much longer period of washing, and (d) reduction of the strength of hydrogen peroxide in his solution "B" from 30 percent to 3 percent. This modified process produced less heavily stained specimens which were more satisfactory for photography.

2. *India ink and benzyl benzoate.* This method was used to study distribution and patency of the vascular system of the eye. The heparinized and anesthetized animal was perfused first with saline and then with a diluted, filtered, ammoniacal suspension of India ink.* The eyes were subsequently fixed, dehydrated, and cleared as above. All

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* Higgins American India ink.

whole mounts were immersed in benzyl benzoate and examined under the binocular dissecting microscope.

EXPERIMENTS

In a preliminary experiment, 20 rats weighing 36 to 42 gm. were fed diet A. They were examined daily by ophthalmoscope. After they died or were killed, random sections of their eyes were prepared.

In the next experiment, 63 animals of similar weights were placed on the same diet and similarly examined except that the eyes were sectioned serially in the frontal plane. Some of those eyes which had shown no evidence of hemorrhage ophthalmoscopically were prepared as whole mounts following benzidine staining.

An additional group of 81 weanling rats were fed diet B and ophthalmoscopic exami-
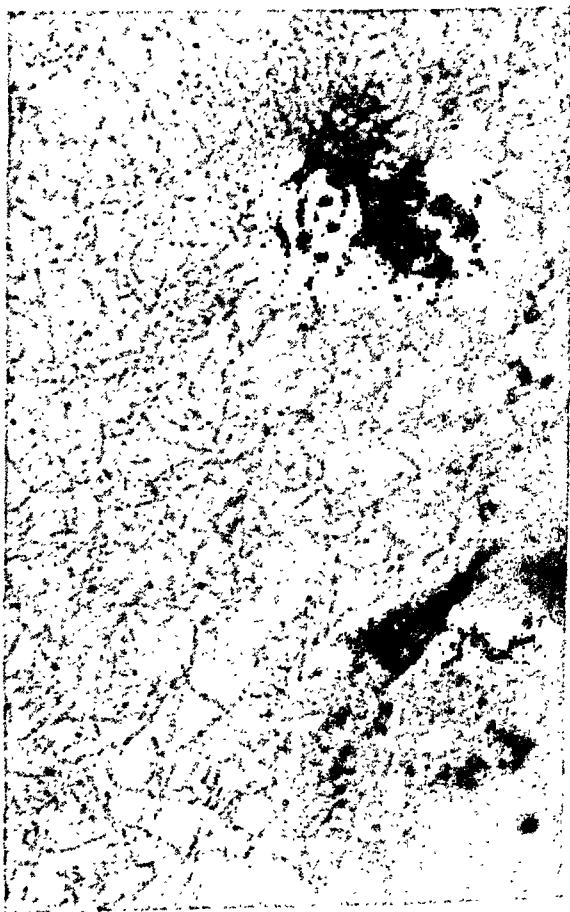
Fig. 6 (Burns and Hartroft). High-power view of marked square in Figure 5.

nations were carried out at appropriate intervals.

To study the possible relation between renal function and this particular form of intraocular hemorrhage, 20 weanling rats were rendered uremic by another means, namely bilateral nephrectomy. Ophthalmoscopic examination was carried out at frequent intervals. The eyes of two animals were serially sectioned for comparison with those of choline-deficient rats and the remaining eyes prepared as benzidine-stained whole mounts.

A group of 20 young adult rats (145-172 gm.) were fed diet A and examined ophthalmoscopically at biweekly intervals over a period of 4½ months. Twenty similar rats were bilaterally nephrectomized and ex-

Fig. 8 (Burns and Hartroft). High-power view of marked square in Figure 7. This shows the hyaloid artery near the posterior pole of the lens surrounded by fibrin and platelets with an adjacent large area of hemorrhage.

Fig. 7 (Burns and Hartroft). The darkly stained central structure is a tangential section of the crystalline lens near its posterior pole. (Plane No. 7 in Figure 10.)

amined frequently by ophthalmoscope. Seventeen comparable normal animals and three weighing 400 to 450 gm. were perfused with India ink and the eyes prepared as unstained whole mounts.

To investigate the possible correlation between ocular hemorrhages and blood levels of N.P.N. in the choline-deficient weanling rats, 30 animals were fed diet A. These were examined ophthalmoscopically at intervals during the first 5 days and daily thereafter. Samples of tail blood were taken at the same times for estimation of nonprotein nitrogen.

Thirteen weanling rats were placed on diet A and a similar group on diet B. Ophthalmoscopic examination was performed daily during the first 4 days and more frequently

thereafter. The nonprotein nitrogen level in the blood of each animal was determined as soon as ocular hemorrhage was noted.

Finally, 11 weanling animals were bilaterally nephrectomized and examined ophthalmoscopically at frequent intervals. Whenever an intraocular hemorrhage was noted, the level of the nonprotein nitrogen was determined.

ratio varying from 1:1 to 3:1 in various groups.

B. Site and morphology. Almost all of the hemorrhages noted in the foregoing experiments were in the vitreous humor or between it and the crystalline lens. An exception was the retinal hemorrhage shown in Figure 9, which occurred in an animal fed diet A.
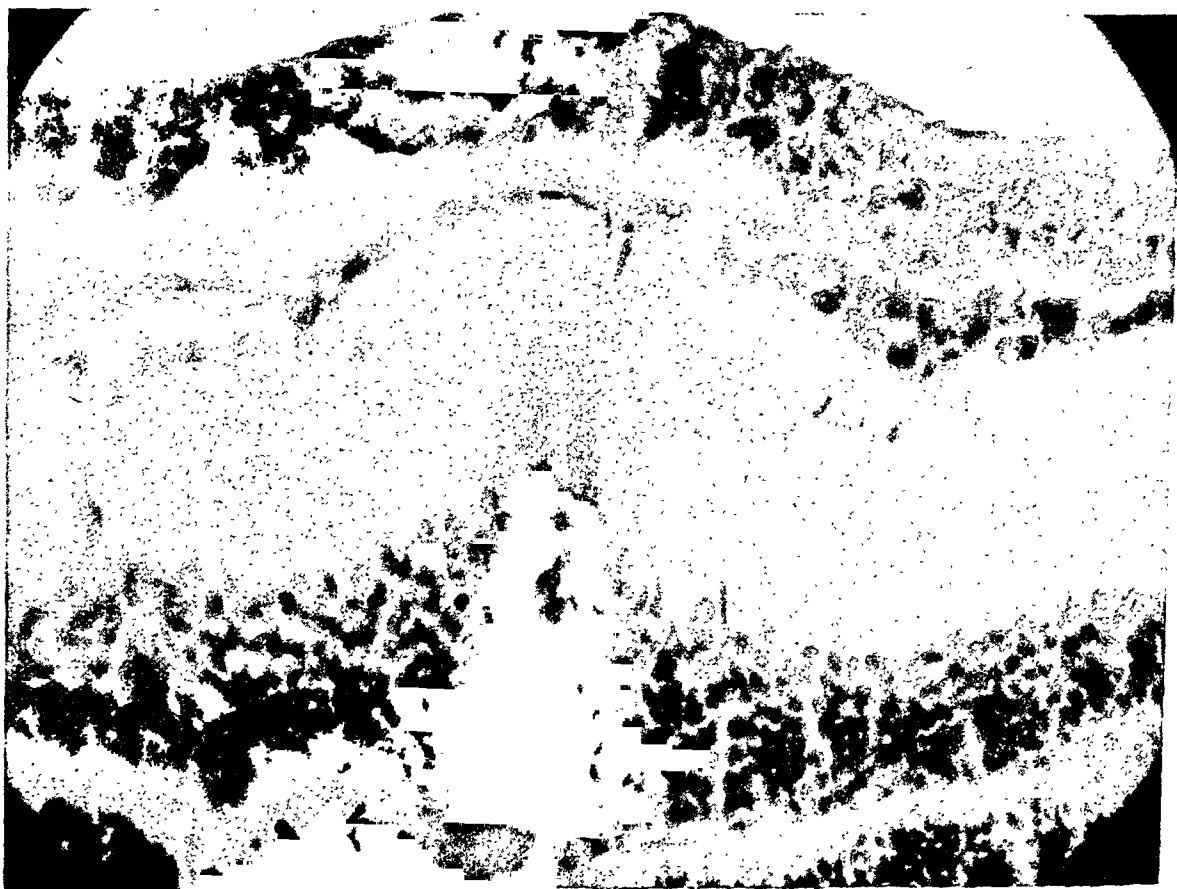
Fig. 9 (Burns and Hartroft). This demonstrates a superficial retinal hemorrhage (top) in a weanling rat fed diet A for seven days. This was the rarest situation in which these intraocular hemorrhages were observed. All others were found around branches of the hyaloid artery. See Figures 1 to 8. (Hematoxylin and eosin stain. ×375).

RESULTS

A. Incidence. In the various dietary experiments, intraocular hemorrhage occurred in one or both eyes of 35 percent to 85 percent of the animals. The difference in the two diets employed did not significantly affect the incidence; nor did the sex, although the females showed a tendency to greater susceptibility than the males, the

A hyaloid arterial system was found in each of the 75 eyes which were serially sectioned. The hyaloid vessels can usually be seen ophthalmoscopically, and in normal eyes they appear as slightly irregular, highly refractile lines. In the hemorrhagic eyes they are surrounded for considerable portions of their lengths by a granular, pale-red sheath (stereoscopic fig. 11). Larger areas of hem-

orrhage are seen as rather "fluffy" enlargements of this sheath, varying greatly in size and density (stereoscopic fig. 12).

Microscopically, also, the commonest site of hemorrhage was between the vitreous and the crystalline lens. The blood and the ac-

C. *Hemorrhage following nephrectomy.* Sixteen of 20 weanling rats (80 percent) suffered hemorrhage in one or both eyes following bilateral nephrectomy. Only 3 of 23 eyes with patent hyaloid arteries were free from hemorrhage. Collections of red cells
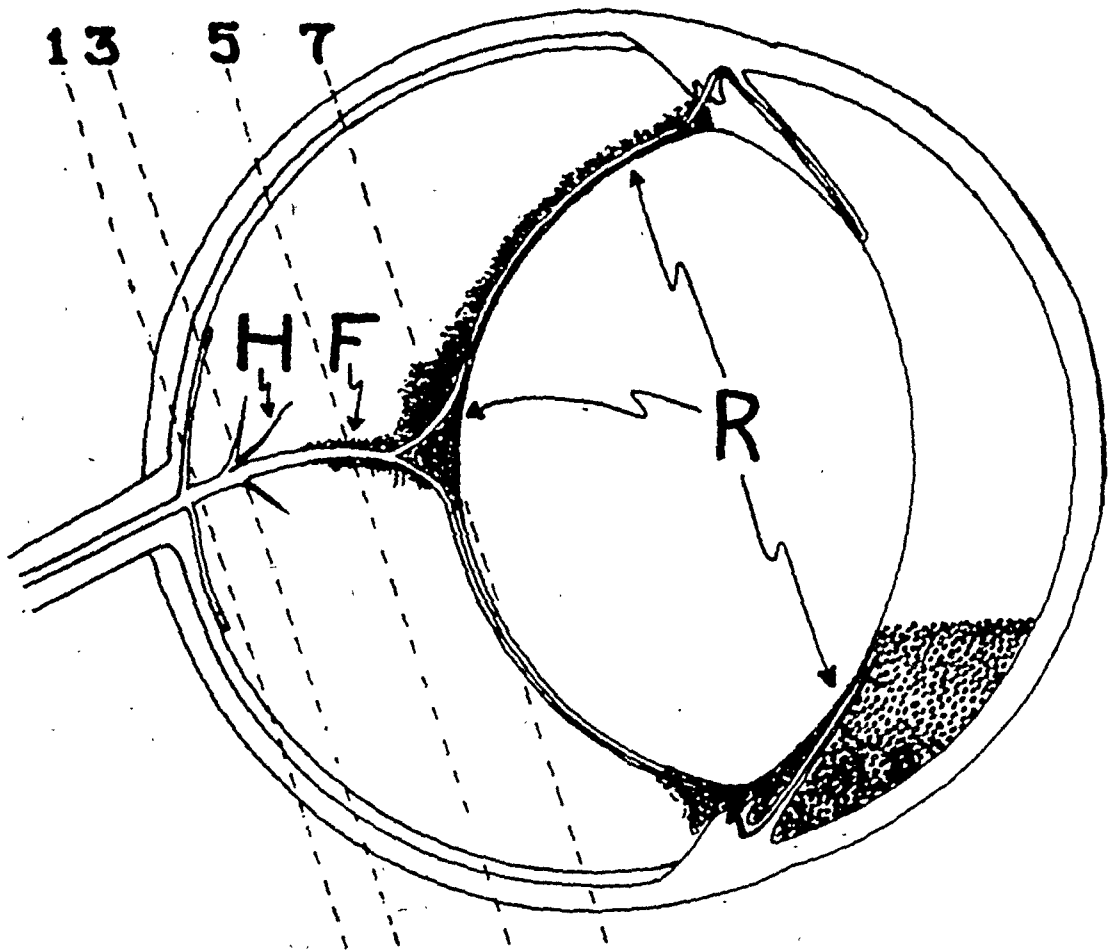
Fig. 10 (Burns and Hartroft). This is a two-dimension, graphic reconstruction of the eye illustrated in Figures 1 to 8. An additional hemorrhage has been shown originating in the ciliary region and extending into the anterior chamber with resultant hyphemia. (H) Hyaloid artery. (F) Fibrin and platelets (without red blood cells). (R) Red blood cells with fibrin and platelets. The dotted lines indicate the planes of the sections illustrated in the correspondingly numbered photomicrographs (figs. 1, 3, 5, and 7).

companying fibrin lay, in almost every case, around the hyaloid artery, or one or more of its branches. In a few cases there were extensions of blood to the ciliary region, and around the lens into the aqueous chambers. Occasionally, hemorrhages limited to the ciliary region were found. In 13 eyes of 10 animals fibrin and platelets without red blood cells were seen adjacent to the hyaloid vessels (fig. 1 to 8 and fig. 10).

could not be demonstrated in any of the eyes without functional hyaloid arteries. Those hemorrhages present were ophthalmoscopically and microscopically identical with those seen in the animals on choline-deficient diets (stereoscopic fig. 13).

D. *Older animals.* Animals, 150 to 170 gm. in weight, fed diet A for 4½ months, did not develop ocular hemorrhages; nor did those which were bilaterally nephrecto-
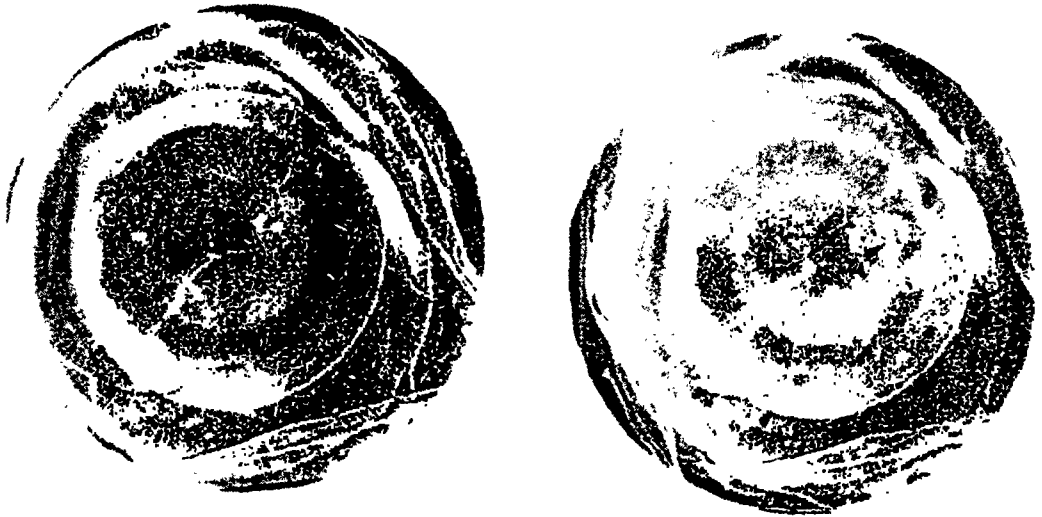
Fig. 11 (Burns and Hartroft). Stereoscopic photomicrograph (×12). This shows an eye from a choline-deficient weanling rat viewed through the pupil. Note the granular sheathing of the hyaloid vessels (lower left and upper right).

mized but fed normal diets. However, examination of the whole mounts from the latter experiment indicated that although the hyaloid artery was present in most of the eyes, it was usually nonpatent. This was confirmed by the India-ink injections, for in only 1 of the 40 eyes examined was any indication of patency found. Even this was limited to a relatively short portion of one of the smaller branches.

E. N.P.N. experiments. Of the first group of animals in which the blood levels of

Fig. 12 (Burns and Hartroft). Stereoscopic photomicrograph (×12). This demonstrates, in a similar specimen to that of Figure 11, a small hemorrhage at the left near the periphery of the lens. A hyaloid vessel can be seen passing across the posterior surface of the lens, through the area of hemorrhage and beyond it to the ciliary body. This view is taken obliquely from behind.

N.P.N. were followed from day to day, 20 (67 percent) developed intraocular hemorrhage in one or both eyes. In 4 of these, the level of nonprotein nitrogen in the blood was within or near normal limits at the time the hemorrhage was first discovered.

In the others it was moderately to markedly increased, but there was no consistency in the levels at which hemorrhage appeared. The hemorrhages which were

nonprotein nitrogen levels in the blood of 3 of these were normal or nearly normal, while those of the remainder were moderately or markedly elevated.

In the bilaterally nephrectomized group, 5 of the 11 (45 percent) weanling rats developed intraocular hemorrhage. In every case the nonprotein nitrogen level in the blood was markedly increased at the time the hemorrhage was discovered.

Fig. 13 (Burns and Hartroft). Stereoscopic photomicrograph (×12). This depicts two hyaloid vessels, each with a small hemorrhage in an eye from a bilaterally nephrectomized weanling rat fed a normal diet. Note the close resemblance of this lesion to those illustrated in Figures 11 and 12 showing hemorrhages in choline-deficient animals. The photographs were taken through the posterior pole.

found in the presence of normal blood levels of N.P.N. occurred on the 4th to 7th days of the experiment. Hemorrhages found in animals with increased concentrations of N.P.N. in the blood occurred on or after the 7th day. The pattern of the N.P.N.-time curve was essentially the same in all animals regardless of the time of hemorrhage. A typical example is illustrated in Graph 1.

In the second group consisting of 13 animals fed each diet (A and B), no essential differences were noted, except that elevation of the blood N.P.N. did not occur as soon in animals fed diet B as those fed diet A. Seventeen of the 26 animals (65 percent) developed intraocular hemorrhages. The

DISCUSSION

There is strong evidence in the foregoing results to show that the intraocular hemorrhage occurring in weanling rats, both on choline-deficient diets and following bilateral nephrectomy, originates from the hyaloid arterial system. Hemorrhages limited to the ciliary region are considered to have originated from the more peripheral portions of the branches of the hyaloid artery, rather than from the vessels within the ciliary body. The capillary dimensions of hyaloid vessels make their detection difficult, especially in the peripheral portions. This difficulty is increased if large amounts of fibrin and blood surround them.

Blood in all the locations mentioned by previous investigators and confirmed by us can be explained on the basis of hemorrhage originating from the hyaloid system. The only exception is the rare retinal hemorrhage. The hyaloid vessels are unusual, for although of the order of arterioles in their position in the vascular tree, their structure resembles that of capillaries. The thin walls, suggests that choline deficiency produces intraocular hemorrhages in weanling rats through the medium of the renal lesions.

Although older rats have frequently been fed choline-deficient diets, no case of intraocular hemorrhage has been reported in such animals and we have found none. Adult rats on a choline-deficient diet do not develop such severe and fulminating renal lesions
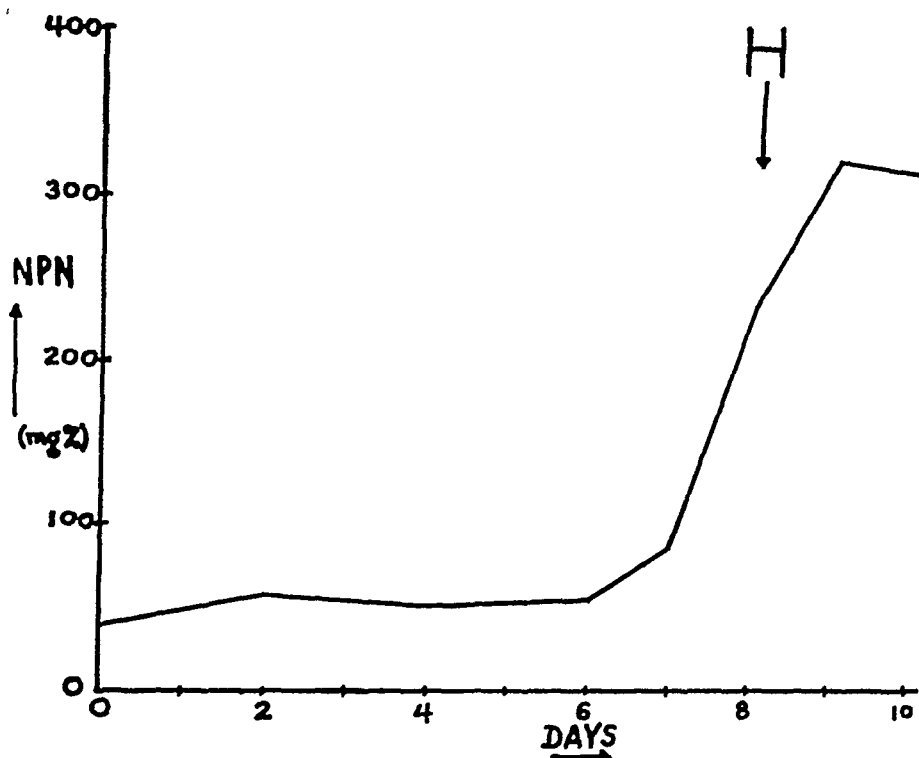
Graph 1 (Burns and Hartroft). This is a typical example of the graphs obtained by plotting the N.P.N. levels of the blood against the number of days weanling rats were fed diet A. (H) indicates the time intraocular hemorrhage was first noted.

subjected to arteriolar pressures and supported only by the vitreous, would appear to be uniquely susceptible to hemorrhage.

The distribution of the extravasated blood extending along the vessels and the presence of fibrin and platelets without red blood cells, in some situations, suggest diapedesis, rather than actual interruption of the continuity of the vessel wall in the early stages. The later formation of "fluffy" hemorrhages may be associated with actual rupture of the vessel wall.

The occurrence of morphologically identical hemorrhages in bilaterally nephrectomized animals on normal diets strongly as do the weanlings. The lack of patency of the hyaloid arteries appeared to be the probable reason why the older animals did not develop intraocular hemorrhage following bilateral nephrectomy. The failure of such animals to develop the hemorrhages on the choline-deficient diet could thus be explained in either of two ways; (1) On the basis of insufficient interference with renal function, and (2) By the lack of patency of the hyaloid arteries.

The occurrence of ocular hemorrhages in 7 animals with normal levels of nonprotein nitrogen in the blood appears to contradict the theory that the hemorrhages are asso-

ciated with renal dysfunction. It must be remembered, however, that determinations of blood N.P.N. levels measure only one aspect of renal function. Histologic evidence of incipient renal damage in such rats has been detected as early as the second day of the experiment (Hartroft; 1948). It is therefore obvious that more detailed studies of all aspects of renal function in these animals must be carried out before suggesting that the ocular hemorrhages may sometimes be unrelated to kidney damage.

The use of nephrectomized weanling rats possessing patent hyaloid arteries, so uniquely susceptible to hemorrhage, may prove of considerable value in investigations of the important relationship between renal dysfunction and ocular changes.

SUMMARY AND CONCLUSIONS

1. Confirming the work of previous investigators, ocular hemorrhages were found in weanling rats deprived of dietary choline. The incidence in our experiments varied from 35 percent to 85 percent of the animals, nearly all of which developed severe renal lesions.

2. All the hemorrhages but one (from the retina) in 209 eyes arose from the hyaloid arterial system. The mechanism appeared to be that of diapedesis rather than rhexis, at least in the early stages.

3. Morphologically identical hemorrhages were observed in bilaterally nephrectomized rats of the same age.

4. Neither deprivation of choline nor bilateral nephrectomy produced intraocular hemorrhages in older rats. Such rats do not develop such severe renal lesions on the choline-deficient diets, nor are their hyaloid arteries usually patent.

5. Of weanling rats whose blood levels of N.P.N. were determined at the time of occurrence of intraocular hemorrhage, 81 percent showed evidence of uremia. The remainder (7 rats) had intraocular hemorrhages in the presence of normal levels of nonprotein nitrogen in the blood.

6. Much of the evidence presented here suggests that the occurrence of intraocular hemorrhages in choline-deficient weanling rats is closely related to the coexistent, extensive renal damage.

695 Broadview Avenue.

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DISCUSSION

DR. A. B. REESE (New York City): Mr. Chairman, I know of one instance in which a severe vitreous hemorrhage occurred in an infant from a persistent hyaloid artery. The

question arose as to whether or not the condition was an intraocular tumor. It was elected to temporize, the hemorrhage absorbed, and the persistent hyaloid artery could be seen. We have a globe removed with the clinical diagnosis of tumor and microscopically no tumor was found. Instead, there was a massive vitreous hemorrhage from a persistent hyaloid artery.

DR. DAVID G. COGAN (Boston, Massachusetts): It seems to me that Dr. Kinsey's studies on the blood-aqueous barrier of young rabbits bears on the essayist's observations. Using ascorbic-acid transfer as an index, Dr. Kinsey found there was a much freer communication between the blood and aqueous humor when the hyaloid system was present than after its resolution.

DR. PARKER HEATH (Boston, Massachusetts): I would like to ask a question, if any of these animals were carried on to their ultimate conclusion, what happened to the hemorrhage? If there was a large volume of hemorrhage, what happened to the eyes?

DR. JONAS S. FRIEDENWALD (Baltimore, Maryland): I am very glad to hear from Dr. Reese that he has seen an actual case of intraocular hemorrhage arising from the hyaloid vessels.

I can't agree with Dr. Burns that the peculiar anatomy of the hyaloid system renders it abnormally susceptible to hemorrhage, at least not in human beings. In a large series of ours from stillborn human beings, we have found intraocular hemorrhages of various sizes in something like 20 percent of the routine sections.

Those hemorrhages have been almost exclusively in the retina and choroid, and out of several hundred cases I have yet to find a hemorrhage arising from a hyaloid system so that as compared with the other vessels in the eye, the hyaloid vessels do not break as easily under the stress of labor, in prematurity as do the other intraocular vessels.

DR. BURNS (closing): Dr. Reese's observations are very interesting to me. I haven't made much of an effort to correlate our findings with those in man. That ties in probably with what Dr. Friedenwald was saying. I don't know, but I would like to know, if, in the eyes Dr. Friedenwald was mentioning, the hyaloid arteries were patent.

DR. FRIEDENWALD: These were premature stillborns with hyaloid arteries.

DR. BURNS: I see. In these rats, as I mentioned, the hyaloid artery does persist into adult life but it is not patent and we felt that if it had been patent, bilateral nephrectomy would have caused intraocular hemorrhage.

As for the question about the ascorbic-acid transfer, I am afraid I am not a nutritionist and whatever I have included in the paper on nutrition has been second-hand from the experts in our department; so I can't make any further comment on that.

Regarding the ultimate fate of these animals, weanling rats on these choline-deficient diets die in from 7 to 10 to 12 days, depending on various factors. There are a few survivors. We had, out of 63 animals, 4 survivors in one experiment, if I remember the figure. Those animals had no intraocular hemorrhage.

Adult rats, if they are fed choline-deficient diets for a prolonged period, will survive for many months. They do have renal lesions but these renal lesions occur more slowly than in the weanlings, and there is apparently time for a repair process to take place, which means that they don't die from the renal lesions. They do, however, go on to cirrhosis of the liver from the piling up of fat there.

I don't know just how long they will survive, if nothing is done except feeding of choline-deficient diets. Dr. Hartroft has been doing some very interesting experiments, in which he has fed weanling rats diets deficient in choline for a period which, as closely as he could judge, was sufficient to produce renal damage of a very severe degree, but not quite enough to produce death; and subsequently switched them to normal diets and allowed them to grow to maturity. A great many of these animals developed hyperten-

sion when they became mature, especially in the case of females who became pregnant.*

We did find one animal in which I had examined the eyes ophthalmoscopically while it was on a choline-deficient diet, and it did have a fairly large hemorrhage in one eye, and that animal was allowed to survive; some three months later I examined the

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*These findings have now been published. Hartroft, W. S., and Best, C. H.: Hypertension of renal origin in rats following less than one week of choline deficiency in early life. Brit. M. J., 1, 423 (Mar.) 1949.

same animal and found that hemorrhage was still present, although it had been absorbed to some extent, and there was a considerable amount of scarring present in the vitreous.

In the weanling rats, over short-time observations, that is from the time the hemorrhage occurred until the animal died, there was evidence that the hemorrhage was absorbed, particularly in the case of small hemorrhages. I couldn't say whether the larger hemorrhages were partially absorbed or not.

THE FATE OF TRANSPLANTED CILIARY-BODY TISSUE*

EDWARD P. DANFORTH, M.D.
New York

The capacity of some types of tissue to survive when transplanted has brought about a considerable amount of experimental investigation and speculation. The object of this paper is to report in detail the results of transplanting pieces of normal, adult, homologous ciliary-body tissue in the rabbit. Sections were transplanted in the anterior chamber, under the bulbar conjunctiva, and subcutaneously. Histologic sections were made at periodic intervals and will be described subsequently.

One of the most spectacular workers in the field of tissue transplants was Voronoff[1] who attempted to prolong life and restore vital energy by transplanting testicular tissue experimentally in rams. He tried various locations in which to place his transplants: under the skin, intraperitoneally, and finally found the tunica vaginalis in the scrotum to be the most favorable site.

Voronoff made observations showing that

the youthful behavior of the old rams correlated with the histologic changes in the biopsies of the transplanted tissue. He noted that the seminiferous tubules of the graft continued for some time to form spermatozoa but that, little by little, the epithelium degenerated, the cells becoming changed into a syncytium containing numerous nuclei which filled the lumen of the tubules. This syncytium was then transformed, starting at the basement membrane, into a reticulated tissue. Depending on the size of the graft, these changes took place over a period of about 18 months. The significance of reporting Voronoff's work will be noted in the investigation which is to follow.

EXPERIMENTAL PROCEDURE

Two rabbits were anesthetized with 0.75 cc. of sodium pentothal (60 mg. per cc.) intravenously. The eyes to be operated were irrigated with zephiran (1:5,000).

Donor rabbit No. 1. An extensive corneal section was made at the limbus and following removal of the lens the iris and ciliary body were removed in toto and placed in a sterile petri dish containing normal saline. Under loupe magnification the ciliary body was easily separated from the iris. A small
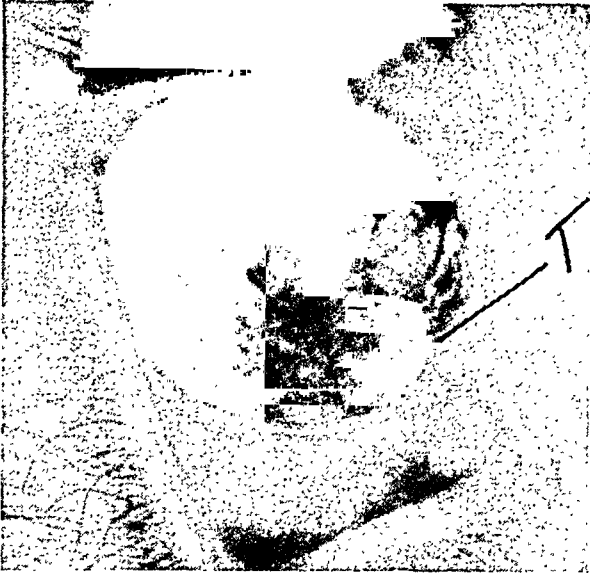
Fig. 1 (Danforth). Photograph of anterior chamber taken at the end of one month showing transplant attached to iris.

Fig. 2 (Danforth). Photomicrograph of normal rabbit ciliary-body tissue.

transplant, 2 by 3 mm., was then cut from this donor tissue.

Recipient rabbit No. 1. A conjunctival flap was made at the 11-o'clock position, followed by a keratome incision through the cornea. The prepared transplant tissue was then introduced into the anterior chamber by manipulating it with iris forceps and an iris spatula. The conjunctival flap was then closed.

Observations. A small amount of hemorrhage in the anterior chamber was noted immediately following the above procedure. This cleared on the third day and at the end of the week the transplanted tissue had moved to the 12-o'clock meridian and appeared to be floating free in the anterior chamber. On the ninth day the tissue appeared to be attached to the anterior surface

Fig. 3 (Danforth). Photomicrograph of section of transplant showing viable tissue with dilated capillaries, migration of pigment through stroma, and beginning atrophy of epithelial cells.

of the iris and was developing a pinkish, translucent color.

At the end of a month an iridectomy was performed removing the section of iris with the transplant for histologic study (figs. 1, 2, and 3).

Donor ciliary body tissue was again prepared as before. This time 0.1 of a unit of curare was added to the sodium pentothal, as advocated by Kirby and Hughson.[2] This practically eliminated the "whipping" which is apt to occur during the excitement stage, and from which one of the previous rabbits was lost from a broken back.

Pieces of ciliary-body tissue were then placed into the anterior chambers of four rabbit eyes in the same manner as previously described, except they were placed in different locations in the anterior chamber, two of them being placed over the pupillary area. A transplant was also made under the
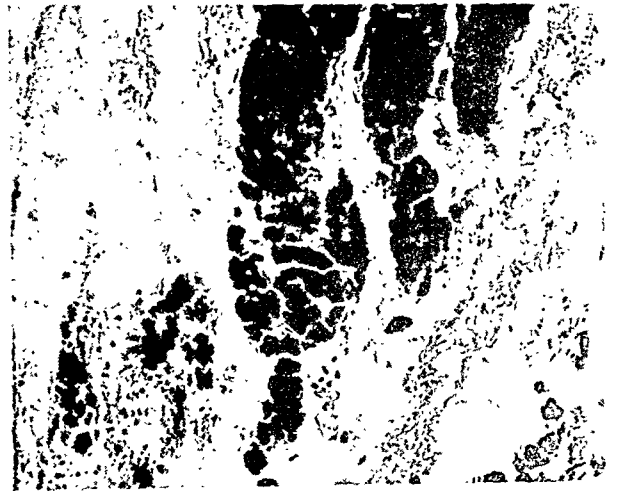
Fig. 4 (Danforth). Photomicrograph of section of subconjunctival transplant after one month, showing disintegration of transplant tissue with a few remnants of pigment.

bulbar conjunctiva and subcutaneously in one rabbit.

Observations of the transplants in the anterior chamber were the same as in the ini-
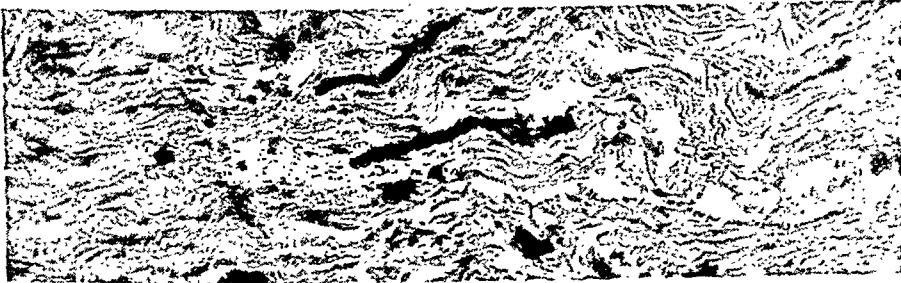
Fig. 5 (Danforth). Photomicrograph of subcutaneous transplant. There is almost complete dissolution of tissue.
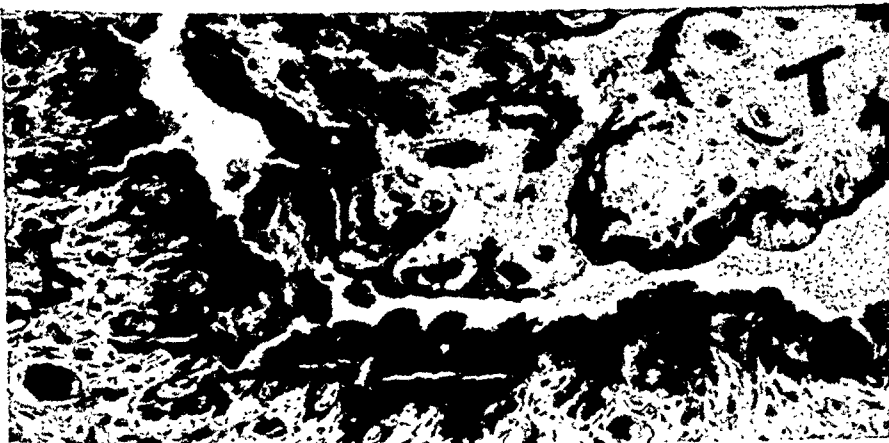
Fig. 6 (Danforth). Photomicrograph of transplant (T) in anterior chamber after two months. The tissue is still viable. There is wider dilatation of the capillaries and further atrophy of epithelial cells. (I) iris.
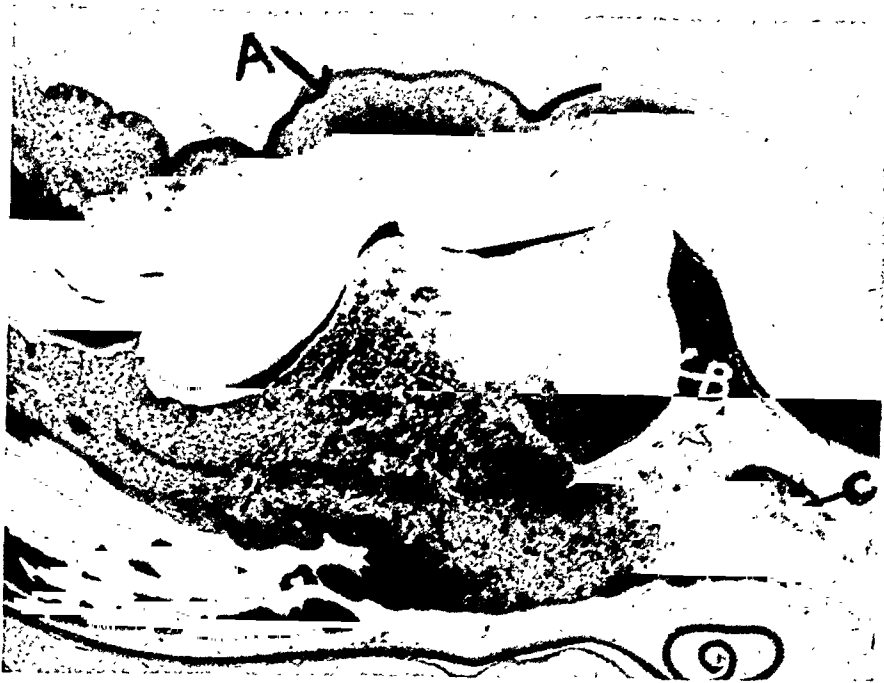
Fig. 7 (Danforth). Photomicrograph of section at six months shows: (A) Cornea, (B) transplant, (C) iris. Section reveals (1) Transplant is attached to iris; (2) there is local dilatation of vessels of the iris in the region of the transplant; (3) only a few attenuated capillaries in the transplant which are nearly empty of blood; (4) cells have nearly lost their identity, appear like a syncytium; (5) epithelial cells can no longer be identified.
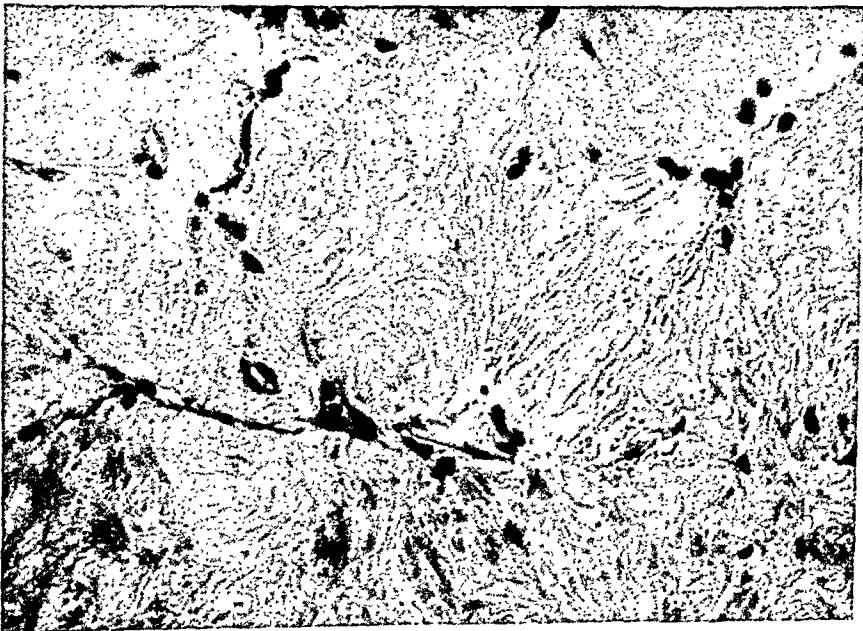
Fig. 8 (Danforth). High-power photomicrograph of the transplant in Figure 7.

tial recipient rabbit. It was noted, however, that during the first week there was a migration of the transplants placed over the pupillary areas to the anterior surface of the iris. They all appeared pink and viable by the 8th to 9th day.

At the end of a month a biopsy was made in the region of the transplants, which were under the skin and conjunctiva. Iridectomies were performed, removing for histologic study a segment of iris and attached ciliary body tissue at the end of 2 months, 5 months, and 6 months (figs. 4, 5, 6, 7, and 8). From the 2nd month until the 6th month there appeared to be a gradual shrinkage and increasing pallor of the transplants on gross inspection.

Discussion

Strangely enough the anterior chamber of the eye as a site for tissue transplants has been extensively exploited, not by ophthalmologists, but by cancer research workers. Greene,[3] whose extensive and painstaking work has been so well summarized by Blake,[4] found that not only was the anterior chamber of the eye the only place where he could cause malignant tissue transplants to survive but that the cornea acted as a window so that he could study the transplants under magnification at any desired interval without disturbing the transplant. He was mainly interested in finding a laboratory animal in which he could grow human cancer tissue and he found that malignant-tumor tissue would not only survive, but that it could be retransplanted in such animals as the rabbit or guinea pig.

Greene also reported that human embryonic tissue would survive and grow in the anterior chamber of the eyes of these animals but that benign-tumor tissue and, with the exception of skin and cartilage, normal-adult tissue would not survive. He also tried transplanting tissue sections from the various endocrine glands and met with constant failure.

We recently transplanted a small piece of tissue from a retinoblastoma into the anterior chamber of a rabbit which failed to survive. There is, however, a very good possibility that the tissue we received was necrotic before removal.

It would be logical to reason that the present work being done by transplanting pieces of placental tissue subcutaneously as advocated by Filatov[5] could have but the same fate as the gonad transplants of Voronoff and the ciliary body. However, there could well be absorption of products during disintegration of these transplants, as was the case with Voronoff's rams, which, by repeated transplants at proper intervals, would make this procedure worth while.

Summary

1. Sections of ciliary-body tissue from the rabbit were transplanted into the anterior chamber, subcutaneously and subconjunctivally, of another rabbit.

2. Periodic histologic sections were taken of the transplants in the anterior chamber up to a period of 6 months for study.

3. Biopsies were taken of the tissue transplanted subconjunctivally and subcutaneously after a period of one month which showed nearly complete absorption of transplanted tissue.

4. In the transplanted tissue in the anterior chamber there was attachment to the iris formed in about a week with dilatation of the capillaries. There was, however, a progressive atrophy of the epithelial tissue and stroma until finally the whole mass appeared to be replaced by a fibrous tissue-appearing syncytium.

5. These observations confirm the work of Voronoff and Greene on the failure of normal, adult, homologous tissue of this type to survive when transplanted.

780 Park Avenue (21).

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EFFECTS OF TESTICULAR EXTRACT ON CERTAIN OCULAR STRUCTURES*

R. K. MacDonald,† M.D.
Toronto, Ontario

INTRODUCTION

Morphologists have appreciated for many years that the fibrous intercellular substances of connective tissue (collagenic, reticular, and elastic fibers) are associated in many parts of the body with nonfibrous jellylike materials. Moreover, they have appreciated that these jellylike materials, commonly called ground or cement substances, are relatively abundant in the tissues of the fetus, and that aging is associated with a decrease in the ratio of jellylike types to fibrous types.

In general, however, the nonfibrous intercellular substances have received little attention and it is only since the relatively recent researchers of Meyer and his associates that they have come to be viewed in a proper perspective. It has become apparent that, in general, the so-called ground or cement substances are mucopolysaccharides—substances of great molecular weight.[1] What is generally termed ground substance is a nonsulphated type of mucopolysaccharide, called *hyaluronic acid*,[2] a composite word from hyaline, meaning glassy or clear, and glucuronic acid of which it is partly composed. Many of the so-called cement substances are sulfated types of mucopolysaccharide.[1]

In sections, the two types may usually be differentiated from one another by their staining reaction with metachromatic dyes.[3] The sulfated types usually take on a different color from that of the dye, for example with toluidene blue they become colored purple or red.

The physical state, and hence the fluidity, of hyaluronic acid differs in different parts of the body. That of the aqueous humor is 95 percent depolymerized.[1] That of ordinary connective tissue, however, is probably highly polymerized and jellylike in consistency. The sulfated mucopolysaccharides commonly exist in the body as firm gels of which the hyaluronic acid sulfate of the cornea and the chondroitin sulfuric acid of cartilage are examples.[1]

Meyer has shown that testicular extracts contain an enzyme that brings about the depolymerization of hyaluronic acid.[1] Hence it has been termed *hyaluronidase*. Either this or other enzymes associated with it in testicular extracts effect the breakdown of sulfated mucopolysaccharides also, but this reaction occurs relatively slowly.[4]

The depolymerization of hyaluronic acid by hyaluronidase affects both its diffusibility and its osmotic pressure. Since the hyaluronic acid of the aqueous is largely depolymerized, and since hyaluronidase has been recovered from macerations of iris and ciliary body[5] and from aqueous,[6] it might be suspected that some normal mechanism operates in the eye both to produce and depolymerize hyaluronic acid. Accordingly, it was thought of interest to investigate the effects on the eye of giving large amounts of hyaluronidase to animals over considerable periods of time.

METHODS

Testicular extract was prepared by the method first described by Madinaveitia.[7] A 50-percent to 100-percent fraction was diluted to 60 turbidity reducing units per cc., sterilized by Seitz filtration, bottled, and refrigerated until used.

One cc. was injected into each of four

6-month-old rabbits and four 2-year-old guinea pigs, twice daily, both intraperitoneally and subcutaneously, for from 20 to 55 days. Two of the guinea pigs and one rabbit given 55 daily injections were allowed a 30-day recovery period before being killed; the others were all killed the morning after their last injection. Eyes were enucleated just before the animals died from ether anesthesia.

Each eye was immersed in formol-saline for 5 minutes in order to harden it slightly before a window was cut in its cornea and sclera to permit of more rapid fixation. After 24-hours' fixation the eyes were dehydrated and embedded in paraffin. Alternate sections were stained with hematoxylin and eosin and with toluidene blue.

In addition to the foregoing material some sections were obtained from normal eyes that were subjected to the action of testicular extract after death as follows:

Two 6-week-old rabbits were killed with ether. A very small opening was then cut in the cornea of each eye. A hypodermic needle was then passed through the sclera near the limbus into the posterior chamber and 2 cc. of testicular extract were slowly perfused under slight pressure into one eye of each animal, great care being taken not to dislocate the lens. Boiled testicular extract was similarly injected into the other eye of each animal. After 30 minutes at room temperature, the eyes were enucleated and sectioned in the same manner as the others.

Observations

The chief morphologic changes that occurred in the experimental animals were found in their anterior ciliary processes. These structures in the normal rabbit are, according to our observations, of two general types, which differ from each other chiefly by the extent and character of their stroma.

Those of the first type are stout (fig. 1) and possess an abundant content of a primitive type of connective tissue which con-

tains star-shaped cells, widely separated by an intercellular substance which stains only very faintly with eosin and is not metachromatic with toluidene blue.

The second type of anterior ciliary process is thin and contains only a scanty amount of a more condensed type of intercellular

Fig. 1 (MacDonald). Normal anterior ciliary process of the stout type in the rabbit. Note the watery nature of the intercellular substance.

substance which stains with eosin, and is metachromatic with toluidene blue.

In sections of the eyes that were injected with testicular extract after death, the most striking change is that the intercellular substance of the stout variety of anterior ciliary processes has almost disappeared leaving only capillaries and concentrations of connective tissue cells. (fig. 2). The ciliary processes of the eyes injected with inactivated extract are still stout and contain their intercellular substance.

The stout type of anterior ciliary process becomes changed in those rabbits given testicular extract for long periods of time. The change essentially is a substitution of a

Fig. 2 (MacDonald). Anterior ciliary process after exposure to testicular extract in vitro. Note loss of intercellular substance and partial separation between epithelial layers.
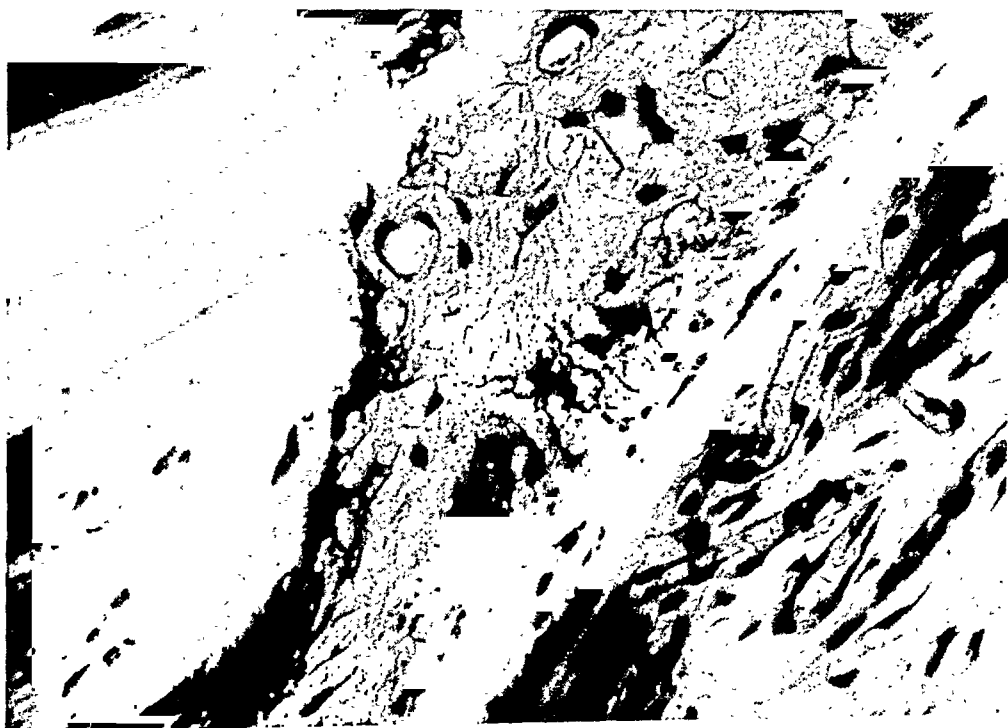

Fig. 3 (MacDonald). Anterior ciliary process after prolonged administration of testicular extract. Note more solid nature of the intercellular substance. Iris is at right, lens at left.

more solid type of intercellular substance of an amorphous character that stains with eosin, and is metachromatic with toluidene blue (fig. 3), for the more fluid and more poorly staining intercellular substance observed in the normal process. In the rabbits allowed a 30-day recovery period after the injections of extract ceased, the altered intercellular substance in the process still persists.

The eyes of guinea pigs possess anterior ciliary processes of a considerably different type from those observed in the rabbit and no change is observed in the intercellular substance of the cores of those of the animals given testicular extract for long periods of time. A change, however, is observed in that the two epithelial layers covering the ciliary body and processes are almost completely separated from each other in the instance of two eyes (fig. 4) and partially separated in two others. No such separation is observed in the eyes of control guinea pigs fixed and sectioned in the same manner.

An additional lesion in the rabbits given testicular extract for long periods of time was observed in the extraocular muscles. These exhibit a patchy distribution of lesions that were of a combination of muscle

Fig. 5 (MacDonald). Extraocular muscle lesion in the rabbit after prolonged administration of testicular extract.

degeneration and cellular proliferation. The latter involves both the endomysium of the muscles and the muscle fibers themselves. In some sites the lesions are associated with a mild infiltration of mononuclear cells (fig. 5).

DISCUSSION

The fact that the intercellular substance of the stout type of anterior ciliary process of the normal rabbit's eye appears in sections to be of a more or less fluid nature, and does not stain with eosin, and is not metachromatic with toluidene blue, suggests that it is hyaluronic acid. The fact that it dissolves away in the instance of eyes injected with testicular extract after death is confirmatory evidence to this effect.

The fact that the intercellular substance of the ciliary processes of the eyes of the rabbits given testicular extract for long periods of time became of such a character that it stained with eosin and was metachromatic with toluidene blue suggests that a sulfated type of mucopolysaccharide be-

Fig. 4 (MacDonald). Separation of epithelial layers of guinea pig following prolonged administration of testicular extract.

came substituted for hyaluronic acid under the conditions of the experiment.

It is difficult to assess the significance of this finding. It is tempting to suggest that this provides evidence of hyaluronidase injected at one site in the body having a pronounced effect at another. But the extract was a relatively wide-range fraction probably containing protein, and hence the possibility of the changes in the ciliary processes being of the nature of a foreign-protein response must be taken into account.

It is of interest that aging is known to be associated with changes in the quality of the intercellular substances of the ciliary processes which are in general in the character of what might be termed a solidifying nature[8] and hence somewhat similar to those obtained in this experiment.

The separation of the layers of epithelium observed in the ciliary processes of the guinea pigs given extract for long periods of time also suggests an effect on the cement substances at a site distant from that of the injection.

Although no precise information is available about the nature of the cement substance assumed to hold these two layers of epithelium together, it is not unlikely that it, like other cement substances, is of the nature of a sulfated mucopolysaccharide. The extract used in this experiment contains, as noted previously, enzymes that react with this type of intercellular substance as well as with hyaluronic acid.

The lesions seen in the extraocular muscles were similar to those found in many other striated muscles of the experimental animals. The nature and cause of the muscle lesion is being investigated in collaboration with other members of the department in which this work was done and who are interested in the effects of hyaluronidase in sites other than the eye.

It may be said, however, that the muscle lesion is not unlike that seen in biopsies of muscle obtained from certain stages of some types of rheumatic diseases. The fact that certain investigators have reported the production of muscle lesions as a result of the injection of foreign protein,[9] however, makes it unwise at this time to attribute the muscle lesion to the enzymes of the extract acting on a substrate in the muscle. Further work will be necessary before any conclusions can be drawn on this matter.

SUMMARY

Two types of ciliary processes were found in the 6-month-old rabbit, a thick and a thin type. The thick type contains a primitive form of connective tissue not unlike that found in umbilical cord. After the thick type is subjected to the action of testicular extract for 30 minutes it loses most of its intercellular substance. This, as well as its morphologic characteristics, suggests that it is hyaluronic acid.

On the other hand, in rabbits injected with testicular extract over long periods of time, the intercellular substance of the thick type of process becomes denser and stains metachromatically. This suggests that hyaluronic acid is here replaced by a sulfated type of mucopolysaccharide under the experimental procedure.

In guinea pigs similarly treated over long periods, the two epithelial layers covering the ciliary body become separated. Also degenerative and proliferative lesions of the extraocular muscles develop in the rabbits injected with testicular extract.

15 Walmsley Boulevard.

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DISCUSSION

DR. JONAS S. FRIEDENWALD (Baltimore, Maryland) : I think that Dr. MacDonald has opened a very interesting and fascinating subject, and I am very glad indeed that he has started to work in this field. What I wanted to ask him was whether he was aware of the technique of Hotchkiss for mucoid stain with the aid of which one can settle some of the problems about which he seems to be in doubt. This Hotchkiss technique is a general stain for mucoids of a much more highly specific character than the faint color difference which one gets with the metachromatic stain and one can stain tissues and see where the mucoids are, and one can take parallel sections and expose them to various enzymes such as hyaluronidase and see whether certain mucoids disappear and thus can identify quite well which mucoids were present.

DR DAVID G. COGAN (Boston, Massachusetts) : I would be interested to know what changes other than those in the ciliary body occur.

DR. ERNST SCHMERL (Toledo, Ohio) : May I ask whether the ocular tension was affected by the administration of the testicular extract?

DR. MACDONALD (closing) : In answer to Dr. Friedenwald's question, we have tried Hotchkiss's technique of staining for hyaluronic acid without very much success, because the ground substance disappeared in our in vitro experiments in which hyaluronidase was acting on the tissues. This along with its other staining qualities led us to believe it was hyaluronic acid. The reason that most of our observations on the eye concerned the anterior ciliary processes in rabbits was because of the simplicity of the primitive type of connective tissue there.

We looked for changes elsewhere but because of complexity of the tissues we were not able to make any definite observations.

In regard to changes in ocular tension, we were not able to establish definitely any changes in intraocular pressures, although we did find changes in the rate of diffusibility of fluorescein using ultraviolet light. Our present experiments involve a much larger series and half these animals demonstrate rapid diffusibility of fluorescein in the aqueous as compared with the normal. It comes in great clouds.

We really have not done enough control animals to know just what the normal range is.

THE USE OF ALKYL-DIMETHYL-BENZYL AMMONIUM CHLORIDE FOR MAINTENANCE OF STERILITY IN SOLUTIONS*

D. T. HUGHSON,† M.D.
Milwaukee, Wisconsin
AND
NORMA C. STYRON,‡ M.S.
New York

Experimental eye surgery on rabbits has several hazards, one of which is postoperative infection. While doing experimental eye surgery it was found on two occasions that the particular organism responsible could be traced to one of the solutions used in connection with the operation. In doing animal work it would be convenient to have freshly autoclaved solutions. However, this is not always possible so that it was deemed worth while to investigate a method whereby the solutions used in experimental ophthalmic surgery could be kept sterile for a reasonable length of time. It also seemed that, if this method were successful, it could be used to keep solutions ordinarily used in ophthalmology sterile for longer periods.

Alkyl-dimethyl-benzyl ammonium chloride solution, known by its trade name Zephiran chloride, seemed a suitable bactericidal agent because it is compatible with all drugs used in ocular surgery except eserine salicylate. It is, however, compatible with eserine sulphate. It has been shown by Domagk[1] and Walter[2] to be nontoxic when given to animals internally and also to be noninjurious in the conjunctival sac of human beings in concentrations of 1:1,000 to 1:5,000. It has been used to maintain the sterility of vaccines by Maier,[3] and has been shown to be an efficient bactericide by the work of Dunn,[4] Hoyt, Fisk, and Burde,[5] also Heineman[6] and Thompson.[7] This chemical has been shown to be suitable for ocular use by O'Brien.[8] It also has the advantage of being thermostabile as was demonstrated by Dunn.[9] Sevag and Ross[10] used it as a fungicide and Dunn[11] also used it against molds.

In order to test further the toxicity of this chemical agent, the aqueous of one eye of each of three rabbits was replaced by Zephiran chloride in saline in a concentration of 1:3,000, 1:6,000, and 1:7,500. The aqueous of the fellow eye of these animals was replaced by normal saline. In three animals in which the 1:3,000 solution was used, and the three animals in which the 1:6,000 solution was used, endothelial edema was caused which, however, disappeared in from 6 to 8 weeks. The degree of edema was in direct proportion to the concentration of the solution. In three animals in which the aqueous was replaced by a saline solution of Zephiran chloride in a concentration of 1:7,500, no visible evidence of damage could be ascertained with a hand slitlamp.

At the time this work was done we were unaware of the work of Post.[12] Post did very much the same type of experiment but used concentrations of Zephiran chloride of 1:500, 1:1,000, and 1:3,000, and stated that there was necrosis of the iris in all of these concentrations.

PROCEDURE

In order to simulate actual conditions, but to an exaggerated degree, the following drugs were dissolved in an aqueous solution of Zephiran chloride of 1:5,000: atropine sulphate (1 percent), pilocarpine (1 percent), pontocaine (0.5 percent), fluorescein (2 percent), eserine sulphate (0.5 percent). These solutions were placed in bottles such as are

ordinarily used for containing ophthalmic solutions, and were capped with rubber stoppers which were held in place by bandages. As a control to test and compare the efficacy of Zephiran chloride the drugs mentioned above were dissolved in triple-distilled water, and capped in similar manner. All the solutions were then autoclaved in the bottles. The bottles had a capacity of 60 cc. The opening was one centimeter in diameter.

Twelve hours later the rubber stoppers were removed from the bottles, samples of the drugs were taken immediately, and cultured in bacteriologic culture media to test the sterility of the solutions. The bottles were allowed to stand open in the laboratory, unprotected for 19 days. Samples were taken subsequently after 1, 7, 14, and 19 days from each of the bottles and inoculated in liquid media in tubes. Several different media were used. These will be described subsequently.

The inoculations were done in quadruplicate and the inoculated tubes were incubated aerobically and anaerobically, both at 37°C. and room temperature. The room temperature during the time of the experiment ranged from 16°C. to 24°C. (60° to 75°F.).

After 3 to 5 days, the cultures were examined macroscopically and any gross changes in the media noted. Smears were made from each tube. These were stained by Gram's method and examined. Whenever bacteria were observed in the smears the different morphologic types, their Gram reaction, and their relative number were recorded. No further identification was attempted.

The final experimental procedure was the subculturing of each of the primary cultures. This was done by preparing agar pour plates. Approximately 0.5 cc. of the primary culture was used to inoculate these plates. The pour plates were incubated aerobically at 37°C. for 5 days and examined daily for the presence or absence of bacterial colonies. In most cases where colonies were present, representative colonial forms were selected, smears were made, stained by Gram's

method, and examined. Except for the unstoppered bottles of the drugs, aseptic technique was observed throughout the experimental procedure.

The volume of drug tested each time was 0.5 cc. in 7 cc. of medium. The volume of the medium was such that culture tubes 6 by ⅝ inches could be used. This was an advantage as all of the tubes at any one sampling interval could be placed in four anaerobic jars and incubated anaerobically. This ratio gave a final dilution of Zephiran chloride of 1:75,000 in each tube. This dilution was considered to be sufficiently high so as not to exert any bacteriostatic or bactericidal effect during the period of incubation. However, as a control of bacteriostasis, the primary cultures, as stated in the preceding paragraph, were always subcultured.

Dunn[4] reported the dilution ratios of Zephiran chloride capable of destroying various organisms in 10 minutes but not in 5 minutes at 20°C. and at 37°C. With the exception of a strain of Hemolytic streptococcus, which was destroyed by a solution of Zephiran chloride 1:95,000 at 20°C., the species of bacteria and cryptococcus which he tested were destroyed by a dilution of 1:70,000 or less.

Using a Gram-positive and a Gram-negative organism, we tested the action of Zephiran chloride in a dilution of 1:75,000 in sterile evaporated milk. Two-mm. loopfuls of a broth culture of Staphylococcus aureus and of E. coli were inoculated at 37°C. and at room temperature for 24 hours. At the end of this time, the growth was abundant in all four tubes. It may be mentioned now, but referred to later, that in parallel tests with blood broth Staphylococous aureus failed to grow in the broth plus Zephiran, both at 37°C. and at room temperature. The strain of E coli appeared to grow equally as well in the broth with Zephiran as in the broth without Zephiran.

The media used for testing the sterility of the drugs were whole evaporated milk and

TABLE 1*

ATROPINE SULFATE (1 PERCENT) IN ZEPHIRAN (1:5,000)†

Intervals of Sampling	Media for Primary Culture — Kind	pH	Explanation of Observations Columns 4 to 5	Line	Zephiran 1:5,000 Aerobic 37°C	R.T.	Anaerobic 37°C	R.T.	Organisms in Smears Line 2	Sterile Distilled Water Aerobic 37°C	R.T.	Anaerobic 37°C	R.T.	Organisms in Smears Line 2
Col. 1	Col. 2		Col. 3		Col. 4					Col. 5				
Imm.	Whole Evap. Milk	5.90	*Line 1* Macroscopic change noted in primary culture after 2–5 days incubation (primary cultures = 0.5 cc. of solution in 7 cc. of medium)	1	−	−	−	−		−	−	−	−	
				2	−	−	−	−		−	−	−	−	
				3	−	−	−	−		−	−	−	−	
	Rabbit Blood Neopep. Broth	7.20		1	−	−	−	−		−	−	−	−	
				2	−	−	−	−		−	−	−	−	
				3	−	−	−	−		−	−	−	−	
1 Day	Whole Evap. Milk	5.90		1	−	−	−	−		−	−	−	−	
				2	−	−	−	−		−	−	−	−	
				3	−	−	−	−		−	−	−	−	
	Rabbit Blood Neopep. Broth	7.20		1	−	−	−	−		−	−	−	−	
				2	−	−	−	−		−	−	−	−	
				3	−	−	−	−		−	−	−	−	
7 Days	Whole Evap. Milk	5.90	*Line 2* Smears of primary culture stained by Gram's method.	1	−	−	−	−		PC	PC	−	−	(Gr.+rods (2 types) Gr.+cocci.)
				2	−	1ᵃ	−	−		4+	3+	2+	−	
				3	−	−	−	−		4+	4+	4+	4+	
	Rabbit Blood Neopep. Broth	7.20		1	−	−	−	−		T	T	T	−	(Gr.+rods (2 types) Gr.+cocci. and molds)
				2	−	−	−	−		4+	3+	4+	±	
				3	1ᵃ	−	−	−		4+	4+	4+	4+	
14 Days	Whole Evap. Milk	5.90		1	−	−	−	−		−	−	−	−	(Gr.+rods (1 type))
				2	−	−	−	−		4+	3+	±	±	
				3	−	−	−	−		4+	4+	4+	4+	
	Whole Evap. Milk	5.90	*Line 3* Colonies present in pour plates made of primary culture after 2–5 days incubation. (Pour plates were incubated aerobically at 37°C.)	1	−	−	−	−		−	−	−	−	(Gr.+rods (1 type))
				2	−	2ᵃ	−	−		4+	4+	4+	4+	
				3	−	−	−	−		4+	4+	4+	4+	
19 Days	Dil. Evap. Milk	7.00		1	−	−	−	−		−	−	−	−	(Gr.+rods. (1 type))
				2	−	−	−	−		3+	3+	±	±	
				3	−	−	−	−		4+	4+	2+	2+	
	Dil. Evap. Milk	7.00		1	−	−	−	−		−	−	−	−	(Gr.+rods (1 type))
				2	−	−	−	−		3+	3+	±	±	
				3	−	−	−	−		4+	4+	2+	2+	
	Rabbit Blood Neopep. Broth	7.20		1	−	−	−	−		T	T	T	T	(Gr.+rods (1 type))
				2	−	−	−	−		±	±	±	±	
				3	−	−	−	45ᵇ		4+	4+	2+	2+	

*EXPLANATION OF SYMBOLS IN TABLES

Imm.: immediately
Whole evap. Milk: whole evaporated milk
Dil. Evap. Milk: diluted evaporated milk
Rabbit Blood Neopep. Broth: rabbit blood neopeptone infusion broth
R.T.: room temperature

LINE 1
Minus sign: no macroscopic change in the primary culture
C: coagulation
PC: partial coagulation
T: turbidity

LINE 2
Minus sign: no microorganisms seen in the smear of the primary culture stained by Gram's technique
Plus over minus to 4 plus: the relative numbers of microorganisms seen in the smears of the primary cultures stained by Gram's technique

LINE 3
Minus sign: no colonies in the pour plates made of the primary cultures.
Plus over minus to 4 plus: the relative number of colonies in the pour plates. When the number of colonies per plate is 100 or less the exact number is recorded.

pH of the primary cultures after inoculation with the solutions:

Whole Evap. milk plus atropine sulfate in Zephiran	= 5.90
Whole Evap. milk plus atropine sulfate in distilled water	= 5.90
Rabbit Blood Neopep. Broth plus atropine sulfate in Zephiran	= 7.18
Rabbit Blood Neopep. Broth plus atropine sulfate in distilled water	= 7.20

† Sterile distilled water was used. Solutions and media were sterilized by autoclaving.
ᵃ Colonies are probably surface contaminants.
ᵇ Molds.

TABLE 2*
ESERINE SULFATE (0.5 PERCENT) IN ZEPHIRAN (1:5,000)†

Intervals of Sampling	Media for Primary Culture		Explanation of Observations Columns 4–5		Zephiran 1:5,000					Sterile Distilled Water				
					Incubation of Primary Culture				Organisms in Smears Line 2	Incubation of Primary Culture				Organisms in Smears Line 2
					Aerobic		Anaerobic			Aerobic		Anaerobic		
	Kind	pH			37°C.	R.T.	37°C.	R.T.		37°C.	R.T.	37°C.	R.T.	
Col. 1	Col. 2		Col. 3		Col. 4					Col. 5				
Imm.	Whole Evap. Milk	5.90	*Line 1* Macroscopic change noted in primary culture after 2–5 days incubation (primary cultures = 0.5 cc. of solution in 7 cc. of medium)	1 2 3	— — —	— — —	— — —	— — —		— — —	— — —	— — —	— — —	
	Rabbit Blood Neopep. Broth	7.20		1 2 3	— — —	— — —	— — —	— — —		— — —	— — —	— — —	— — —	
1 Day	Whole Evap. Milk	5.90		1 2 3	— — —	— — —	— — —	— — —		— — —	— — —	— — —	— — —	
	Rabbit Blood Neopep. Broth	7.20		1 2 3	— — —	— — —	— — —	— — —		— — —	— — —	— — —	— — —	
7 Days	Whole Evap. Milk	5.90	*Line 2* Smears of primary culture stained by Gram's method.	1 2 3	— — —	— — —	— — —	— — 1ᵃ		— — —	— 1ᵇ —	— 1ᵇ —	— — —	
	Rabbit Blood Neopep. Broth	7.20		1 2 3	— — —	— — —	— — —	— — —		— — —	— — —	— — —	— — 4ᶜ	
14 Days	Whole Evap. Milk	5.90	*Line 3* Colonies present in pour plates made of primary culture after 2–5 days incubation. (Pour plates were incubated aerobically at 37°C.)	1 2 3	— — —	— — —	— — —	— — —		— — 3ᶜ	— — —	— — —	— — —	
	Whole Evap. Milk	5.90		1 2 3	— — —	— — —	— — —	— — —		— — 4	— — —	— — —	— — —	
19 Days	Dil. Evap. Milk	7.00		1 2 3	— — —	— — —	— — —	— — —		— — —	— — —	— — 1ᵈ	— — 60ᵈ	
	Dil. Evap. Milk	7.00		1 2 3	— — —	— — —	— — —	— — —		— — —	— — —	— — 2ᵈ	— — 1+ᵈ	
	Rabbit Blood Neopep. Broth	7.20		1 2 3	— — —	— — —	— — —	— — —	— — —	— — —	— — —	— — —	T — 4+ᵈ	

* See * of Table 1 for explanation of symbols.
† Sterile distilled water was used. Solutions and media were sterilized by autoclaving.
a Mold, surface contaminant.
b Opaque white surface colonies (Gram +cocci). Probably surface contaminants.
c Opaque yellow surface colonies (Gram +cocci). Probably surface contaminants.
d Subsurface colonies (Gram +rods).

evaporated milk diluted with equal parts of neopeptone infusion broth and 5-percent rabbit blood neopeptone infusion broth. The pH of the whole evaporated milk was not adjusted. After autoclaving it was found to have pH of 5.90. The pH of the diluted evaporated milk and of the blood broth was adjusted so as to be between pH 7.0 to pH 7.2 after autoclaving. Toward the end of the experiment, because of the viscosity of the whole evaporated milk, the diluted milk was used as a substitute. The diluted milk not

only facilitated a more uniform mixing of drugs and media, but it also insured more accurate measurement of the volume of the culture used in the agar pour plates.

The evaporated milk was considered to be a better medium for this work than the blood broth, since McCulloch[13] reported that false disinfection velocity curves are produced by quaternary ammonium compounds, of which group Zephiran chloride is a member. He found that sterile evaporated milk allowed the growth of organisms exposed to solu-.

TABLE 3*
FLUORESCEIN (2 PERCENT) IN ZEPHIRAN (1:5,000)†

Intervals of Sampling	Media for Primary Culture		Explanation of Observations Columns 4–5		Zephiran 1:5,000					Sterile Distilled Water				
					Incubation of Primary Culture				Organisms in Smears Line 2	Incubation of Primary Culture				Organisms in Smears Line 2
					Aerobic		Anaerobic			Aerobic		Anaerobic		
	Kind	pH			37°C	R.T.	37°C	R.T.		37°C	R.T.	37°C	R.T.	
Col. 1	Col. 2		Col. 3		Col. 4					Col. 5				
Imm.	Whole Evap. Milk	5.90	*Line 1* Macroscopic change noted in primary culture after 2–5 days incubation (primary cultures =0.5 cc. of solution in 7 cc. of medium)	1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—7	—	—	
				3	—	—	—	—		—	—	—	—	
	Rabbit Blood Neopep. Broth	7.20		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
1 Day	Whole Evap. Milk	5.90		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
	Rabbit Blood Neopep. Broth	7.20		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
7 Days	Whole Evap. Milk	5.90	*Line 2* Smears of primary culture stained by Gram's method.	1	—	C	—	—	{Hyphae of molds}	—	—	—	—	
				2	—	4+	—	—		—	—	—	—	
				3	—	4+[a]	—	—		—	—	—	—	
	Rabbit Blood Neopep. Broth	7.20		1	—	—	—	—		—	—	—	—	{Gr. −cocci}
				2	—	—	—	—		—	1+	—	—	
				3	1[b]	—	—	—		—	1[b]	1[c]	50[d]	
14 Days	Whole Evap. Milk	5.90	*Line 3* Colonies present in pour plates made of primary culture after 2–5 days incubation. (Pour plates were incubated aerobically at 37°C.)	1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	1[c]	—	—	—		—	—	1[c]	—	
	Whole Evap. Milk	5.90		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
	Dil. Evap. Milk	7.00		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	1[c]	1[c]	—	—		—	1[d]	1[c]	—	
19 Days	Dil. Evap. Milk	7.00		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
	Rabbit Blood Neopep. Broth	7.20		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	3[d]	—	

* See * of Table 1 for explanation of symbols.
† Sterile distilled water was used. Solutions and media were sterilized by autoclaving.
a Molds.
b Subsurface colonies (Gram −cocci).
c Opaque yellow surface colonies (Gram +cocci). Probably surface contaminants.
d Subsurface colonies and cream-colored surface colonies (Gram +rods).

tions of these compounds, while parallel inoculations into broth failed to grow. We found this to be true in the case of Staphylococcus aureus.

The media used for the samples taken at the 5 intervals were as follows:

For the first 3 intervals whole evaporated milk and 5-percent rabbit blood neopeptone infusion broth were used. For the 4th interval on the 14th day whole evaporated milk in parallel series was used. At the 5th interval on the 19th day after the start of the experiment, diluted evaporated milk and 5-percent rabbit neopeptone infusion broth were employed.

The observations are recorded in Table 1 through Table 5, inclusive. The macroscopic changes in the culture media are recorded in line 1 of columns 4 and 5. The observations of smears stained by Gram's

TABLE 4*
PILOCARPINE (1 PERCENT) IN ZEPHIRAN (1:5,000)†

Intervals of Sampling	Media for Primary Culture — Kind	pH	Explanation of Observations 4 Columns 4–5	#	Zephiran 1:5,000 — Aerobic 37°C	R.T.	Anaerobic 37°C	R.T.	Organisms in Smears Line 2	Sterile Distilled Water — Aerobic 37°C	R.T.	Anaerobic 37°C	R.T.	Organisms in Smears Line 2
Col. 1	Col. 2		Col. 3		Col. 4					Col. 5				
Imm.	Whole Evap. Milk	5.90	*Line 1* Macroscopic change noted in primary culture after 2–5 days incubation (primary cultures =0.5 cc. of solution in 7 cc. of medium)	1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
	Rabbit Blood Neopep. Broth	7.20		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
1 Day	Whole Evap. Milk	5.90		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
	Rabbit Blood Neopep. Broth	7.20		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
7 Days	Whole Evap. Milk	5.90	*Line 2* Smears of primary culture stained by Gram's method.	1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	2^a	2^a	—		—	—	1	1^a	
	Rabbit Blood Neopep. Broth	7.20		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		30^c	±/3^d	1^b	—	{Gr.+rods}
				3	1^b	—	—	—						
14 Days	Whole Evap. Milk	5.90	*Line 3* Colonies present in pour plates made of primary culture after 2–5 days incubation. (Pour plates were incubated aerobacially at 37°C.)	1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	1^b	—	—	
	Whole Evap. Milk	5.90		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
	Dil. Evap. Milk	7.00		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
19 Days	Dil. Evap. Milk	7.00		1	—	—	—	—		—	—	—	—	
				2	—	—	—	—		—	—	—	—	
				3	—	—	—	—		—	—	—	—	
	Rabbit Blood Neopep. Broth	7.20		1	—	—	—	—		—	—	—	—	{Gr.+rods}
				2	—	—	—	—		—	—	±/4+^{e}	—	
				3	—	—	—	—		—	—			

* See * of Table 1 for explanation of symbols.
† Sterile distilled water was used. Solutions and media were sterilized by autoclaving.
a Subsurface colonies (Gram+cocci). Probably contaminants.
b Opaque yellow and white surface colonies. (Gram+cocci). Probably contaminants.
c Subsurface and surface colonies of molds and bacteria. The bacteria are Gram+cocci and Gram+rods.
d Subsurface colonies (Gram+rods). Probably contaminants.
e Subsurface and grayish white, flat surface colonies (Gram+rods and Gram−rods).

method are in line 2 of columns 4 and 5, and the observations of the pour plates in line 3 of the same columns.

CONCLUSIONS

TABLE 1

Atropine sulphate (1 percent) dissolved in aqueous solution of Zephiran chloride re-mained sterile under conditions described for a period of 14 days to 19 days at which time the solution was contaminated by molds.

TABLE 2

Eserine sulphate (0.5 percent) in Zephiran chloride 1:5,000 remained sterile during the 19 days.

TABLE 5*
PONTOCAINE (0.5 PERCENT) IN ZEPHIRAN (1:5,000)†

Explanation of Observations, Columns 4–5:
- Line 1: Macroscopic change noted in primary culture after 2–5 days incubation (primary cultures = 0.5 cc. of solution in 7 cc. of medium)
- Line 2: Smears of primary culture stained by Gram's method.
- Line 3: Colonies present in pour plates made of primary culture after 2–5 days incubation. (Pour plates were incubated aerobically at 37°C.)

Intervals of Sampling	Media — Kind	pH	Line	Zephiran 1:5,000 Aerobic 37°C	Aerobic R.T.	Anaerobic 37°C	Anaerobic R.T.	Organisms in Smears Line 2	SDW Aerobic 37°C	Aerobic R.T.	Anaerobic 37°C	Anaerobic R.T.	Organisms in Smears Line 2
Imm.	Whole Evap. Milk	5.90	1	−	−	−	−		−	−	−	−	
			2	−	−	−	−		−	−	−	−	
			3	−	−	−	−		−	−	−	−	
	Rabbit Blood Neopep. Broth	7.20	1	−	−	−	−		−	−	−	−	
			2	−	−	−	−		−	−	−	−	
			3	−	−	−	−		−	−	−	−	
1 Day	Whole Evap. Milk	5.90	1	−	−	−	−		−	−	−	−	
			2	−	−	−	−		−	−	−	−	
			3	−	−	−	−		−	−	−	−	
	Rabbit Blood Neopep. Broth	7.20	1	−	−	−	−		−	−	−	−	
			2	−	−	−	−		−	−	−	−	
			3	−	−	−	−		−	−	−	−	
7 Days	Whole Evap. Milk	5.90	1	−	−	−	−		−	−	−	−	
			2	−	−	−	−		−	−	−	−	
			3	−	−	−	−		1[a]	−	2+[d]	−	
	Rabbit Blood Neopep. Broth	7.20	1	−	−	−	−		−	−	−	−	
			2	−	−	−	2[b]		−	−	−	−	
			3	−	−	−	−		−	−	1[a]	−	
14 Days	Whole Evap. Milk	5.90	1	−	−	−	−		−	−	−	−	
			2	−	−	−	−		−	−	−	−	
			3	−	−	−	−		3[c]	−	−	−	
	Whole Evap. Milk	5.90	1	−	−	−	−		−	−	−	−	
			2	1[c]	−	−	−		−	−	−	−	
			3	−	−	−	−		−	−	−	−	
	Dil. Evap. Milk	7.00	1	−	−	−	−		−	−	−	−	
			2	−	−	−	−		−	1[a]	−	−	
			3	−	−	−	−		−	−	−	3[c]	
19 Days	Dil. Evap. Milk	7.00	1	−	−	−	−		−	−	−	−	
			2	−	−	−	−		−	−	−	−	
			3	−	−	−	−		−	−	−	−	
	Rabbit Blood Neopep. Broth	7.20	1	−	−	−	−		−	−	−	−	
			2	−	−	−	−		−	−	−	−	
			3	−	−	−	−		−	−	−	−	

* See * of Table 1 for explanation of symbols.
† Sterile distilled water was used. Solutions and media were sterilized by autoclaving.
[a] Subsurface and opaque, yellow surface colonies (Gram + cocci). Probably contaminants.
[b] Subsurface and opaque, white surface colonies (Gram − rods). Probably contaminants.
[c] Subsurface and opaque, white surface colonies (Gram + cocci). Probably contaminants.
[d] Subsurface and opaque, yellow surface colonies (Gram + cocci).

TABLE 3

Fluorescein (2 percent) in 1:5,000 solution of Zephiran chloride was contaminated by molds when cultured at the end of 7 days, but was sterile at the 14- and 19-day periods.

TABLE 4

Pilocarpine (1 percent) in 1:5,000 Zephiran chloride remained sterile during the 19 days of the experiment.

TABLE 5

Pontocaine (0.5 percent) in 1:5,000 Zephiran chloride remained sterile during the 19 days of exposure.

When 1 or 2 colonies were present in the pour plate, it was considered to be due to contamination at the time of subculturing, rather than that the organism was present in the primary culture.

Under the conditions of the experiment,

the control solutions of the drugs in sterile water all became contaminated, while the drugs in the 1:5,000 Zephiran-chloride solution remained sterile with the exception of

the fluorescein which became contaminated by molds at the 7-day period, but which became sterile at the 14- and 19-day samplings.

208 East Wisconsin Avenue (2).

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DISCUSSION

DR. M. H. POST, JR. (St. Louis Missouri): I had the privilege of some correspondence with Dr. Hughson concerning the injection of Zephiran chloride into the anterior chamber of the rabbit eye. The subject has been of interest to me, inasmuch as I have been recommending the use of Zephiran chloride in conjunction with other sterilizing solutions for the prevention of infection in cataract surgery.

A few experiments were carried out. In these it was found that: Using a solution of Zephiran chloride varying in strength from 1:3,000 to 1:500 the corneas of the injected eyes became diffusely cloudy in 5 or 6 days.

They remained so for about 5 weeks, clearing up at the end of that time. The irides on the other hand began to show signs of localized atrophy near the site of injection. This change was first manifest about 2 weeks after the injection, gradually becom-

ing more marked as long as the animal survived.

Just a word, however, in conjunction with its effects on cataract surgery seems in order. It is of interest that, through a miscalculation a solution of Zephiran chloride, 1:500 was used in the operating rooms of the McMillan Hospital for a period of 30 days, and that during that time there were no complaints of corneal or iris disturbances. It would appear, therefore, that the small amount of Zephiran introduced into an open eye even though much stronger than necessary cannot be likely to produce any great damage.

Relative to maintenance of sterility in solutions, I am tremendously interested in what Dr. Hughson has had to say. I have found that the sterile water exposed to air for a few minutes in the trays in our operating rooms would result in 100-percent con-

tamination of the instruments after they had been supposedly completely sterilized by the other solutions.

By replacing the sterile water in these trays by Zephiran solution, (1:3,000) this difficulty was completely overcome, since the Zephiran solution, thus substituted, remained sterile for a period of 5 hours, that is, as long as the experiments upon it were conducted.

DR. ALSON BRALEY (New York, New York): I would like to ask a question. What effect does Zephiran chloride have on the presence of viruses in the solution?

DR. DAVID G. COGAN (Boston, Massachusetts): I would like to ask the essayist if he has had any experience with allergy to this drug.

DR. PHILLIPS THYGESON (San Jose, Calfornria): I might say that the problem of sterility of solutions is quite an important one now that epidemic keratoconjunctivitis is so widespread. The question as to whether or not Zephiran is protective against this virus is still open.

DR. HUGHSON (closing): When I first started to use Zephiran to replace the aqueous in the animal eye, it was to find out its effect, as I was curious to find out what would happen if any of the solution adhered to a knife or keratome and to see how strong a solution the eye could tolerate.

I think that with one drop of the Zephiran adhering to the instrument and diluted by the total aqueous, provided a solution of 1:3,000 or 1:5,000 is used, you have a safe antiseptic agent.

The answer to Dr. Braley's question concerning viruses. There has been no work done on that as far as I could find in the literature; the only thing that I can find that might have some bearing on this is: I think some authorities have an idea that possibly bacteriophage may be allied to a virus. At least, they resemble each other morphologically under the electron microscope and Maier did some work with that on vaccines and bacteriophage to preserve the sterility of the solution; and as far as he could see, Zephiran did not have any ill effect on the quality of the bacteriophage, so I would possibly deduce from that, that it would not have any effect on the virus. I realize that is a long stretch, but to my knowledge no work has been done directly against the virus.

As to the question concerning allergy, I haven't found anyone who is particularly sensitive. Occasionally, you will get a slight hyperemia of the eye from the solution both in human beings and in animals, but the toxicity of it or the lack of toxicity is pretty well proven. Domagk, the original worker, used Zephiran undiluted as the sole source of fluid for animals for several months and could find no damage of any sort. You do get, occasionally, a case of slight hyperemia in some people from it.

EFFECTIVENESS OF STREPTOMYCIN IN TREATMENT OF EXPERIMENTAL CONJUNCTIVITIS CAUSED BY *HEMOPHILUS SP.**

DORLAND J. DAVIS,[†] M.D.

AND

MARGARET PITTMAN,[‡] PH.D.

Bethesda, Maryland

Epidemic conjunctivitis, commonly called "gnat sore eyes," has been described in certain sections of southern United States.[1,2] In a bacteriologic study of 50 cases in Georgia, in 1932, Bengtson[2] isolated organisms resembling the Koch-Weeks bacillus from 80 percent of the cases. While the disease is usually mild, is of short duration, and leaves no sequelae, severe and prolonged cases do occur, and the high incidence especially in school children renders it one of major public health importance in certain areas.

During October, 1947, a study of the disease in the Rio Grande River Valley, where it has been prevalent for many years, was initiated at the request of the Hidalgo-Starr Counties Medical Society and the National Society for the Prevention of Blindness. This investigation was directed toward the elucidation of the etiology and epidemiology of the disease as it occurred in that region.

During the course of this investigation scrapings and cultures were taken from the conjunctivas of 45 acute cases and examined for pathogenic organisms. From 24 of these cases a small, gram-negative bacillus resembling Hemophilus influenzae was isolated. All strains failed to grow on plain nutrient agar. Twelve were lost before the growth factor requirements could be determined. The remaining 12, however, required both X and V factors, and reduced nitrates to nitrites. Eleven appeared to be non-type-specific, the other was type b. Only

the latter produced indol. Because of the lack of any criteria for differentiation, the Koch-Weeks bacillus and the influenza bacillus have been considered as belonging to the same species.[2,3] However, until further study has been made, we prefer not to designate the strains recovered from the eye in this study as Hemophilus influenzae. For convenience they will be referred to as Hemophilus sp.

Hewitt and Pittman[4] reported the sensitivity of H. influenzae to streptomycin in vitro. With their technique the Texas eye strains were found to be inhibited by 0.625 or 1.25 micrograms (units) of streptomycin per ml., which falls within the range of sensitivity of H. influenzae. Rivanol lactate (2-ethoxy-6, 9-diaminoacridine lactate) was bactericidal in concentrations of 12.5 to 25 micrograms per ml.

Despite the frequent occurrence of this organism in the conjunctivas of acute cases, the question remained whether this agent by itself could cause a conjunctivitis in human beings or was merely incidental or accessory to an undetected cause. Attempts to induce infection in the eyes of rabbits and monkeys with cultures of these strains alone, mixed with cultures of Staphylococcus albus, or subsequent to scarification failed.

EXPERIMENTAL STUDY

SUBJECTS

However, an opportunity was afforded to inoculate 8 human volunteers with a strain of Hemophilus sp. The volunteers were healthy young adult white men, aged 19 to 39 years, who had had experimentally induced common colds 10 days previously, but had become almost entirely free of symptoms.[5] They were kept together in a ward, iso-

lated by strict techniques, and observed constantly by a male nurse and trained attendants. Temperatures were recorded at least every four hours during the daytime. Urinalysis and leukocyte counts were done daily and differential leukocyte determinations made every other day.

Bacteriologic cultures of each eye were taken before inoculation and each day during the course of the infection. Cotton swabs moistened with broth were rubbed gently along the lower conjunctival sac, incubated in 0.15-percent agar infusion broth containing approximately 3-percent Fildes peptic digest of blood to supply the X and V growth factors for 3 to 4 hours, and then streaked on blood agar and nutrient agar also containing peptic digest of blood.

STRAIN USED FOR INOCULATION

The strain used for inoculation, No. 48, had been isolated from the conjunctiva of a 7-year-old Hidalgo County school girl who had a mild conjunctivitis of 30 hours' duration. It had been preserved in the dried state soon after the original isolation. A 5-hour broth culture was diluted with normal saline solution so that the inoculum of 0.1 ml. contained not more than 10,000,000 bacteria. This was instilled directly into the right eye of each volunteer about 3 P.M. on the first day of the study.

RESULTS

Six of the 8 inoculated volunteers developed a severe conjunctivitis corresponding clinically to that observed among the population of the Rio Grande River Valley, and a hemophilic bacterium indistinguishable from the inoculated one was recovered from the affected eyes. The other 2 volunteers showed evidence of slight conjunctival hyperemia only on the first day after inoculation.

The signs and symptoms in all 6 cases were uniform, although there was variation in the degree of intensity in individual cases. Despite the recent convalescence from the

common cold, respiratory symptoms were minimal throughout the course of the infection. A representation of the degree of intensity of the clinical findings including conjunctival injection, mucopurulent discharge, edema, pain, and photophobia is presented in the chart along with the record of the isolation of Hemophilus sp. and the type of therapy employed.

In general the first symptom noticed by the patients was an itching or scratching of the inoculated eye about 6 hours after instillation of the culture. The following morning the eyelids were adherent with dried exudate, the eye was painful, the bulbar and palpebral conjunctivas were hyperemic, and a moderate amount of yellow mucopurulent material was present in the conjunctival sac. In some there was definite bipalpebral edema.

On the third day, 48 hours after inoculation, all the signs and symptoms were exaggerated and the bipalpebral edema was increased to the extent of closing the eye in some cases. Photophobia was more pronounced. In general there was slight elevation of temperature, not exceeding 1-degree Fahrenheit, and no marked change in leukocyte count or urinalysis.

In 2 cases (Cases 1 and 2), not specifically treated till the 8th and 9th day, the disease progressed to a severe, acute manifestation of all the local signs and symptoms, as well as definite general malaise. In three instances (Cases 2, 6, and 8,), the left or uninoculated eye became infected spontaneously as shown by the clinical appearance and the presence of Hemophilus sp. in culture.

On the third day, or 48 hours after inoculation, the 8 patients were separated into 3 groups for evaluating specific treatment. Streptomycin hydrochloride* in a concentration of 1 mg. per ml. of 0.85 percent NaCl solution was applied locally with an eyecup to the affected eye of three patients (Cases 3, 5, and 6) every 2 hours from 6 A.M.

INOCULATED WITH FIVE HOUR CULTURE OF HEMOPHILUS IN THE RIGHT EYE

DAYS	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
CASE 1 EYE L	0	0	0	0	0	0	0	0	0	0	0	0			0
R	+*	+	+	+	+	+	+	+	0	0	0	0			0
			0.85% NaCl SOLUTION					STREPTOMYCIN →							
CASE 2 EYE L	0	0	0	0	0	0	+	+	+	0	0	0			0
R	0	+	+	0	0	0	+	+	+	0	0	0			0
			0.85% NaCl SOLUTION					STREPTOMYCIN →							
CASE 3 EYE L	0	0	0	0	0	0	0	0	0	0					
R	0	0	+	0	0	0	0	0	0	0					
			STREPTOMYCIN												
CASE 4 EYE L	0	0	0	0	0	0	0	0	0	0					
R	0	0	0	0	0	0	0	0	0	0					
			STREPTOMYCIN RIVANOL												
CASE 5 EYE L	0	0	0	0	0	0	0	0	0	0	0				
R	0	+	+	0	0	0	0	0	0	0	0				
			STREPTOMYCIN												
CASE 6 EYE L	0	0	0	+	0	0	0	0	0	0	0				
R	0	+	+	0	0	0	0	0	0	0	0				
			STREPTOMYCIN												
CASE 7 EYE L	0	0	0	0	0	0	0	0	0	0	0				
R	0	+	+	0	0	0	0	0	0	0	0				
			STREPTOMYCIN RIVANOL												
CASE 8 EYE L	0	0	+	0	0	0	0	0	0	0	0				
R	0	+	+	0	0	0	0	0	0	0	0				
			STREPTOMYCIN RIVANOL				STREPTOMYCIN								
DAYS	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15

KEY
- \+ HEMOPHILUS ISOLATED
- 0 HEMOPHILUS NOT ISOLATED
- * HEMOPHILUS INFLUENZAE ISOLATED
- ■ CLINICAL EVALUATION

Chart 1 (Davis and Pittman). Clinical evaluation, isolation of Hemophilus sp., and type of therapy in eight human cases of experimental conjunctivitis.

until 10 P.M. for various time periods as indicated in the chart.

A second group (Cases 4, 7, and 8) was treated similarly with a mixed solution of streptomycin in the same concentration, and rivanol lactate in a concentration of 0.2 mg. per ml.

Patients in Cases 1 and 2 were treated locally with 0.85-percent NaCl solution till the 8th and 9th day as a control for the specific therapy administered to the other cases. Patients in Cases 3 and 4 showed only slight evidence of infection on the 2nd day and were treated as a check on the possible

irritative effect of the two specific solutions.

The four cases (Cases 5, 6, 7, and 8) manifesting acute disease and treated early with specific therapy showed marked clinical improvement beginning about 8 or 10 hours after the start of treatment, with definite relief of pain and diminution of the exudate. The following day there was less conjunctival hyperemia and Hemophilus sp. could no longer be recovered from the treated eye. Convalescence was rapid and progressive, and the eye cultures remained negative.

Since there was such a uniformity of clinical findings and the experimental conditions of the disease were relatively constant, only two case histories are presented. Case 1 on the 3rd day appeared to have a representative case and, as a control, specific therapy was withheld till the 8th day. Case 6 was more severe, and streptomycin eye washes were administered 48 hours after inoculation and continued for 3 days.

CASE REPORTS

Case 1. This 39-year-old volunteer first noticed itching, burning, exudate, and conjunctival injection of the right eye upon awakening in the morning, 15 hours after inoculation. The signs and symptoms became more severe and on the 3rd day, 48 hours later, there was moderate bipalpebral edema as well.

As a control for those patients receiving specific therapy, the affected eye was treated with 0.85-percent NaCl solution as an eye wash in an eyecup for the affected eye every 2 hours from 6 A.M. until 10 P.M.

The severity of the disease increased till the 8th day when there was marked bipalpebral edema, pain, severe hyperemia, and injection of the bulbar and palpebral conjunctivas, and profuse mucopurulent exudate. At this time he complained of a dry nonproductive cough.

The temperature reached 99°F. on the 6th day and 99.2°F. on the 8th day. Leukocyte counts varied from 7,600 to 12,000 cells per cubic mm. and the urinalysis was normal. On the 8th day streptomycin therapy was instituted. The following morning the patient reported marked lessening of pain, discomfort, and exudate, and the conjunctival injection was less intense. Improvement was steady till the 13th day when therapy was discontinued, and the only sign remaining was a slight hyperemia of the right conjunctivas.

Bacteriologic culture taken just before inoculation revealed the presence in the right eye of a non-type-specific strain of Hemophilus influenzae which produce indol. Cultures made daily from each eye showed a heavy growth, from the 2nd until the 8th day, of a strain of Hemphilus which was indistinguishable from No. 48, the inoculated strain. At no time was an organism isolated which resembled H. influenzae, the one originally found in the right eye. No hemophilic organisms were recovered from the eye subsequent to the institution of streptomycin solution eye washes.

Case 6. This 22-year-old volunteer reported itching at the right eye about 6 hours after inoculation, and on the following day there was marked conjunctival injection, pain, and a moderate amount of mucopurulent discharge from the right eye. On the 3rd day the disease had progressed, palpebral edema was marked, and the right nostril was obstructed and draining a watery discharge.

At this time local application every 2 hours of streptomycin solution (1 mg. per ml.) employing an eyecup was started. About 8 hours after the start of specific therapy, the patient reported a lessening of discomfort.

On the 4th day there was much less exudate and edema and somewhat less conjunctival hyperemia. However, the left eye was acutely inflamed, edematous, painful, and discharged mucopurulent material. Streptomycin eye washes were instituted for this eye at this time.

On the 5th day there was marked improvement in both eyes, and on the 6th day

only a mild conjunctival hyperemia remained in either eye after 72 hours of treatment for the right eye and 48 hours for the left eye. Therapy was discontinued and no recurrence of symptoms was noted during the following week of close observation.

There was a slight elevation of temperature not exceeding 1-degree Fahrenheit from the 2nd to the 6th day and occasionally thereafter, possibly due to a subcutaneous inflammation on the left cheek of unknown cause. The highest leukocyte count was 7,700 cells per cubic mm. and the daily urinalysis was normal.

Bacteriologic culture from the eyes taken before inoculation of the infecting organism revealed no known pathogen. Hemophilus sp. was recovered from the right eye in heavy growth on the 2nd and 3rd day and from the left eye on the 4th day. It was not recovered from either eye after specific therapy was started.

Discussion

The immediate effectiveness of streptomycin and streptomycin in combination with rivanol lactate applied locally to the infected eye in relieving the signs and symptoms and reversing the cultural findings is encouraging. It remains to be determined whether other methods of topical application—that is, by instillation or irrigation—and a less rigid treatment schedule would be as effective.

It should be emphasized that the infection treated in this series was localized in the eye and not the respiratory tract, and that intensive treatment was directed against the primary focus. It is possible that cases of conjunctivitis due to Hemophilus influenzae which may be secondary to or concurrent with a primary infection of the respiratory tract would not respond to topical therapy in the same way.

Summary

Acute conjunctivitis resembling clinically that seen in the Rio Grande River Valley was induced in 6 of 8 human volunteers with a culture of Hemophilus sp. isolated from a Texas case, and an organism indistinguishable from the one inoculated was recovered from the affected eyes.

Two acute infections were treated with a solution of streptomycin hydrochloride, (1 mg. per ml.) applied locally in an eyecup, and 2 cases were similarly treated with a combination of streptomycin and rivanol in solution.

The clinical condition improved rapidly, and Hemophilus sp was not isolated from the eyes after the institution of treatment. In 2 cases treated with 0.85-percent NaCl solution as an eye wash, the disease progressed and Hemophilus sp. persisted until the 8th and 9th day when the institution of streptomycin therapy was followed by rapid clinical improvement, and failure to recover the organisms.

National Institute of Health.

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DISCUSSION

DR. KENNTH C. SWAN (Portland, Oregon): In January, 1947, I reported to the Research Study Club of Los Angeles an epidemic of acute conjunctivitis. With some 30 cases, it was possible to treat one eye with streptomycin ointment and the other eye with the ointment base alone. I have forgotten the concentration of streptomycin in the ointment. In that particular oubreak which occurred in Portland, Oregon, the organism was Hemophilus influenzae, although the type was not determined. The results in the streptomycin-treated eye were quite spectacular. In many of the patients, symptoms in the treated eye subsided rapidly after two applications several hours apart. This led several patients to discontinue the ointment in the treated eye and to apply it to the control eye, and then to discontinue treatment. Two of these patients had recurrences. In treatment of the recurrences, the streptomycin ointment was not nearly so effective. We interpreted this decreased response as illustrative of the fact that organisms rapidly became fast to the streptomycin, if treatment is inadequate. I would like to hear the essayist comment on this matter.

Another outbreak of Hemophilus influenzae conjunctivitis occurred last spring in the Portland area but the infection was so mild and of such short duration that it was not always possible to tell the difference between the treated and the untreated eye. The conjunctivitis would clear up in 36 hours; therefore, I did not feel justified to use streptomycin in the hundred or so mild cases of this second outbreak.

DR. JAMES H. ALLEN, (Iowa City, Iowa): In the Midwest we do not find the Koch-Weeks organism, but we do see many cases of conjunctivitis caused by H. influenzae or H. hemolyticus. It is our impression that these infections usually respond readily to treatment with any of the usual conjunctival antiseptics. The lesion most frequently seen is acute catarrhal conjunctivitis with an occasional severe purulent conjunctivitis.

However, I do recall one severe and prolonged unilateral case of conjunctivitis due to H. influenzae. It finally responded to the instillation of drops of streptomycin (100 mg. per cc.). Therefore I would like to ask Dr. Davis if any of his cases tended to remain unilateral? And if he has an explanation for the apparent unusual resistance of these strains of hemophilus to chemotherapy?

DR. ALSON E. BRALEY (New York City): I was very much interested in the disease down there in Texas, this "gnat" conjunctivitis. I saw several of the slides and from the description obtained from the patients with the disease some time ago, there were many particles or whatever you might call them in the slides that could be a very small Hemophilus influenzae. I thought they might possibly be Rickettsia. In the next paper, I think we will have something much more valuable than streptomycin.

DR. PHILLIPS THYGESON (San Jose, California): I should like to make a few comments. When I first became interested in the bacteriology of the eye, while at the University of Iowa, I tried to find a typical Koch-Weeks organism. We had many cases of rather mild, subacute conjunctivitis, such as Dr. Allen has described, but there was only one case that turned out to be typical Koch-Weeks conjunctivitis; this was in a student who was on a motor trip from California.

It seemed to me that there was a clinical distinction, in any event, between the subacute conjunctivitis, from which morphologically typical influenza bacilli could be demonstrated, and the acute conjunctivitis containing typical Koch-Weeks bacilli. In the former the bacilli were characteristically coccobacilli and there was usually an excess of mucus over polys, while in the latter, or typical Koch-Weeks conjunctivitis, the bacilli were slender rods and the exudate was

frankly purulent with a minimum amount of mucus. Thus there appeared to be two types of conjunctivitis associated with hemophilus organisms.

It is true that by ordinary culture methods there were no differences between the hemophilus organisms from these two types of cases, but no typing was done and I have seen no reports as yet of the typing of hemophilus organisms from conjunctivitis. I should therefore like to ask the essayist if he thinks it is possible to settle this question of the relationship or identity of the influenza and Koch-Weeks bacilli.

I should like to comment on the so-called "gnat" conjunctivitis that we have in the Imperial Valley of California. The Imperial Valley, particularly around Indio, is a very hot, dry area comparable, I think, to southern Texas, and there are the same types of recurrent periodic epidemics of acute conjunctivitis associated with gnats and apparently aggravated during the gnat-breeding season, and in which the typical Koch-Weeks organism has been found.

The cases of this condition that I have seen have all been of the acute, severe type and none have been of this milder type observed in Iowa and described by Dr. Allen. I am wondering if the essayist can make any comments on the possible relationship of this California gnat conjunctivitis to the south Texas type.

DR. DAVID G. COGAN (Boston, Massachusetts) : I believe I am correct in saying that in Boston conjunctivitis from Hemophilus influenzae is practically nonexistent in adults. We do have an occasional infection in children, perhaps preferentially in girls, caused by this organism but the clinical picture is unlike that described by the authors in being bilateral and having more evidence of keratitis (lacrimation, photophobia, punctate fluorescein staining) along with the conjunctivitis. I should like to ask the essayist or Dr. Thygeson if they are familiar with such a clinical picture occurring predominantly or exclusively in children.

DR. DAVIS (closing) : First, in regard to this problem of the fastness or resistance of a hemophilus organism to streptomycin, we were well aware of that and made some laboratory experiments to try to shed some light on it. We carried this strain and several strains for about 15 passages through increasing amounts of streptomycin and we were able to increase its resistance about 80 times to streptomycin.

At the same time, Dr. Pittman felt that perhaps if we added another antibacterial agent to the streptomycin, we might be able to reduce that tendency to develop resistance. We selected rivanol. She found in some preliminary experiments that the organisms apparently did not develop resistance to streptomycin as readily in solution of rivanol as when it was in streptomycin alone, and that was the reason we used the streptomycin and rivanol, particularly in these patients.

In regard to the disease in Texas, it is a very severe disease; my experience with conjunctivitis in the rest of the country is extremely limited, but it does not correspond with the ordinary conjunctivitis which has been described, and as Dr. Thygeson said, it does seem to be somewhat different.

As far as the other causes of the disease, we did everything we could with material from these cases to find out some other cause. We searched the stained slides for evidence of Rickettsial bodies or the elementary bodies of trachoma or inclusion conjunctivitis and were able to identify only one case of trachoma among a large number of cases.

We inoculated a great many animals with material that was brought back in a frozen state to the laboratory but we were able to secure no evidence at all of any other cause of the disease.

In regard to this problem of Koch-Weeks, I am sorry that Dr. Pittman isn't here because she could discuss it much more capably than I. As you know, Koch reported seeing the organism in Egypt and Dr. Weeks was

able to culture it, but only in association with another organism, in New York in 1886 and 1887.

This organism which we dealt with down there could be the same as Koch and Weeks wrote about; however, taxonomically, the Koch-Weeks bacillus is not a recognized species, and there are no type strains; none of the organisms which were originally described of course are in existence now.

The organisms which were subsequently isolated from the eye have been indistinguishable from Pfeiffer's influenza bacillus according to our present methods of bacteriologic technique, and they have been considered the same organism in Bergey's *Manual of Determinative Bacteriology.* However, with more recent advances in technique, particularly in the knowledge of the nutritional requirements of this very interesting group of Hemophilic organisms, we may be able to determine whether these strains recovered from the eye are the same as those recovered from respiratory infections.

As far as this disease compares with other conjunctivitis, particularly among children in other parts of the country, I cannot discuss that adequately because of my limited experience with the disease in other parts of the country. However, it is a very severe disease, as you can see, in the southern United States. It is a disease chiefly of children and occurs mainly in the group under five years of age; it is a disease of people of poor and economically low status, although it spares no one.

It is both highly contagious and infectious. Whole families will be infected and one after the other will come down with it. It may last for a short period of time only with a very mild case, and many are self-limited; or it may persist for several weeks, up to six weeks or longer. Some of the patients we saw were said to have had it for six weeks or two months.

AUREOMYCIN IN OCULAR INFECTIONS*

A STUDY OF ITS SPECTRUM

ALSON E. BRALEY, M.D., AND MURRAY SANDERS, M.D.
New York

Aureomycin is an antibiotic obtained from a mold belonging to the Streptomyces group. It was isolated by workers at the Lederle Laboratories of the American Cyanamid Company.[1] This antibiotic was found by these workers to be effective against both Gram-positive and Gram-negative organisms, and their work suggested a wide range of activity. It has been made available to us in two forms, Aureomycin hydrochloride and Aureomycin borate.

Aureomycin HCl is a dry, crude, crystalline substance, yellow in color. When in aqueous solution it is an acid with a pH of 3.0 and is stable either in the dry form or in solution without refrigeration. In solution it can be injected intramuscularly. The dry material is quite soluble in water or normal saline; 20 mg. will dissolve in 1 cc. to 1.5 cc. of normal saline. This material is moderately irritating when injected intramuscularly, but with the addition of a small amount of procaine hydrochloride there is little or no discomfort.

A borated salt of Aureomycin was also manufactured and dried into a fine, yellow, stable powder. In aqueous or physiologic saline solution the pH is 7.5 to 7.8. It is very soluble in nearly all concentrations; however, in solution at room temperature the material loses its antibiotic activity within approximately 24 hours. Various concentrations of the borate were used, but it was found that a 0.5-percent solution was the one best tolerated. The activity of the 0.5-percent solution is retained for several days when it is stored at +4°C. Freshly prepared Aureomycin-borate solution is a light golden-yellow color;

after it has remained at room temperature for 24 hours, it turns a golden-brown.

Wong and Cox[2] have shown in experimental infections with a wide range of microörganisms, rickettsia, and viruses that Aureomycin was unusually potent and active. Since this was true experimentally, it was felt that this new antibiotic should be tried in many types of ocular infections. The antibiotic was used in this study much the same as penicillin might be used clinically. The borated salt was used locally in eyes for infections of the conjunctiva and cornea. When infection was present in the deeper structures of the eye, such as uveitis and in ocular infections associated with general disease, the local application was augmented by intramuscular injections of Aureomycin HCl.

In a previous report 100 patients with conjunctival and corneal infections have been reported.[3] It was found from this study that local use of Aureomycin borate effectively inhibited staphylococci, pneumococci, and H. influenzae. It was also active against the virus of inclusion conjunctivitis and appeared to have some value in herpes simplex corneae and to a lesser extent in epidemic keratoconjunctivitis. Since that time additional information has been obtained regarding these same organisms, as well as other ocular infections.

The present study was made in an attempt to find the number of diseases and microorganisms in which Aureomycin might be effective. The use of Aureomycin in 401 unselected cases showed that the antibiotic was effective in the treatment of 303 and of no value in 98. This can be further separated into 383 cases in which the infection was primarily of the conjunctiva and cornea and

18 cases in which the infection was primarily of the uvea.

STAPHYLOCOCCAL INFECTIONS

In all, 202 patients with various types of staphylococcal infections were treated. The majority had blepharitis combined with a conjunctivitis, and keratitis. There were, however, a fair number of cases with marginal infiltrates and marginal ulcers associated with the chronic conjunctivitis. A few patients had hordeola and chalazia complicating the blepharitis.

For statistical purposes we divided staphylococcal infections into mild and severe cases. There were 47 patients in the group considered mild, those with a blepharitis squamosa and a chronic conjunctivitis associated with a slight discharge. Severe staphylococcal infections were those with a blepharitis with an acute or subacute conjunctivitis combined with corneal changes such as superficial punctate keratitis, marginal infiltrates, or marginal ulcers.

The evaluation of the results of Aureomycin in staphylococcal infections was difficult because of the tendency for recurrence of all types of staphylococcal infections, and the inclination of the patient to discontinue treatment as soon as the acute symptoms subsided. In order to evaluate the effectiveness of the antibotic an arbitrary 48 hours was chosen as the time limit for disappearance of symptoms; if there was no improvement in the objective appearance or symptoms, the action of the antibiotic was considered unfavorable.

There is little doubt, as reported in the previous publication, that Aureomycin is very active against the staphylococcus, whether the disease produced by it is mild or severe. From experience with these patients it seems to be as potent as local penicillin (1,000 units per cc).

Staphylococcal conjunctivitis had a tendency to recur when therapy was discontinued; recurrences were about the same with Aureomycin as with other local antibiotics. Aureomycin was potent in patients with staphylococcal conjunctivitis who had developed a sensitivity to the local use of penicillin.

Staphylococcal infections require local therapy for a long period of time and since a transition occurs in Aureomycin borate solution, an attempt was made to prepare an ointment with both the hydrochloride and the borate. The hydrochloride ointment was irritating to nearly all of the patients although it seemed to be active against the infection. The ointment prepared with the borate was nonirritating but it probably lost its activity after a short period. Further investigation will be necessary to determine the best means of retaining this antibiotic effect for the required prolonged use in staphylococcal infections.

There were 12 unfavorable responses to Aureomycin in the entire group. The organisms could have been assayed to determine the amount of the antibiotic necessary to inactivate them, but it is possible that the patients did not use the antibiotic as directed.

PNEUMOCOCCAL CONJUNCTIVITIS

The second largest group of patients with bacterial conjunctivitis was infected by the pneumococcus. The patients with pneumococcal conjunctivitis have been treated; there were excellent results and no recurrences.

MENINGOCOCCAL CONJUNCTIVITIS

In one case the response to local Aureomycin was prompt.

INFLUENZAL CONJUNCTIVITIS

The response of 8 patients from whom influenza bacilli were cultured from the conjunctiva was rapid and efficient. In all of the patients the purulent discharge was entirely gone within 24 hours. It was difficult to evaluate the antibody response to influenzal conjunctivitis since the duration of this infection without treatment varied considerably. From the appearance of the conjunctiva, however, we felt that Aureomycin

was potent against H. influenza. Further investigation will be necessary, particularly in influenzal meningitis, to determine the degree of potency.

DIPLOBACILLARY INFECTIONS

The diplobacillus of Morax-Axenfeld has been an organism which has not responded well to any form of therapy. In 5 cases the symptoms were relieved and no bacteria found on scrapings of the conjunctiva after local use of Aureomycin. In one patient a recurrence developed in one eye shortly after the antibiotic was discontinued, while in 3 patients no definite improvement was noted. From all clinical appearances, however, Aureomycin is much more effective against the diplobacillus than any other therapy.

E. COLI

Aureomycin borate was used in only one case of infection of the conjunctiva by E. coli. A pure culture of E. coli was obtained from the conjunctiva after several months of conjunctivitis. Following the use of this antibiotic for 24 hours, conjunctival symptoms were entirely gone and the conjunctiva was free of organisms.

PROTEUS VULGARIS INFECTIONS

Of 3 cases, one showed improvement following Aureomycin therapy. There was one recurrence which responded to a second course of treatment. The third case showed no improvement.

VIRAL INFECTIONS

Two viruses involving the conjunctiva and cornea have been treated with Aureomycin, 21 cases of dendritic keratitis and 53 cases of epidemic keratoconjunctivitis. Clinically Aureomycin appears to be more useful in the herpes corneae virus than in epidemic keratoconjunctivitis.

DENDRITIC KERATITIS

All 21 of the patients with dendritic keratitis had an associated beginning involvement of the corneal stroma with an area of infiltration under the dendritic figure. In 13 of these patients the results after use of Aureomycin were rapid and beneficial. The ulcer was healed in 24 hours and there was no increase in the size of the infiltrate beneath the ulcer, and in most of the patients the infiltrate disappeared entirely. In one patient who had a recurrent dendritic keratitis with a large disciform keratitis there was no appreciable change in the involvement of the corneal stroma after Aureomycin. Seven patients showed no improvement. From our experience thus far with the antibiotic, it seems to be a valuable therapeutic agent for dendritic keratitis.

EPIDEMIC KERATOCONJUNCTIVITIS

The use of Aureomycin in the treatment of epidemic keratoconjunctivitis does not appear effective from the data presented. Fifty-three patients with the infection have been followed after the use of the antibiotic. There were many more patients with epidemic keratoconjunctivitis who had used Aureomycin, but their follow-up was not entirely satisfactory and they cannot be included in the series.

The course of the disease was not affected in 28 of the 53 patients, but 25 showed a definitely favorable reaction. These patients taught us a good deal as to how this new antibiotic should be used. Certainly in epidemic keratoconjunctivitis, Aureomycin must be used before corneal opacities begin, since in several of the 28 patients it was started after corneal opacities were first noted.

It appears that if Aureomycin can be started before the 3rd to 5th day of the disease and used continually for at least a week or 10 days there is some beneficial effect. If the material is instilled in the conjunctival sac every one-half to one hour and continued, even though the symptoms and edema of the conjunctiva increase, there will certainly be some favorable result.

Most of the 25 favorable cases developed 1

or 2 typical corneal opacities at about the same time as they would had the disease been allowed to run its normal course, but the conjunctival findings and the corneal changes were considerably decreased as compared to control cases. Even though Aureomycin was used, a few developed conjunctival scars and minimal symblepharon.

Patients who used the antibiotic a few times and discontinued its use after 24 or 48 hours because of its slight irritability received no benefit from the antibiotic. The method of choice, therefore, in treatment of epidemic keratoconjunctivitis should be the instillation of Aureomycin borate every hour for at least 10 days with a fresh supply of the antibiotic given at 48-hour intervals. Blood has been obtained from the patients for neutralization of the virus to determine the presence of antibodies.

FOLLICULAR CONJUNCTIVITIS, UNKNOWN ETIOLOGY

The evaluation of the use of Aureomycin in follicular conjunctivitis is rather difficult since this group contains a number of patients with what clinically appeared to be a Beal's type of conjunctivitis. This type of follicular conjunctivitis is notoriously inconsistent in the duration of symptoms. With Aureomycin, however, none of the cases of follicular conjunctivitis lasted more than 48 hours.

INCLUSION CONJUNCTIVITIS AND TRACHOMA

Local Aureomycin was used in 6 cases of inclusion conjunctivitis. Most of these were in the newborn infant after the disease had been present for from 5 days to 2 weeks. The response to Aureomycin was prompt and the purulent discharge was entirely gone after 24 hours of its use. The conjunctiva returned to normal within 3 days to 1 week. Some of the cases have been followed with daily scrapings from the conjunctiva; no inclusion bodies could be found after 24 hours on Aureomycin.

One case of trachoma III which had been recurrent for 20 years was treated. This patient had developed anuria on sulfanilamide. Following treatment with local Aureomycin there was rapid disappearance of corneal infiltrates and conjunctival symptoms. No inclusion bodies could be demonstrated from the conjunctival scrapings. From the effect of Aureomycin on inclusion conjunctivitis and lymphogranuloma we feel that it should also be effective in trachoma.

MOLLUSCUM CONTAGIOSUM

One patient with molluscum contagiosum has been treated with Aureomycin locally. There was no effect on the tumor or on the appearance of the conjunctiva.

KERATITIS

Of the various types of keratitis, 34 cases have been treated. Some of these have been remarkable, particularly one patient with a severe marginal keratitis of unknown etiology. This patient had marked thinning of the periphery of the cornea, and the central cornea was necrotic. His vision was reduced to hand movements in one eye and 20/400 in the other eye. After local and parenteral Aureomycin the process stopped and the central portion of the cornea became clear while the periphery vascularized. The vision was restored to 20/25 in one eye and 20/20 in the other.

Six cases of acne rosacea keratitis have been treated, 1 with some beneficial effect and 5 without any effect. It is doubtful that any of the various types of keratitis profunda or severe types of keratitis are particularly benefited by Aureomycin although 9 of the 16 cases improved under Aureomycin therapy.

Pyocyaneus infections of the cornea were not helped by treatment.

Two patients with neurotropic type of keratitis were unaffected by Aureomycin.

PARINAUD'S CONJUNCTIVITIS

Only 2 patients with Parinaud's conjunctivitis were treated with Aureomycin with no

effect on the progress of the disease in one case and slight improvement in the other.

VERNAL CONJUNCTIVITIS

Of the 8 cases of vernal conjunctivitis which have been treated with varying amounts of local Aureomycin, 6 were unchanged but 2 showed a disappearance of the filmy membrane and some relief of symptoms, although there was no changt in the papillary hypertrophy in the conjunctiva. It is probable that the improvement was due to the antibiotic action on the secondary infection.

UVEITIS

All of the patients with uveitis have been treated with local borate salt and intramuscular Aureomycin HCl. Of the 18 patients with various types of uveitis, 8 have shown beneficial results while 10 have remained unchanged.

The most striking in this group are 2 patients with scrofuloderm combined with keratitis and uveitis. Not only was the eye restored to normal vision, but there was also marked improvement in the draining sinuses and skin reaction associated with the underlying lymph-node disease. In one of these patients tubercle bacilli were demonstrated in biopsies of the lymph nodes, and in the other the biopsy and guinea-pig inoculation were unsatisfactory.

There are under observation at the present time two other patients with tuberculous lymphadenopathy and keratitis. The response of the cornea has been prompt, but there has been no change in the lymphadenopathy so that these cases have not been included in this study. The response to Aureomycin in these cases is certainly as satisfactory as with streptomycin.

One patient with a recurrent unilateral uveitis in whom a positive Frei test was found responded dramatically to treatment with Aureomycin. She developed a recurrence two weeks after receiving 100 mg. intramuscularly and was given another course of 100 mg. with complete recovery.

Seven cases of uveitis of unknown etiology have received Aureomycin; 4 have shown definite improvement while 3 have remained unchanged. Several more patients are under observation at the present time, but the effectiveness of the antibiotic is doubtful.

Two cases of sympathetic ophthalmia were given Aureomycin without any beneficial result, although one patient insisted on receiving it for a long period of time because he stated that his eyes felt better; there was no change in the clinical appearance of the eye.

One patient with a metastatic endophthalmitis of unknown etiology has been treated. She had developed a large abscess in the vitreous with pus in the anterior chamber following considerable abdominal surgery. She was given 300-mg. intramuscular Aureomycin and local drops after which all of the pus disappeared. A red reflex could be obtained from the fundus but, because of the vitreous opacities, it was impossible to see the fundus details at the time of her discharge from the hospital. The eye has remained quiet since that time.

COMMENTS

We have previously reported on the antibiotic properties of local Aureomycin in staphylococcal, pneumococcal, and influenzal conjunctivitis. To this group we are adding the diplobacillus of Morax-Axenfeld and E. coli. Several diseases of unknown etiology were treated in an attempt to determine the spectrum of the antibiotic.

The validity of Aureomycin in some of the virus infections was not anticipated. From the experiments of Wong and Cox[2] we learned that it should be of value in the psittacosis-lymphogranuloma group and in rickettsial diseases.

In our experience Aureomycin was excellent in the treatment of inclusion conjunctivitis. Because of the similarity between the virus of trachoma and the virus of inclusion, it should be a useful therapy for trachoma.

Aureomycin seems to have some antibiotic properties to the virus of herpes simplex. The results of its use on herpes infections of the cornea were striking. Experimental herpes-simplex infections will be reported later, although at the present time they indicate had been used for a period of 48 hours, it became somewhat irritating to the conjunctiva, in cases of epidemic keratoconjunctivitis particularly, and many patients thought it produced a more severe conjunctivitis. We found that the applications

TABLE 1

RESULTS OBTAINED IN AUREOMYCIN TREATMENT OF 401 OCULAR INFECTIONS

Infection	No. of Cases	Clinical Cure	No Improvement
Conjunctivitis			
Staphylococcus aureus			
mild	47	40	7
severe	155	150	5
D. pneumoniae	10	10	
Meningococcus	1	1	
H. influenzae	8	8	
Moraxella lacunata (diplobacillus of Morax-Axenfeld)	9	5	4
E. coli	1	1	
Proteus vulgaris	3	2*	1
Follicular (etiology unknown)	17	17	
Inclusion conjunctivitis	6	6	
Trachoma	1	1	
Vernal	8	2	6
Epidemic keratoconjunctivitis	53	25	28
Molluscum contagiosum	1		1
Parinaud's conjunctivitis (leptothricosis)	2		2†
Keratitis			
P. Pyocyaneus	2		2
Dendritic (herpes simplex)	21	13	8
Unclassified (etiology unknown, probably infectious)	16	9	7
Acne rosacea	6	1	5
Superficial punctate (virus?)	7	2	5
Neurotropic	2		2
Marginal, severe	3	2	1
Herpes zoster	2		2
Pinguecula	1		1
Episcleritis	1		1
Uveitis			
Idiopathic	7	4	3
Lymphogranuloma	1	1	
Scrofuloderm with uveitis and keratitis	2	2*	
Sympathetic ophthalmia	2		2
Endophthalmitis, metastatic	1	1	
Ritter's syndrome	1		1
Bechet's syndrome	2		2†
Harada's syndrome	2		2
Total	401	303	98

* One case recurred but responded to a second course of treatment.
† One case showed some improvement.

cate that Aureomycin has some antiviral properties.

Its use in epidemic keratoconjunctivitis is not entirely satisfactory, but there is a strong indication from several patients that if the antibiotic is used properly considerable benefit may be expected. After Aureomycin bor-

of the antibiotic must be continued in spite of increased symptoms in order for it to be beneficial. There is no change in epidemic keratoconjunctivitis much short of a week. If the material was used conscientiously by the patient, the period of morbidity was shortened from approximately 3 weeks to a

TABLE 2

OCULAR INFECTIONS WHICH SHOULD RESPOND WELL TO AUREOMYCIN THERAPY

Virus infections
  inclusion conjunctivitis*
  trachoma*
  lymphogranuloma venereum†
  herpes simplex corneae*
  follicular conjunctivitis*
Hemolytic streptococcus infections
  conjunctivitis† (membranous)
  corneal ulcers†
  endophthalmitis†
  orbital cellulitis†
  impetigo*
Staphylococcus infections
  dacryocystitis
  conjunctivitis*
  ulcers*
  endophthalmitis†
  blepharitis*
  orbital cellulitis
  impetigo*
Pneumococcus infections
  dacryocystitis
  conjunctivitis*
  ulcers†

  endophthalmitis
  orbital cellulitis
Conococcus infections
  conjunctivitis
  iridocyclitis
Proteus infections
  conjunctivitis
Coliform group infections
  conjunctivitis*
H. influenzae infections
  conjunctivitis*
  ulcers†
  orbital cellulitis
Diplobacillus (Morax-Axenfeld)
  conjunctivitis*
  ulcers†
Friedländer bacillus infections
  ulcers†
  conjunctivitis*
  meibomitis†
  dacryocystitis
Meningococcus infections
  endophthalmitis
  conjunctivitis

* Local therapy preferred.
† Combined intramuscular and local therapy preferred.

TABLE 3

OCULAR INFECTIONS IN WHICH AUREOMYCIN MAY BE OF VALUE AND DESERVES TRIAL

Virus infections
  epidemic keratoconjunctivitis*
  herpes zoster†
  herpes simplex corneae*
Tuberculosis
  conjunctivitis* (ulcers)
  uveitis†
  keratitis
  scrofuloderm†
  kerato-uveitis
Nonhemolytic streptococcus infections
  orbital cellulitis
  endophthalmitis
  corneal ulcers

Brucella melitensis-abortus-suis
  keratitis
  uveitis
  choroiditis
Moraxella duplex (diplobacillus of Petit)
  central ulcers
H. Ducreyii
  soft chancre of lid or conjunctiva
Syphilis
  chancre of lid
  choroiditis
  optic atrophy
Keratitis (marginal) unknown etiology
Uveitis (idiopathic)

* Local therapy preferred.
† Combined intramuscular and local therapy preferred.

TABLE 4

OCULAR INFECTIONS IN WHICH AUREOMYCIN PROBABLY IS OF NO VALUE

Erythema multiforme
  conjunctivitis
  keratitis
Ocular pemphigus
Parinaud's conjunctivitis
  leptothricosis

Pyocyaneus infection
  ulcer
Sympathetic ophthalmia
Vernal conjunctivitis
Molluscum contagiosum
Mooren's ulcer
Streptothrix concretions

period of 10 days. The corneal opacities which developed were usually minimal as compared to control cases.

Aureomycin had no effect on the virus of molluscum contagiosum.

Aureomycin was surprisingly effective in 14 cases of follicular conjunctivitis. In none of these was it possible to determine the etiology.

Six cases of vernal conjunctivitis were treated and no particular result was anticipated. It is well known that any of the antibiotics will have some tendency to give a certain degree of subjective improvement, and it is doubtful if Aureomycin will have any effect on vernal conjunctivitis.

Although one case of Parinaud's conjunctivitis due to the leptothrix was treated, no beneficial effect was anticipated because of the similarity between the leptothrix and the actinomyces from which Aureomycin is made.

In the treatment of uveitis and keratitis, it was not possible to determine in advance which patients would be improved. There is little doubt in our minds that there was marked improvement in the patients with scrofulous keratitis and scrofuloderm. There is also little doubt that the antibiotic produced improvement in several cases of uveitis of unknown etiology.

muscularly in 401 patients with a wide range of ocular infections. The local use of 0.5-percent solution produced no damage to the conjunctiva or cornea.

This antibiotic was found to be effective against some of the Gram-positive cocci and several Gram-negative bacilli. It was also found to be an effective therapeutic agent in inclusion conjunctivitis and in herpes simplex of the cornea.

Its therapeutic effect in epidemic keratoconjunctivitis will require further investigation before results can be evaluated. It is, however, more effective in epidemic keratoconjunctivitis than any of the other antibiotics or drugs tried.

The intramuscular administration of Aureomycin HCl did not give rise to any toxic reactions and in only one individual was any general effect noted. The patient developed a secondary anemia which was easily controlled by the administration of iron.

The HCl is somewhat irritating on intramuscular injection, but this irritation can be controlled by the addition of a small amount of procaine hydrochloride.*

There is some indication that Aureomycin may be a valuable antibiotic in the treatment of uveitis.

Aureomycin has a wide spectrum of activity in ocular infections.

635 West 165th Street (32).

SUMMARY

Aureomycin borate has been used locally and Aureomycin HCl has been used intra-

* Because of the pain associated with intramuscular Aureomycin, since this report most of the antibiotic has been given intravenously without pain or side effects.

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DISCUSSION

DR. PHILLIPS THYGESON (San Jose, California): I realize that Aureomycin has not been available for general use. I begged a small supply of it from Dr. Braley and Dr. Sanders for a case of bilateral tuberculous keratitis which had responded temporarily

to streptomycin but had subsequently relapsed, and I am very happy to say that this man's keratitis quieted down very rapidly on 40 mg. a day and that his vision has improved in one eye from 20/100 to 20/50, and in the other eye from hand movements to 20/70.

I used Aureomycin topically in one other case, that of a nurse with what we considered to be an epidemic keratoconjunctivitis, prior to onset of corneal lesions. She had been exposed to a known case of epidemic keratoconjunctivitis and had the preauricular adenopathy, follicle formation, and mononuclear cell exudate typical of epidemic keratoconjunctivitis.

The borate was administered topically only. The patient failed to develop any corneal signs and the course was much milder than in any of the previous cases we had studied.

DR. BRALEY (closing) : I would like to thank Dr. Thygeson for his remarks. I am extremely enthusiastic about this material and feel that it would certainly justify wide trial when and if the material is available.

UVEITIS AND TOXOPLASMIN SENSITIVITY*

J. K. FRENKEL, M.D.
Hamilton, Montana

During an experimental and clinicopathologic study of toxoplasmosis, a skin testing antigen (toxoplasmin) has been developed[1] providing a basis for a relatively rapid and accurate diagnosis of past and chronic[2] infection with toxoplasma. This paper serves as a preliminary report on studies of patients with uveitis, designed to draw further attention to an etiologic entity more prevalent than generally suspected. Previous studies of ocular toxoplasmosis, such as those of Koch, Wolf, Cowen, and Paige,[3] Heath and Zuelzer,[4] and of others,[4a] dealt with histopathologic aspects of the infection. Vail, Strong and Stephenson,[5] Heidelman,[6] Johnson,[7] and others[7a-e] investigated patients with chorioretinitis for the presence of neutralizing antibodies to toxoplasma, as demonstrated by the rabbit test of Sabin and Ruchman.[8]

The toxoplasmin skin test served as diagnostic agent in the study reported here. It was controlled by the use of (a) the toxoplasma neutralizing antibody test (on the rabbit skin), (b) the toxoplasma complement-fixation test[†, 9, 10] and (c) a survey of toxoplasmin sensitivity in two groups of individuals without eye diseases, selected for their age only. A detailed evaluation of the results obtained by the use of these tests and correlation with the clinical syndromes exhibited by patients will be reported in a more extensive publication. Suffice it to say that the skin test proved to be simpler and more reliable than the other two tests used.[‡, 1]

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† Performed by Dr. Carl M. Eklund and Dr. David B. Lackman, both of the Rocky Mountain Laboratory, Hamilton, Montana.

‡ Recently Sabin and Feldman[11] described a serologic test for toxoplasma antibody, employing dyes as microchemical indicators, which is more informative than the more easily performed skin test. Their new test provides quantitative data in all stages of the disease; whereas, the results of the skin test are qualitative only and its main usefulness is in chronic toxoplasmosis (uveitis) and in surveys.

J. K. FRENKEL

CLINICAL STUDIES

The majority of the patients with uveitis were seen in the eye clinic of the University of California Hospital, San Francisco, where a study on the etiology of uveitis, supported by the Francis I. Proctor Foundation for Research in Ophthalmology, was being conducted. As part of that study patients' sera were submitted for serologic tests for syphilis. Brucellergin tests were performed and,

mal individuals. Hence, evaluation of data not pertaining to toxoplasmosis will be deferred.

The results of toxoplasmin tests conducted in 1947 and 1948 on groups of patients with chorioretinitis and anterior uveitis, and on two control groups of young healthy individuals and of older hospital patients with cardiac or neoplastic diseases, are presented in Table 1.

TABLE 1

TOXOPLASMIN SENSITIVITY

Grouping	Years of Age	Total No.	Numbers Pos.	Numbers Neg.	Percent Pos.	Percent Neg.
Patients with chorioretinitis	Mean 23	28	20	8	71	29
Patients with anterior uveitis	Mean 35	40	13	27	33	67
Mothers of toxoplasmin-positive patients		8	8	0	100	0
Young healthy individuals	20–35	50	5	45	10	90
Older hospital patients	50–83	50	14	36	28	72

when positive, were followed up by agglutination and complement-fixation tests with Brucella antigen. Tuberculin, coccidioidin, histoplasmin, and Frei tests were also done routinely and, occasionally, the Kveim test for sarcoidosis was carried out.

None of the patients revealed any data as to previous illness, residence, or animal contacts that could be correlated in respect to toxoplasmosis. Apart from the tests for toxoplasmosis, enumerated above, electroencephalograms, skull roentgenograms, and psychometric studies were made on many toxoplasmin-positive patients.

Relatively few of the tests for diseases other than toxoplasmosis were positive. Certain patients had a history, with physical signs as well as laboratory evidence, of syphilis; others had lymph-node biopsies and radiologic findings suggestive of sarcoidosis. In only one of the toxoplasmin-positive patients with chorioretinitis and taboparesis, were significant dual etiologic factors uncovered. In addition to the statistically small and scattered number of positives that implicated other etiologic factors, evaluation of such tests was made difficult, since they had not as yet been conducted on groups of nor-

CHORIORETINITIS (GRANULOMATOUS POSTERIOR UVEITIS)

The incidence of toxoplasmin sensitivity in patients with chorioretinitis was 71 percent as compared to an incidence of 10 percent in a group of healthy individuals of similar age. Although the mean age of toxoplasmin reactors with chorioretinitis when first seen was 23 years, their mean age when the disease was first noted was 13 years. This contrasts with an average of 28 years, for both date of onset and when first seen, in toxoplasmin-negative patients with chorioretinitis. The high incidence of toxoplasmin sensitivity in this group is considered very significant. The actual difference between the incidence of toxoplasmin positivity in patients with chorioretinitis and the control group is 5.5 times the standard error of the difference.*

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* The following formula to test for significance of the difference between proportions was used:

$$\sigma_{D\%} = \sqrt{pq\left(\frac{1}{N_1} + \frac{1}{N_2}\right)}$$

where p is the total percentage of occurrence
$q = 1 - p$
$N_1 =$ number in first sample
$N_2 =$ number in second sample

ANTERIOR UVEITIS

Although the incidence of toxoplasmin sensitivity (33 percent) in this group exceeds the incidence in the control group (10 percent) of comparable age, the difference is not as great as in the patients with chorioretinitis. A breakdown of positive and negative reactors according to the type of uveitis is presented in Table 2.

TABLE 2

TOXOPLASMIN REACTION IN PATIENTS WITH ANTERIOR UVEITIS

| Skin Test | | Numbers | |
		Granu-lomatous	Nongranu-lomatous
Positive	13	10	3
Negative	27	15	12
Total	40	25	15

The predominance of granulomatous (10 cases or 77 percent) over nongranulomatous anterior uveitis (3 cases or 23 percent) in the toxoplasmin positive group and the relative scarcity of positive skin tests in the nongranulomatous group of patients (only 3 out of 15 cases, or 20 percent), suggest certain correlations. The actual difference between the incidence of toxoplasmin sensitivity in the patients with granulomatous anterior uveitis and the normal control group is 3.06 times the standard error of the difference. Comparing the nongranulomatous and the control groups the difference is not significant.

Wood[13] presents evidence "that in granulomatous uveitis the various recognized, specific etiologic agents are present in living form in the uveal tract," associated with a bacterial type of hypersensitivity. In nongranulomatous uveitis a sensitization without infection of ocular tissues, which may be either bacterial or both anaphylactic and bacterial, is thought to be present.

As will be further discussed below, in toxoplasmic uveitis, organisms are likely to be present within the uveal tract. This further supports the statistical evidence in favor of a toxoplasmic etiology in 10 out of 25 cases, or 40 percent of all patients with granulomatous anterior uveitis. According to the interpretation of the survey, a small majority of patients with granulomatous anterior uveitis and most of the patients with nongranulomatous uveitis must be assigned an etiology other than toxoplasmosis for their ocular disease.

OTHER GROUPS

The frequent concurrence of positive tests for toxoplasmosis in young patients and their mothers has frequently been noted. Their similar habitat with equal chances for exposure may account for these instances, while transmission of the infection from mother to infant in utero has also been observed.

The increased incidence with age of toxoplasmin sensitivity in the general population is noteworthy and suggests that infection is contracted throughout life. None of the 19 positive individuals in the control group and none of the 8 mothers had uveitis. Only one young man had a history of an obscure disease with a rash and encephalitic symptoms when aged 21 years. In general, the impression is gained that more damage may be produced if toxoplasmic infection occurs in the young; whereas, in older individuals asymptomatic infection appears to be the rule.

SEX DISTRIBUTION.

Comparison of toxoplasmin sensitivity in males and females is presented in Table 3. Patients with chorioretinitis and anterior uveitis are listed as in Table 1, the grouping "Mothers of toxoplasmin positive patients" has been omitted, and the control group consists of individuals without eye disease, without regard to age, essentially a merging of the two control groups of Table 1.

In the control group, 24 percent of women but only 16 percent of men were toxoplasmin positive. Again, among patients with chorioretinitis, more women reacted to toxoplasmin (82 percent) than did men (55 percent). There were more than twice as many toxo-

plasmin sensitive women (14, or 70 percent) than men (6, or 30 percent) with chorioretinitis. Patients with anterior uveitis showed the reverse relationship. The numbers recorded here merely indicate a trend; they are not large enough to be statistically significant.

induration appear 24 to 72 hours after injection of toxoplasma antigen. Histologically, there is vascular damage, with exudation of fluid and cells, sometimes accompanied by necrosis, if the amount of antigen is large.

Chorioretinitis is thought to be due to the rupture of a pseudocyst in the retina, which

TABLE 3

SEX DISTRIBUTION OF TOXOPLASMIN SENSITIVITY

Group of Patients	Skin Test	Total No.	Numbers		Percent	
			Males	Females	Males	Females
Chorioretinitis	Positive	20	6	14	55	82
	Negative	8	5	3	45	18
	Total	28	11	17	100	100
Anterior uveitis	Positive	13	8	5	42	24
	Negative	27	11	16	58	76
	Total	40	19	21	100	100
Control	Positive	22	10	12	16	24
	Negative	90	53	37	84	76
	Total	112	63	49	100	100

TREATMENT

PATHOGENESIS OF TOXOPLASMIC UVEITIS

In another paper[2] the pathogenesis of toxoplasmosis was discussed. For the purpose of developing a rationale for the treatment used, it is essential here only to keep in mind the persistence of organisms long after the acute infection. This has been proven visually and by isolation in animals[12] and it is likely to occur also in man, judging from autopsy observations.[17]

Toxoplasma in both man and animals has been found in so-called "pseudocysts," which have a definite cyst wall that is argyrophilic. Such pseudocysts or cysts may lie dormant for long peroids of time in the brain as well as in the eye as indicated by the lack of host reaction to their presence. If such a cyst ruptures, organisms and soluble antigen are released and the resulting tissue reaction is characteristic of the delayed (bacterial) type of hypersensitivity.[12]

This hypersensitivity reaction is also the basis for the skin test, where erythema and

is accompanied by an intense hyperergic inflammatory reaction. Pseudocysts have been seen in the retina of patients with subacute toxoplasmosis at autopsy, and in both retina and iris of experimental animals with chronic toxoplasmosis.[12]

Due to the relative poverty of humoral antibody in the neuro-ectodermal tissues and fluids (associated with the blood—neuro-ectodermal barrier for protein), much time passes before organisms and antigen released by the pseudocyst can be neutralized or phagocitized. Treatment was aimed, therefore, at increasing the antibody level in the blood and intercellular fluid by injections of carefully graded and increasing doses of toxoplasma antigen. The greater amount of available free antibody may then be capable of binding and neutralizing the antigen in the intercellular fluids, thereby minimizing the intensity of the same reaction taking place on the more vulnerable cell surfaces.

INDICATION FOR TREATMENT USED

Such toxoplasma antigen injections have

been given to patients with chorioretinitis who were toxoplasmin positive and who showed active chorioretinitis, usually accompanied by vitreous exudate. In these patients the correlation between the eye lesions and toxoplasmin sensitivity was deemed significant and no definite evidence of other etiology was uncovered. One patient was treated who suffered with both chorioretinitis and a granulomatous anterior uveitis. She also had a positive tuberculin test, but without evidence of chest disease, and had been treated unsuccessfully with tuberculin for several years. No patient with anterior uveitis alone was treated since the correlation between toxoplasmin sensitivity and the granulomatous eye lesions was not made until later.

Since nonspecific protein therapy is thought to increase the shedding of antibody into the blood stream, intravenous typhoid bacterin injections were frequently used in conjunction with toxoplasma antigen.

Although sulfonamide therapy suppresses toxoplasmic proliferation, it was not considered useful in the cases under study. The chorioretinal lesions are thought to be due more to the liberated antigen, which does not quickly diffuse out of the interstitial fluid and vitreous, than due to proliferation of toxoplasma within the retina. Actually, sulfonamide therapy had been given to several patients before they were seen by me. In no case did the referring physician note any improvement of the lesions that could be attributed to that therapy.

TECHNIQUE OF TREATMENT

After the initial toxoplasmin skin test, every patient who appeared to fufill the indications for treatment was informed as fully as possible (or the parents, in case of a minor) of the experimental nature of the treatment contemplated. This was instrumental in securing full coöperation of all patients and gained their enthusiasm for repeated venipunctures to follow antibody levels.

Depending on the amount of redness and induration developed in the skin test, a dose was chosen between one tenth and one hundredth of the skin test dose to commence potentially immunizing, intradermal antigen injections (desensitization). It was desired to keep the resulting skin reactions under 10 millimeters of redness with a minimum of induration. These injections were given twice weekly and the dose of antigen was increased as tolerated. At every visit the visual acuity was determined and the fundus was visualized, while fundus photographs or drawings and visual field measurements were made at irregular intervals to record the changes occurring.

RESULTS OF TREATMENT

Of the 9 patients treated by toxoplasmin injections, the lesions became inactive during treatment in 8 as indicated by disappearance of the vitreous exudate, decreased retinal edema and infiltration, and beginning pigment deposition. One of these patients was treated for nearly a year until the acute perimacular lesions became quiescent and started to become pigmented.

A 9th patient, who had both chorioretinitis and a granulomatous iridocyclitis, associated with a positive tuberculin test, did not improve during 6 weeks of toxoplasma antigen and typhoid bacterin injections and her anterior uveitis became more severe during that period. Subsequently, she had a course of treatment consisting 2 gm. each of sulfadiazine and sulfamerazine and paracentesis of the anterior chamber daily for 10 days, followed by 1 gm. streptomycin daily for a month. Neither of the therapeutic regimes was accompanied by improvement of the uveitis. Previously, she had had a course of penicillin injections and tuberculin therapy, likewise without effect.

Since the course of the lesions cannot be predicted, any improvement in the 8 patients, occurring during treatment, cannot necessarily be ascribed to it. The results of this experimental treatment are recorded here to

point a way for careful and prolonged clinical research work, which should be controlled by the immunologic and serologic tests for toxoplasmosis already mentioned.

DISCUSSION

SPECIFICITY OF THE TOXOPLASMIN SKIN TEST

Comparison of toxoplasmin sensitivity in normal guinea pigs and in those with chronic, latent toxoplasmosis showed a high degree of specificity for the test. These findings were supported by a significant degree of correlation between skin hypersensitivity and the presence of toxoplasma neutralizing antibodies in man.[1] Further confirmation was obtained by the anamnestic appearance or the rise of complement-fixing and neutralizing antibodies, following injection of the skin test antigen into indivdiuals exhibiting dermal hypersensitivity. The high incidence of toxoplasmin sensitivity in patients with chorioretinitis and in the mothers of such patients is significant.

Due to its wide host range Toxoplasma is a unique protozoan organism. No related organisms are known, and hence no information is available as to possible cross-reactions of dermal hypersensitivity, such as between the two fungus diseases of histoplasmosis and coccidioidomycosis and their respective skin-testing antigens.

ETIOLOGY OF UVEITIS

Reviewing the literature on uveitis[14] many causal factors have been listed. The importance attributed to each parallels to some degree the history of recognition of rheumatism, gout, tuberculosis, syphilis, focal pyogenic infections, gonorrhea, brucellosis, and sarcoidosis[15] as etiologic and clinical entities. This study, therefore, may merely reflect the enthusiasm kindled by the discovery of another "new" disease.

However, in following Woods,[13] the patients under study have been classified as having either granulomatous or nongranulomatous uveitis. Furthermore, they were subdivided as having predominantly either anterior or posterior uveal tract lesions. The results of this survey show a high incidence (71 percent) of toxoplasmin sensitivity in patients with granulomatous posterior uveitis (chorioretinitis) and a lesser, but still elevated, incidence of positivity among patients with granulomatous anterior uveitis (40 percent).

Control groups of individuals of comparable age (20 to 35 years) showed a 10-percent incidence of toxoplasmin sensitivity. A seven-fold greater incidence was found in the patients with chorioretinitis (mean age 23 years) and a four-fold greater incidence in the patients with granulomatous anterior uveitis (mean age 35 years). While these data proved statistically significant (5.5 and 3 times the standard error), no significant correlation was found between dermal hypersensitivity to toxoplasmin and the occurrence of nongranulomatous uveitis.

The findings reported here on the concurrence of chorioretinitis and toxoplasmosis are in general agreement with those made by Heidelman[6] and Johnson.[7] A comparison with the detailed studies on uveitis by Woods and Guyton[14,15] is difficult to make, since they did not distinguish in their tables between predominantly anterior and posterior uveal tract involvement, nor between granulomatous and nongranulomatous lesions.

Diagnosis made by exclusion of other known etiologic factors, or on the basis of a positive tuberculin test or a calcified pulmonary focus, or from the results of a therapeutic test with tuberculin may easily be fallacious. At the time that their studies were made, much less was known about the incidence of toxoplasmosis and perhaps also about the incidence of sensitivity to tuberculin and other antigens in the population as a whole.

It is felt, therefore, that, in this study, by suitable differentiation of clinical syndromes and by integration with controlled experimental data, two groups of patients have been singled out, a significant proportion of

whom may be assigned toxoplasma as the etiologic agent of their uveal tract lesions. Further serologic studies being carried out at present may serve to distinguish between active and inactive chronic toxoplasmosis.[11]

SUMMARY

1. Toxoplasmin, a skin test antigen made from toxoplasma, evokes reactions of a delayed (tuberculin) type of hypersensitivity in certain individuals.

2. The incidence of toxoplasmin sensitivity was 10 percent in a group of young healthy individuals and 28 percent in a group of older hospital patients with cardiac or neoplastic diseases.

3. Of 28 young patients with chorioretinitis 20, or 71 percent, were sensitive to toxoplasmin.

4. Among 40 young patients with anterior uveitis, 13, or 33 percent, were toxoplasmin sensitive. The incidence was 40 percent for the granulomatous cases and only 20 percent for the nongranulomatous cases.

5. The incidence of toxoplasmin sensitivity was higher in women than in men both in the control and the chorioretinitic group of patients.

6. Reasons for assuming a toxoplasmic etiology for a certain percentage of granulomatous uveitis cases are given. The pathogenesis of toxoplasmic uveitis is discussed, as well as the rationale, indications, technique, and results of treatment with toxoplasma antigen.

Rocky Mountain Laboratory.

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DISCUSSION

DR. PARKER HEATH (Boston, Massachusetts) : I think this is a very interesting and important paper. One suggestion of importance from the paper is that it offers another breakdown in the group of unknown causes of uveitis.

Gabriel Steiner sometime ago reported a direct relationship between the active lesion and the breaking of the pseudocyst wall and the free parasite.

DR. LORAND V. JOHNSON (Cleveland, Ohio) : I have enjoyed this very much. It seems to me that this has been one of the big years in the increasing knowledge of toxoplasmosis.

Dr. Leslie Alm in Sweden has described a nutrient embryo test for toxoplasmosis, as well as a method for growing the organisms on the chick embryo. I understand that Sabin has a new sensitive skin test, using an antigen obtained from the chorion-allantoic membrane, as well as a new methylene-blue test, whereby the cytoplasm of the organism will take up methylene blue and thus be stained deeply when untreated or when treated with normal sera. If it is treated with serum from a patient with toxoplasma infection, the organism loses its affinity for methylene blue and will not stain (will soon be published in *Science*).

I hope that in your publication you will describe your method of producing toxoplasmin.

DR. FRENKEL (closing) : In answer to Dr. Heath's question, vitreous exudates were almost always associated with active chorioretinal lesions and they disappeared during subsidence of the lesion during treatment, whether it was due to it or not. It is too early to say whether the treatment had any effect. However, according to the judgment of clinicians who are well acquainted with the natural history of uveitis, treatment seemed to be accelerating subsidence.

The diagnosis of chorioretinitis due to toxoplasmosis was made on the basis of skin tests, and the neutralizing antibody tests. We did not biopsy any eyes and, therefore, could not demonstrate organisms. These are all chronic cases in whom organisms are sparse. An enucleation has been done by Dr. Fry (published together with Dr. Schwartz in the new journal *Pediatrics*) and no organisms were found histologically.

Steiner and Kaump,[16] to whom you refer, showed that there is a cellular reaction to the presence of extracellular proliferative forms, such as are present in the subacute and the acute disease. They did not talk of pseudocysts as far as I can determine. Most authors do not differentiate between intracellular proliferative forms and pseudocysts

of toxoplasma, since they are not aware of the argyrophilic cyst wall. I have found the latter to be present in three strains of toxoplasma which I carry and undoubtedly it is a significant structure. The cyst walls of Coccidioides immitis spherules and the cyst walls of the rabbit coccidium Eimeria stiedae stained similarly with Wilder's silver stain. However, this does not imply a relationship between these organisms.

An account of the production of toxoplasmin has been published.[1] There is no great difficulty in preparation of the antigen.

Dr. Johnson's exhibit, showing some of Dr. Alm's technique, is very interesting. The latter is probably an improvement of the neutralizing antibody technique, since it lends itself better to statistical analysis. As may be inferred from one of my lantern slides, differentiation between positive and negative neutralization tests is not always easy to make. I am looking forward with great interest to the results obtainable with the new dye test, which, as Dr. Sabin mentioned to me, is beginning to show much promise.

EXPERIMENTAL STUDIES WITH ANTIBIOTICS*

BACITRACIN, STREPTOMYCIN, PENICILLIN, AND ANTIBIOTIC MIXTURES IN INTRAOCULAR
INFECTIONS WITH PENICILLIN-RESISTANT STAPHYLOCOCCI

JOHN C. LOCKE, M.D.
New York

Pathogenic Staphylococcus aureus is one of the most frequent etiologic agents in postoperative and posttraumatic purulent endophthalmitis.

In 1943, von Sallmann[1,2] demonstrated that experimental intraocular infections in rabbits, caused by penicillin-sensitive staphylococci, responded favorably in a high percentage of cases to local treatment with penicillin iontophoresis.

However, from 10 to 38 percent of staphylococci, isolated from clinical sources, have variously been reported by different authors to be relatively resistant to penicillin;[3-9] and some authorities believe that this frequency will increase.[9, 10]

The purpose of this study, therefore, was to investigate the comparative values of various antibiotics (penicillin, streptomycin, and bacitracin) and antibiotic mixtures (penicillin-sulfacetimide, penicillin-streptomycin, streptomycin-sulfacetimide) in the local treatment of experimental intraocular infections caused by penicillin-resistant staphylococci.

Leopold and Nichols[11] reported finding high concentrations of streptomycin in the aqueous of normal rabbit eyes, following iontophoresis; and this finding was confirmed by Bellows and Farmer.[12]

Bacitracin, discovered by Meleney and coworkers,[13] is one of the newer antibiotics. Having an antibacterial spectrum very similar to that of penicillin, it has given good results in the local treatment of surgical infections caused by penicillin-resistant staphylococci.[7] No reports have yet appeared concerning its use in ophthalmology.

Conflicting results have been reported on the effects of combined chemotherapy,[14-21] but the majority of investigators have observed synergistic or additive activity.

The high solubility of sodium sulfacetimide, at a neutral pH, makes it a satisfactory sulfonamide for use in mixtures with antibiotics. It reaches the aqueous in high concentrations, following iontophoresis;[2, 22] and

it is effective against staphylococci and other sulfonamide-sensitive organisms in conjunctival and corneal infections.[23-26]

The feasibility of applying combined chemotherapy to the eye by iontophoresis was demonstrated by von Sallmann,[2] who found approximately the same concentrations of penicillin and sulfacetimide in rabbit aqueous after iontophoresis with solutions containing both their sodium salts, as after iontophoresis with solutions containing the respective salt alone.

Preliminary experiments were carried out

The eyes were examined during the course of the instillations and 15 hours following the last one.

Results. A concentration of 5,000 units per cc. was very irritating and caused marked chemosis, conjunctival congestion, and belpharospasm, but no corneal damage, in all eyes, commencing soon after the first instillation (Table 1).

A concentration of 1,000 units per cc. was relatively well tolerated, but did cause a mild conjunctival congestion and a very slight degree of chemosis in 8 out of 11 eyes.

TABLE 1

EFFECTS OF SIX TO SEVEN HOURLY INSTILLATIONS OF BACITRACIN SOLUTIONS IN NORMAL RABBIT EYES

Lot No.	Units per mg.	Concentration (U/cc.)	Solvent	No. of Eyes	Ocular Reaction	
					Immediately after Last Instillation	15 Hours after Last Instillation
B130	25	5,000	Distilled water	5	Marked chemosis, conjunctival congestion and blepharospasm; no corneal damage.	
B471212S	50	5,000	Distilled water	3		
B471212S	50	5,000	Normal saline	3		Lids, conjunctivas, and cornea essentially normal.
B130	25	1,000	Distilled water	5	Mild conjunctival congestion, very slight chemosis in 8 of 11 eyes.	
B471212S	50	1,000	Distilled water	3		
B471212S	50	1,000	Normal saline	3		

to determine the irritability and penetrability of bacitracin in the normal rabbit eye, and to determine if any chemical or therapeutic incompatibilities existed between the antibiotics which we wished to use in therapeutic mixtures.

IRRITABILITY OF BACITRACIN

I. INSTILLATION OF DROPS

Technique. Three drops of bacitracin solution were instilled into the conjunctival sacs of 22 normal rabbit eyes, every hour, for 6 to 7 instillations, using two different concentrations (5,000 units per cc. and 1,000 units per cc.), two different solvents (distilled water and normal saline), and two different lots (No. B130, prepared in September, 1947, containing 25 units per mg.; and No. B471212S, prepared in January, 1948, containing 50 units per mg.).

The findings were the same for both lots and for both solvents.

Fifteen hours following the last instillation, all eyes had returned to normal.

Comment. Among the factors influencing the irritability of ophthalmic solutions are pH and tonicity. The pH of these solutions was 6.5 to 6.8. Fifteen hundred units per cc. of the lot containing 25 units per mg. was approximately isotonic with normal saline.[38]

Johnson[28] found the nephrotoxicity of bacitracin in mice to be very much less when the antibiotic was dissolved in saline, but the reason for this was not understood. The possibility existed that sodium chloride might neutralize some toxic component of the bacitracin. The use of normal saline as solvent in our experiments, however, did not lessen the irritability of the drug to the eye.

II. CORNEAL BATH AND IONTOPHORESIS

Technique. Aqueous solutions of bacitracin in three different concentrations (5,000 units per cc., 2,500 units per cc., and 1,000 units per cc.) were applied for 5 minutes by corneal bath and iontophoresis (cathode on the eye; current at 1.6 ma.) to 40 normal rabbit eyes, after local anesthesia with 0.1-percent nupercaine solution. Twenty-four hours later, the corneas were stained with 2-percent sodium fluorescein and studied.

Results. Using a concentration of 5,000 units per cc., a single corneal bath or iontophoretic application for 5 minutes produced extensive corneal abrasions in all eyes (5 eyes by each method).

Using a concentration of 2,500 units per cc., a single corneal bath or iontophoretic application for 5 minutes produced corneal abrasions in a majority of cases (3 out of 5 eyes, and 4 out of 5 eyes, respectively).

With a concentration of 1,000 units per cc., however, repeated applications were well tolerated, providing that the intervals between applications were not less than 9 to 12 hours. If the intervals were reduced to 5 hours, two consecutive applications produced corneal abrasions in most cases (corneal bath: 3 out of 5 eyes; iontophoresis: 4 out of 5 eyes). In every case of iontophoresis, a transient haziness of the corneal epithelium was observed immediately following the application. This was similar, but denser, than that seen after penicillin iontophoresis.

Comment. These findings limit the concentration of bacitracin that can be applied to the rabbit eye, by any of the three types of administration tested, to 500 to 1,000 units per cc. The practical, therapeutic significance of this is discussed later.

PENETRABILITY OF BACITRACIN

Technique. Under 0.1-percent, local nupercaine anesthesia, a concentration of 1,000 units of bacitracin per cc. of distilled water was applied for 5 minutes by corneal bath and by iontophoresis (cathode on the eye;

current at 1.6 ma.), to 4 normal rabbit eyes, 2 determinations being made for each method of application. Aqueous was withdrawn 45 minutes later and assayed for its bacitracin content.*

Results. The concentrations in the aqueous following corneal bath were 4 units per cc. in each case (Table 2); those following

TABLE 2

CONCENTRATION OF BACITRACIN IN AQUEOUS OF NORMAL RABBIT EYE, FORTY-FIVE MINUTES AFTER APPLICATION OF 1,000 UNITS OF BACITRACIN PER CC. DISTILLED WATER AFTER 0.1 PERCENT LOCAL NUPERCAINE ANESTHESIA

Method	Rabbit	Concentration in Aqueous (Units per cc.)
Corneal bath	1	4
	2	4
Iontophoresis	3	8
	4	12

iontophoresis were 8 and 12 units per cc., respectively, or 2 to 3 times as much.

Comment. These concentrations are considerably higher than those necessary to inhibit most strains of staphylococci in vitro (about 0.5 to 1.0 unit per cc.[27]).

The differences between the concentrations obtained by corneal bath, on one hand, and by iontophoresis, on the other, are not as great for bacitracin as for the sulfonamides,[22, 29] atropine,[30] penicillin,[31] or streptomycin.[12] Greater transient damage to the corneal epithelium by bacitracin probably permits a larger proportion of that reaching the aqueous to do so by simple diffusion.

COMPATIBILITIES OF ANTIBIOTICS

I. CHEMICAL COMPATIBILITIES

Technique. Appropriate mixtures were made and observed for evidences of incompatibility.

Results. An aqueous solution containing streptomycin calcium-chloride complex,

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* Miss B. Johnson of the Department of Surgical Bacteriology, College of Physicians and Surgeons, Columbia University, assayed the aqueous samples for bacitracin, and, in the experiments discussed later, carried out the bacitracin sensitivity tests.

20,000 units per cc., and 10-percent sodium sulfacetimide formed a thick insoluble precipitate, which would not disappear on heating or on raising or lowering its pH. No precipitate formed if the concentration of streptomycin calcium chloride in the mixture was 10,000 units per cc. A solution containing streptomycin sulfate, 20,000 units per cc., and 10-percent sodium sulfacetimide, remained clear.

There was no incompatibility in a mixture containing streptomycin calcium-chloride complex, 20,000 units per cc., and sodium penicillin, 1,000 units per cc.

That sodium penicillin and the sulfonamides are compatible is already well known.

Comment. Calcium is known to precipitate many anions. Chlorides on the other hand (except for those of bismuth, lead, mercury, and silver) are generally water-soluble. The incompatibility between streptomycin calcium-chloride complex and sodium sulfacetimide is probably due to the calcium cation combining with the sulfacetimide anion to form a less soluble compound, calicum sulfacetimide.

II. THERAPEUTIC COMPATIBILITIES

Waksman and his co-workers[32] reported the detrimental effects of glucose, sodium chloride, and sodium phosphate on the antibacterial activity of streptomycin; and Berkman and his colleagues[33] demonstrated a marked in vitro inhibition of the antibacterial activity of streptomycin by physiologic concentrations of sodium chloride, potassium chloride, sodium sulfate, sodium tartrate, and ammonium acetate.

In vitro experiments were, therefore, indicated to determine if any such inhibition occurred when streptomycin was combined with sulfacetimide, penicillin, or bacitracin, in the proportions which we wished to use therapeutically.

Technique. The serial dilution method employed at the Presbyterian Hospital, New York City, for testing in vitro streptomycin sensitivities, was used in these experiments.

The test organism was a streptomycin-sensitive strain of Bacillus aerogenes.

Aqueous solutions were prepared, containing: (1) Streptomycin CaCl complex, 10,000 units per cc. and 10-percent sodium sulfacetimide; (2) streptomycin sulfate, 10,000 units per cc. and 10-percent sodium sulfacetimide; (3) streptomycin CaCl complex, 10,000 units per cc., and sodium penicillin, 1,000 units per cc.; (4) streptomycin CaCl complex, 10,000 units per cc., and bacitracin, 1,000 units per cc.

The antibacterial activity of each of these mixtures was compared to that of solutions containing streptomycin, sulfacetimide, penicillin, and bacitracin, alone, and in the same concentrations as in the mixtures.

Rows of eight tubes were set up, the tubes of each row containing 2, 4, 6, 8, 10, 12, 15, and 20 units per cc. of streptomycin respectively and/or the corresponding proportional amount of the second drug being investigated.

The standard inoculum was added, the tubes were incubated for 72 hours, and then examined for evidence of bacterial growth, as determined by the presence of visible turbidity.

Results. Growth of the organisms was not inhibited by any of the concentrations of sulfacetimide, penicillin, or bacitracin, where these agents were used alone.

Growth was inhibited in all rows containing streptomycin, alone or in mixtures: in four rows, by solutions containing 6 and more units of streptomycin per cc.; and, in the remaining three rows, by solutions containing 8 and more units per cc.

Comment. The difference between inhibition by 6 units or by 8 units per cc. is negligible and has no significance, being within the limits of experimental error of the test. The results indicate that there was no inhibition of the antibacterial activity of streptomycin by sodium sulfacetimide, sodium penicillin, or bacitracin, in the proportions used.

Since completing these experiments, re-

ports have appeared in the literature confirming the results: Bondi and Dietz[21] reported a slight degree of synergistic or additive activity between streptomycin and penicillin, in vitro, against Staphylococcus aureus; and Klein and Kimmelman[20] found both sulfadiazine and penicillin to be synergistic with streptomycin, in vitro, against the same organism.

TREATMENT OF INTRAOCULAR INFECTIONS

Technique. A search was made for strains of pathogenic Staphylococcus aureus, resistant to penicillin, but sensitive to streptomycin and bacitracin. For this purpose, the in vitro sensitivities of a large number of strains were determined, and their ability to hemolize red blood cells, ferment mannitol, and coagulate plasma, was noted. Three such strains were found.

The technique of inoculation, described by von Sallmann,[1] was used throughout, 0.05 cc. of inoculum being injected into the anterior chamber, after extensive damage to the lens with the needle. In every instance, counts were made of the numbers of organisms injected.

Preliminary inoculations, with varying dilutions in normal saline, of 18-hour broth cultures of the three strains were first made in rabbit eyes to determine the dilutions that would give satisfactory test lesions.

Experimental intraocular infections were then produced, with the appropriate dilutions, in 115 rabbit eyes, and were treated locally by corneal iontophoresis (cathode on the eye; current at 1.6 ma.), after local anesthesia with 0.1-percent nupercaine, and commencing 4 to 6 hours after inoculation. Iontophoresis was applied for 5 minutes, twice a day, for 5 days, with intervals of at least 9 hours between successive applications. It was discontinued on any eye that perforated or became frankly suppurative. In the case of one strain (strain C), a five-minute corneal bath was given instead of the second daily iontophoresis.

The drugs* were applied, both alone and in the mixtures, in the following concentrations: sodium sulfacetimide, 10 percent; sodium penicillin, 1,000 units per cc.; streptomycin, 20,000 units per cc.; bacitracin, 1,000 units per cc. The mixtures used were: penicillin and sulfacetimide; penicillin and streptomycin; streptomycin and sulfacetimide. Streptomycin sulfate was used in the streptomycin-sulfacetimide mixture, but otherwise the calcium-chloride complex was used.

Results. The first strain (strain A) fermented mannitol, but did so slowly; it was nonhemolytic and coagulase negative. It was highly resistant in vitro to penicillin, requiring 10 units per cc. for inhibition, and had an average sensitivity to streptomycin (8 units per cc.). Injection of 0.05 cc. of a 10^{-1} dilution (1,200,000 organisms) caused self-limited infections only, in all eyes, and these were not affected by any of the solutions used.

The second strain (strain B) was hemolytic, mannitol positive, and coagulase positive. It was moderately resistant in vitro to penicillin, requiring 1 unit per cc. for inhibition. It had an average sensitivity to streptomycin (9 units per cc.) and to bacitracin (0.62 units per cc.). Injection of 0.05 cc. of a 10^{-4} dilution (900 to 1,100 organisms) produced severe suppurative panophthalmitis in all control eyes.

The results of treatment, in the case of this strain, are listed in Table 3, under three headings:

1. Excellent Results. These eyes showed signs of intraocular inflammation for 24 to 72 hours following inoculation, but were quiet by the 5th day. At this time, there was alway some organizing exudate in the anterior chamber, adhering to the anterior surface of the lens in the pupillary area (fig. 1C), which disappeared during the next two weeks, leaving the anterior chamber clear.

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* The sodium sulfacetimide for this study was kindly furnished by the Schering Corporation; the streptomycin CaCl complex by Merck and Co., Inc.

TABLE 3

EXPERIMENTAL INTRAOCULAR STAPHYLOCOCCAL INFECTIONS,* TREATMENT WITH
IONTOPHORESIS TWICE A DAY
STRAIN B†

Treatment	No. of Eyes	Results		
		Excellent	Intermediate	No Effect
Penicillin	6	6	—	—
Penicillin-sulfacetimide	6	5	—	1
Penicillin-streptomycin	6	6	—	—
Streptomycin	6	4	1	1
Streptomycin-sulfacetimide	6	1	2	3
Sulfacetimide	5	—	—	5
Bacitracin	6	—	2	4
Controls	7	—	—	7

* Inoculum: 900–1,100 organisms.
† Hemolytic, mannitol positive, coagulase positive. Inhibited by: penicillin, 1 unit per cc.; streptomycin, 9 units per cc.; bacitracin, 0.62 units per cc.

A thin-linear opacity always remained in the lens, where it had been incised (fig. 1D).

2. Intermediate Results. These eyes responded, but less dramatically, and retained sequelae, such as synechias, pupillary membranes, and corneal opacities (fig. 1B).

3. No Effect. These eyes developed severe suppurative panophthalmitis (fig. 1A).

Penicillin gave excellent results in 6 out of 6 eyes when used alone, in 5 out of 6 eyes when combined with sulfacetimide, and in 6 out of 6 eyes when combined with streptomycin.

Streptomycin gave excellent results in 4

TABLE 4

EXPERIMENTAL INTRAOCULAR STAPHYLOCOCCAL
INFECTIONS,* IONTOPHORESIS ONCE A DAY,
CORNEAL BATH ONCE A DAY
STRAIN C†

Treatment	No. of Eyes	Results	
		Benefited	Not Benefited
Penicillin	6	—	6
Penicillin-sulfacetimide	6	1	5
Penicillin-streptomycin	6	1	5
Streptomycin	6	2	4
Streptomycin-sulfacetimide	3	1	2
Sulfacetimide	5	—	5
Bacitracin	4	—	4
Controls	9	—	9

* Inoculum: 1,500 to 1,700 organisms.
† Hemolytic, mannitol positive, coagulase positive. Inhibited by: penicillin, 10 units per cc.; streptomycin, 8 units per cc.; bacitracin, 0.75 units per cc.

out of 6 eyes and an intermediate result in 1 eye, when used alone. It gave an excellent result in 1 out of 6 eyes and an intermediate result in 2 eyes when combined with sulfacetimide.

All 5 eyes treated with sulfacetimide alone were lost. Bacitracin alone gave 2 intermediate results, and 4 eyes were lost.

The third strain (strain C), also hemolytic, mannitol positive, and coagulase positive, was highly resistant in vitro to penicillin, requiring 10 units per cc. for in-vitro inhibition. It had an average sensitivity to streptomycin (8 units per cc.) and to bacitracin (0.75 units per cc.). Injection of 0.05 cc. of a 10^{-4} dilution (1,500 to 1,700 organisms) produced a severe suppurative panophthalmitis in all control eyes (fig. 2A).

Table 4 lists the results of treatment in the case of this strain. Favorable responses were less numerous and not as dramatic, all eyes retaining some inflammatory sequelae (fig. 2B). None of the 6 six eyes treated with penicillin alone were benefited. Only 1 out of 6 eyes treated with the penicillin-sulfacetimide mixture responded. One out of 6 eyes treated with the penicillin-streptomycin mixture, 2 out of 6 eyes treated with streptomycin alone, and 1 out of 3 eyes treated with the streptomycin-sulfacetimide mixture also were benefited. All other eyes were lost, including 5 treated with sulfacetimide alone, and 6 treated with bacitracin alone.

Fig. 1 (Locke). Results of treatment, Strain B. (A) Control eye showing severe suppurative panophthalmitis. (B) Intermediate result, showing retained inflammatory sequelae. (C) Excellent result five days after inoculation, showing organizing exudate in anterior chamber adherent to anterior surface of lens in pupillary area. (D) Excellent results three weeks after inoculation, showing anterior chamber clear following absorption of exudate. Linear opacity remains where lens was incised.

Comment. Inoculation with 1,200,000 organisms of strain A caused mild, self-limited infections in all eyes, while inoculation with 900 to 1,100 organisms of strain B and 1,500 to 1,700 organisms of strain C resulted in severe progressive panophthalmitis in all control eyes. Thus there was a dramatic correlation between the findings of the in-vitro pathogenicity tests and the in-vivo results.

Strains of staphylococci requiring 1 unit of penicillin per cc. for in vitro inhibition are generally considered to be relatively penicillin-resistant, since injections of massive doses are required to attain these concentrations of penicillin in the blood.[34-36] The good results obtained with penicillin against strain B, however, in these intra-

ocular infections are not entirely unexpected when it is realized that a concentration of penicillin as high as 2.2 to 3.3 units per cc. is obtained in the aqueous, following iontophoresis with 1,000 units per cc.. for 5 minutes.[37]

In the case of this strain, it appeared to make little difference whether penicillin was used alone, or in combination with sulfacetimide or streptomycin.

Streptomycin, giving the next best results against strain B, was fairly effective. It was less effective when combined with sodium sulfacetimide, but a larger number of eyes are needed to give this finding statistical significance.

The ineffectiveness of penicillin against strain C, requiring 10 units per cc. for in-
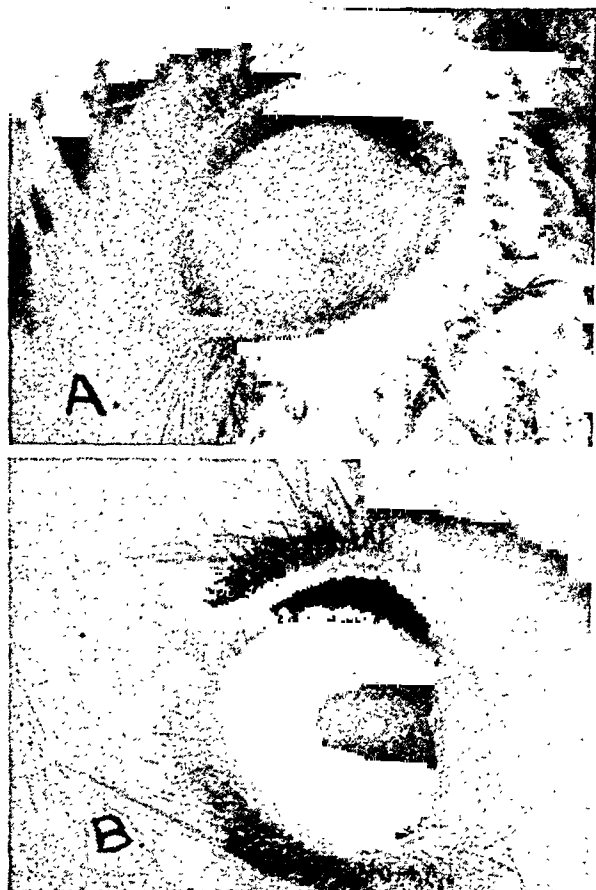
Fig. 2 (Locke). Results of treatment, Strain C. (A) Control eye, showing severe suppurative panophthalmitis. (B) Eye benefited from treatment, showing retained inflammatory sequelae.

hibition, correlates with our knowledge of penicillin aqueous levels.

Against this strain, streptomycin, apparently, was the only effective agent, since of 5 eyes benefiting from treatment, all but 1 received streptomycin, either alone or in a mixture. Even the effectiveness of streptomycin, however, was limited, since of 15 eyes receiving it, only 4, or 27 percent, responded; and the responses were not as marked as in the case of the previous strain. The fact that the second daily treatment was by corneal bath, rather than by iontophoresis, may have been the reason.

The rapid development of an intensely purulent inflammatory response suggests that the production of sulfonamide inhibitors may have been an important factor in the ineffectiveness of sulfacetimide against all strains.

Our conclusions regarding the ineffectiveness of bacitracin in these experimental intraocular infections should not be extended to exclude its possible value in other types of ocular infection. However, our findings limiting the concentrations that can be used in the eye do impose a limitation on its possible usefulness in local ophthalmic therapy. In vitro, the ratio of the antistaphylococcal activity of bacitracin to that of penicillin, in terms of units per cc. required to inhibit sensitive strains, is about 1 to 10.[27] In vivo, certain factors, such as the slower diffusion and excretion of bacitracin[39] and, in some instances, the inhibition of penicillin by penicillinase,[40-42] might effect a lowering of this ratio. But nevertheless, against organisms sensitive to both, a given concentration of bacitracin must be expected to have an antistaphylococcal activity considerably less than the same concentration of penicillin.

Bacitracin is still in the early stages of its development. Further purification, making possible the use of higher concentrations, may yet render it an effective agent in the treatment of experimental intraocular staphylococcal infections.

From a consideration of our in-vivo and in-vitro results, and the results of the in-vitro experiments by Klein and Kimmelman[20] and Bondi and Dietz,[21] the use of penicillin and streptomycin in combination would appear to be a sound therapeutic procedure, especially when an exact bacteriologic diagnosis has not been made, or if the sensitivities of the infecting organisms are not known.

SUMMARY

1. Bacitracin, in a concentration of 1,000 units per cc., is relatively well tolerated by the normal rabbit eye, but higher concentrations are irritating.

2. Therapeutic concentrations of bacitracin can be obtained in the aqueous by corneal bath and iontophoresis.

3. Sodium sulfacetimide is incompatible

with streptomycin calcium chloride in certain concentrations, but is compatible with streptomycin sulfate.

4. The antibacterial activity of streptomycin against a strain of B. aerogenes, in vitro, was not inhibited by sodium sulfacetimide, sodium penicillin, or bacitracin.

5. Penicillin was the drug of choice, over streptomycin, bacitracin, and sulfacetimide, in the local iontophoretic treatment of intraocular staphylococcal infections caused by a strain requiring 1 unit per cc. for in-vitro inhibition. Used alone, and in mixtures with streptomycin and sulfacetimide, it controlled the infection in 17 out of 18 eyes. Against a strain requiring 10 units per cc. for inhibition, it was ineffective.

6. Streptomycin was the second most effective agent. When applied twice daily, by iontophoresis, against a sensitive strain, it controlled the infection in 4 out of 6 eyes.

7. Bacitracin and sulfacetimide were of no value in these infections.

8. The use of penicillin and streptomycin in combination is a sound therapeutic procedure, especially if the sensitivities of the infecting organisms are not known.

635 West 165th Street (32).

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DISCUSSION

DR. HOWARD P. VENABLE (St. Louis, Missouri): I would like to ask Dr. Locke if, in his experience, his work would suggest that the 30-percent sodium-sulfacetimide which is advocated by the company would be a little too irritating?

DR. LOCKE (closing): In answer to Dr. Venable's question: I myself have never used 30-percent sodium sulfacetimide, but Dr. von Sallmann has had a great deal of experience with it, and we felt we could not go higher than a 10-percent solution for iontophoresis. Of course, the 30-percent solution is used as drops. It is considered to be too strong for iontophoresis in this concentration.

INDUSTRIAL VISION TECHNIQUES*

HENRY A. IMUS, LT. COMDR. H(S), USNR (INACTIVE)
Alexandria, Virginia

INTRODUCTION

The emphasis upon vision testing in industry has shifted from primary concern for first aid following accidents to selection and classification of personnel for job placement. The value of this new approach has been demonstrated to labor and management. Better placement in industrial jobs has resulted in greater job satisfaction, increased earning power, as well as promotion and advancement in his craft for the individual worker. These results have been reflected in the reduction of overhead, wastage, and inefficient operation, which are of vital importance to management. The greater productivity of the worker, also, tends toward greater profits for industry. Finally, the detection of abnormal ocular or visual conditions is important for the health and safety of the worker.

Vision testing, which is aimed primarily at the selection and classification of personnel for special visual tasks in industry, must be administered quickly by trained technicians rather than by ophthalmologists. The development of machine vision-testing equipment has made possible the routine administration of visual tests by technicians, who do not need to know anything about the usual clinical tests of vision, and are not required to make any interpretation of the results. The machine tests are contained in a single instrument, are administered according to a standardized procedure, and are scored according to arbitrary scales.

For classification and assignment, the comparison of scores on the visual tests with criteria of performance on the job, whether these be foreman's ratings, units produced, breakage, or earnings, determine the profile of "cut-off" scores for a particular job.

Usually, the personnel department is responsible for the testing of the applicants, the validation against criteria of performance, and the establishment of the profile scores. The industrial medical department, by reference to a table of clinical equivalents, may establish certain minimum scores for referral of patients to the clinic or to outside practitioners for evaluation and treatment of the ocular condition suggested by the tests.

For job placement, it is not necessary that visual screening tests predict the results of the corresponding clinical tests. If the test predicts performance on the job, that is sufficient. However, from the clinical and safety points of view, as well as for selecting procedures for rapid military mobilization, it is desirable that the machine visual tests predict with fair accuracy the clinical measures of vision.

In order to determine the reliability and validity of the current industrial vision screening devices, a number of research projects were established in the military services.[14]

The first test of the Ortho-Rater was conducted at Fort Eustis, Virginia, an antiaircraft artillery replacement training center, in connection with the selection of stereoscopic rangefinder operators, during the spring of 1943. Although the results of this study have not been published, the prediction of visual acuity at the level of 20/20 vision was found to be very good.

The next study was conducted at the U. S. Naval Training Center, Sampson, New York, in connection with the selection of

stereoscopic rangefinder operators for the Radar and Rangefinder School, Fort Lauderdale, Florida. A test-retest analysis[15] was made of the results of 234 administrations of the Ortho-Rater by 26 newly trained examiners. These examiners were optometrists enlisted in the Hospital Corps of the U. S. Navy.

The results of this study, which was concerned only with reliability (the coefficients of reliability varied from 0.49 to 0.83), emphasized the importance of careful training of the technicians who are to operate the machine tests. The standard instructions[16] to the examinee must be memorized perfectly, and each examinee must be encouraged to do his best after the examiner is convinced that he understands the directions given on each subtest. It is important that each examinee be treated in the same way.

These two preliminary tests showed that the Ortho-Rater could be used satisfactorily for mass testing in the military situation. The validation of the Ortho-Rater test of depth perception for the selection of stereoscopic rangefinder operators has been demonstrated adequately.[17]

At the U. S. Naval School of Aviation Medicine and Research, Pensacola, Florida, a test-retest study[12, 13, 18] of the Bausch & Lomb Ortho-Rater and of the corresponding clinical tests was made in 1945. This study shows, in general, that the visual tests incorporated in the Ortho-Rater are as consistent in the measures obtained as the clinical tests. The measures of far visual acuity agree satisfactorily with those obtained clinically. Measures of heterophoria do not agree closely, but, in view of the variability of heterophoria itself, the relationship may be as close as can be expected for any two measures of this anomaly.

The Medical Field Research Laboratory, Camp LeJeune, North Carolina, also reported on a comparative study[5, 6] of visual screening devices.

The most extensive studies[7-11, 19, 20] of the three available commercial screening devices were conducted at the U. S. Naval Medical Research Laboratory, Submarine Base, New London, Connecticut. Some of the statistical analyses of these data were undertaken by The Adjutant General's Office in connection with their intensive investigation of tests of visual acuity at Fort Dix, New Jersey, in coöperation with the Army-Navy-NRC Vision Committee.[1, 2] These statistical analyses are incorporated in a report[3] issued by The Adjutant General in 1947.

DISCUSSION OF RESULTS

The results of the evaluation of the various machine vision-testing devices, which are discussed in this paper, have been taken from the various aforementioned reports and the sources are acknowledged in the various tables or charts and in the list of references.

The test-retest reliability of the various instruments is indicated by the coefficients of correlation presented in Table 1. In general, the coefficients of this table show that the Ortho-Rater provides the most consistent measures and the Telebinocular the least consistent.

For far and near lateral phoria, the coefficients range from 0.75 to 0.92, and the instruments are more nearly equivalent. It should be noted that the reliabilities of the clinical measures are of the same order of magnitude.

For monocular far acuity, the Ortho-Rater and Sight-Screener are practically equal in consistency, the coefficients ranging from 0.81 to 0.90. The Telebinocular is only slightly less good in this aspect with coefficients ranging from 0.78 to 0.86. Only in the Pensacola study did the clinical measure of far monocular acuity appear to be more reliable than a machine test.

For the near tests of acuity, both binocular and monocular, the consistency of the Ortho-Rater is noticeably greater than that of the other two instruments.

The reliabilities of measures of far ver-

TABLE 1

Coefficients of reliability of tests*

Test	Ortho-Rater	Sight-Screener	Telebinocular	Clinical
Far vertical phoria	0.79	0.61	0.63	0.64
Far lateral phoria	0.87	0.80	0.75	0.81
Binocular far	0.88–0.93	0.70	—	0.81–0.97
Monocular far	0.81–0.90	0.84	0.78–0.86	0.80–0.97
Depth	0.83	0.57	0.79	0.62–0.72†
Binocular near	0.84–0.87	0.70	0.72	0.67
Monocular near	0.80–0.90	0.77	0.71	0.75–0.78
Near vertical phoria	0.73	0.55	—	0.74
Near lateral phoria	0.81–0.92	0.83	0.85	0.90

* The data for this Table were selected from the Pensacola (N=100), New London (N=128) and the Adjutant General's Office Report No. PRS No. 742. See references 3, 7–13.
† The Howard-Dolman test.

tical phoria by the Sight-Screener, Telebinocular, and clinical tests are equivalent, 0.61 and 0.64, while that of the Ortho-Rater is much higher, 0.79. For near vertical phoria, the reliabilities of the Ortho-Rater and clinical measures are equivalent, 0.73 and 0.74, while that for the Sight-Screener is much lower, 0.55.

In the measures of depth perception, the Ortho-Rater and Telebinocular are nearly[14] equivalent as to reliability, 0.83 and 0.79, whereas the Sight-Screener and Howard-Dolman test are somewhat less consistent, 0.57 and 0.62 to 0.72.

The results of all tests on the instruments were compared with the clinical ophthalmic tests. The coefficients of correlation are presented in Table 2.

For far and near monocular acuity, the

coefficients for the Ortho-Rater and Sight-Screener are approximately 0.75, while those for the Telebinocular are approximately 0.55.

The Ortho-Rater appears to provide a much better measure of far lateral phoria, r = 0.57 to 0.70, as compared with the other two instruments, r = 0.37 for each. For near lateral phoria, however, the three instruments are practically equivalent: Ortho-Rater, 0.67 to 0.77; Sight-Screener, 0.54; and Telebinocular, 0.68.

For all instruments the coefficients of correlation for vertical phoria are relatively low, ranging from 0.29 to 0.50.

The only comparison in measures of depth perception is between the Ortho-Rater and the Howard-Dolman test. These coefficients (0.59 to 0.62) are no greater than those

TABLE 2

Relationships* between instruments and clinical ophthalmic examination

Test	Ortho-Rater	Sight-Screener	Telebinocular
Far vertical phoria	0.29–0.49	0.28	0.43
Far lateral phoria	0.57–0.70	0.37	0.37
Binocular far	0.79–0.90	0.71	—
Monocular far	0.72–0.84	0.74	0.58
Depth	0.59–0.62†	—	—
Binocular near	0.70	0.64	0.55
Monocular near	0.75	0.71	0.55
Near vertical phoria	0.34–0.50	0.34	—
Near lateral phoria	0.67–0.77	0.54	0.68

* The data for this Table were selected from the Pensacola report (N=100), New London report (N=128) and The Adjutant General's Office Report No. PRS No. 742. See references 3, 7–13.
† Howard-Dolman test.

TABLE 3

FACTOR LOADINGS OF FAR VISUAL ACUITY TESTS[*]

Instrument	Resolution	Accommodation	Form	Interference
Snellen Chart	0.70 0.86	0.00 0.12	0.24 0.50	0.01 0.11
Ortho-Rater	0.77 0.86	−0.07 0.07	0.00 0.11	0.23 0.52
Sight-Screener	0.75 0.90	0.06 0.20	0.02 0.26	0.06 0.18
Telebinocular	0.62 0.72	0.15 0.25	0.02 0.07	0.01 0.23

[*] The Adjutant General's Office PRS Report No. 742, August, 1947, p. 54.

generally found between any two tests of depth perception.[*]

A statistical study of the New London data[8] on the comparison of three commercial visual screening devices was conducted by The Adjutant General's Office, using the method of factor analysis. The data of Tables 3 to 7 have been extracted from this report.[3]

For the purpose of this paper a factor loading can be described as the coefficient of correlation between the test and a specific factor. The square of the factor loading represents the proportion of the total variability of the specific test scores which is explained by the factor. This factor is named after careful consideration of the character of the test and the distribution of all factor loadings.

In Table 3 it is shown that the factor loadings for resolution in the far visual

acuity test for the Snellen Chart, the Ortho-Rater, and Sight-Screener are of the same order of magnitude, while those for the Telebinocular are slightly lower. It is shown, further, that a part of the variability of the test scores on the Snellen Chart and Sight-Screener can be attributed to a form factor which is not effective with the other two instruments. The variability of scores on the Ortho-Rater can be attributed in part to a specific interference or machine factor. This might be eliminated by an improvement of the instrument or test targets. The Telebinocular shows both accommodation and machine factors, and represents the least pure test of retinal resolution.

For the near-vision tests the factor loadings are shown in Table 4. Here again the Snellen, Ortho-Rater, and Sight-Screener are practically equivalent as to factor loadings for resolution. The loadings on the Telebinocular are much lower for both letter and circle targets. As would be expected, an accommodation factor appears to be

[*] Unpublished report, "Comparison Between Seven Tests of Depth Perception," Fort Eustis, Virginia.

TABLE 4

FACTOR LOADINGS OF NEAR VISION TESTS[*]

Instrument	Resolution	Accommodation	Form	Interference
Reduced Snellen	0.53 0.60	0.42 0.66	0.19 0.40	0.00 0.15
Ortho-Rater	0.54 0.70	0.57 0.70	0.02 0.14	0.16 0.37
Sight-Screener	0.59 0.69	0.39 0.53	0.01 0.17	0.00 0.23
Telebinocular (letters)	0.41 0.43	0.37 0.47	0.19 0.26	0.02 0.07
Telebinocular (circles)	0.38 0.56	0.39 0.50	0.03 0.18	0.02 0.26

[*] The Adjutant General's Office PRS Report No. 742, August, 1947, p. 54.

TABLE 5

FACTOR LOADINGS OF VERTICAL PHORIA TESTS*

Instrument		Vertical Phoria		Fusion		Specific	
Maddox rod	Far	0.43		−0.27		0.13	
	Near	0.20		−0.33		0.09	
Ortho-Rater	Far	0.50	0.73	−0.05	−0.12	0.22	
	Near	0.49	0.73	−0.04	0.05	0.71	0.76
Sight-Screener	Far	0.40	0.57	0.48	0.78	—	
	Near	0.47	0.54	0.57	0.62	—	
Telebinocular	Far	0.41	0.49	0.10	0.17	—	
	Near	—		—		—	

* The Adjutant General's Office PRS Report No. 742, p. 60.

present in all tests. The Ortho-Rater scores are affected slightly more by this factor as compared with the other devices. A form factor is present in both the Snellen and Telebinocular letters, which would be expected, but these two instruments present the lowest (practically zero) interference factors.

The factor loadings on the vertical phoria tests for distant and near vision on all devices are summarized in Table 5. Two factors, vertical phoria and so-called "fusion," are revealed in this analysis for all tests, while a specific instrument factor appears for the Ortho-Rater only, especially in the test at the near distance.

For the tests of far vertical phoria with the Maddox rod, Sight-Screener, and Telebinocular, the factor loadings for vertical phoria are relatively low and practically equivalent. The Ortho-Rater test shows the highest factor loadings for vertical phoria. On the other hand, the Ortho-Rater shows the lowest factor loadings for "fusion" with the Telebinocular a close second. The variability of the Sight-Screener scores is greatly affected by this factor.

For the tests of vertical phoria at near vision, a large part of the variability of the Ortho-Rater scores is accounted for by a specific machine factor, peculiar to this instrument. This finding points to a definite area in which the Ortho-Rater might be improved. With the high loading already present on vertical phoria, elimination of the machine factor might greatly increase the efficiency of this instrument.

The Telebinocular does not have a test of near vertical phoria. As in the far vertical phoria test the Sight-Screener scores for

TABLE 6

FACTOR LOADINGS OF LATERAL PHORIA TESTS*

Instrument		Lateral Phoria		Fusion		Specific	
Maddox rod	Far	0.60		0.39		—	
	Near	0.58		0.41		—	
Ortho-Rater	Far	0.81	0.92	0.03	−0.10	0.09	0.17
	Near	0.65	0.68	0.06	0.09	0.05	0.11
Sight-Screener	Far	0.71	0.75	−0.04	−0.08	—	—
	Near	0.47	0.49	0.00	0.01	—	—
Telebinocular	Far	0.71	0.77	0.03	−0.04	—	—
	Near	0.57	0.70	0.02	−0.05	—	—

* The Adjutant General's Office PRS Report No. 742, August, 1947, p. 60.

near vertical phoria are greatly influenced by the "fusion" factor. The near Maddox-rod scores are affected, also, by this factor, and present the lowest factor loadings for near vertical phoria.

For the lateral phoria tests on all instruments, the factor loadings for both far and near vision are presented in Table 6.

For far lateral phoria loadings, the devices are ranked as follows: Ortho-Rater highest, 0.81 to 0.92; Sight-Screener and Telebinocular close second, 0.71 to 0.77; and Maddox rod third with 0.60. The Maddox rod is the only test affected significantly

SUMMARY

1. In general, the machine tests are as reliable, or are more reliable, than the corresponding clinical tests.

2. For monocular far acuity, the coefficients of reliability are practically the same for all tests. The coefficients range from 0.78 to 0.97.

3. For monocular near acuity, the consistency of the Ortho-Rater measures is slightly greater (r = 0.80 to 0.90) than for the other devices (r = 0.71 to 0.78).

4. For binocular acuity at both far and

TABLE 7

FACTOR LOADINGS OF DEPTH PERCEPTION TESTS*

Instrument	Depth	Form	Interference	Specific
Ortho-Rater	0.61 0.69	0.04 0.11	−0.02 0.03	—.
Sight-Screener	0.43 0.44	0.03 0.11	0.03 0.06	0.31 0.38
Telebinocular	0.32 0.35	−0.13 −0.17	0.21 0.30	—

* The Adjutant General's Office PRS Report No. 742, August, 1947, p. 54.

by the "fusion" factor, while the Ortho-Rater presents a slight loading on a specific instrument factor.

For near lateral phoria loadings, the Ortho-Rater again ranks the highest, 0.65 to 0.68, with the Telebinocular second, 0.57 to 0.70, Maddox rod third, 0.58, and the Sight-Screener the lowest, 0.47 to 0.49. Again the Maddox-rod scores are the only ones affected, significantly, by the "fusion" factor. There is a very slight machine factor affecting the Ortho-Rater scores.

The factor loadings of the tests of depth perception are presented in Table 7. The Ortho-Rater has the highest factor loading for depth, 0.61 to 0.69, while the Sight-Screener and Telebinocular have relatively low loadings on this factor, 0.43 to 0.44 and 0.32 to 0.35, respectively. The Sight-Screener scores are affected by a specific machine factor, while those of the Telebinocular are affected somewhat by both form and interference factors.

near distances, the reliability of the Ortho-Rater is the highest (r = 0.80 to 0.93) of the three machine tests.

5. The reliability of the clinical test of binocular acuity is equivalent to that of the Ortho-Rater for far vision (r = 0.81 to 0.97), but is lowest of all for near vision (r = 0.67).

6. For far vertical phoria, the Ortho-Rater is most consistent (r = 0.79), while the other three devices are equally less consistent (r = 0.61 to 0.64).

7. For near vertical phoria, the Ortho-Rater and clinical measures are equivalent in reliability (r = 0.73 and 0.74), while the Sight-Screener is much lower (r = 0.55).

8. Except for a slight advantage of the Ortho-Rater on far lateral phoria, all tests are equally consistent for both far and near lateral phoria.

9. The Ortho-Rater test of depth perception is the most reliable (r = 0.83), followed by the Telebinocular (r = 0.79),

Howard-Dolman (r = 0.72), and Sight-Screener (r = 0.57).

10. The validity coefficients of the tests of monocular acuity for both far and near vision are practically equivalent for the Ortho-Rater and Sight-Screener (r = 0.71 to 0.84), as compared with the Telebinocular (r = 0.55 to 0.58).

11. For binocular acuity, both far and near, the validity coefficients for the Ortho-Rater are the highest (r = 0.90 to 0.70), for the Sight-Screener next (r = 0.71 to 0.64), and for the Telebinocular lowest (near only) (r = 0.55).

12. For vertical phoria, both far and near, the validity coefficients are quite low for all devices (r = 0.29 to 0.50).

13. For far lateral phoria, the validity coefficients for the Ortho-Rater are much higher (r = 0.57 to 0.70), than for the other two devices (r = 0.37) each.

14. For near lateral phoria the validity coefficients of the Ortho-Rater and Tele-binocular are practically equivalent (r = 0.67 to 0.68), while that for the Sight-Screener is somewhat lower (r = 0.54).

15. In the factor analysis of far visual acuity, the Sight-Screener and Ortho-Rater are equivalent to the Snellen chart on the factor of resolution; whereas, the Tele-binocular loadings are lower on this factor. Significant form factors are revealed in the Snellen and Sight-Screener tests, while accommodation and interference factors affect the Telebinocular test and a specific machine factor affects the Ortho-Rater test.

16. For near vision, the factor loadings for resolution are lowest for the Telebinocular while for the other three devices the loadings are equivalent. A factor of accommodation affects all tests of near vision, but affects the Snellen and Ortho-Rater tests more than the others. A form factor is present in the Snellen and Telebinocular tests of near vision, while a specific machine factor is present in the Ortho-Rater test.

17. Although the Ortho-Rater shows the highest loading for vertical phoria for both far and near, it suffers from a specific instrument factor, especially at near. On the other hand, it reveals the lowest factor loading for "fusion."

18. The Ortho-Rater leads all instruments in factor loadings for lateral phoria, both far and near. All machine tests show higher factor loadings for lateral phoria than the Maddox Rod test. The latter is affected, also, by the "fusion" factor.

19. The Ortho-Rater presents the highest factor loadings for depth perception. The other two devices are affected by form, interference, or specific machine factors.

CONCLUSIONS

1. It is evident that a machine test of visual factors can be used to predict clinical factors with a fair degree of accuracy and consistency.

2. For visual acuity measures, the Ortho-Rater is slightly more reliable and valid than the other devices.

3. For vertical phoria, the Ortho-Rater is most consistent, but the validity coefficients for all devices are relatively low.

4. For far lateral phoria, the Ortho-Rater is slightly more consistent and is definitely more valid than the other devices.

5. In the measurement of far visual acuity, the Ortho-Rater and Sight-Screener are equivalent as to the factor of resolution, but all three instruments are adversely affected by one or more other factors.

6. All tests for near vision are affected by factors other than resolution.

7. The Ortho-Rater presents the highest factor loading for vertical phoria, but suffers from a specific machine factor.

8. The Ortho-Rater presents the highest factor loading for lateral phoria.

9. The Ortho-Rater presents the highest factor loading for depth perception and is least affected by other factors.

907 Crescent Drive (25).

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STUDIES OF HUMAN TEARS*

Joseph Smolens, B.S., Irving H. Leopold, M.D., and James Parker, M.D.

Philadelphia, Pennsylvania

The first chemical analysis of tears was recorded in 1791 by Fourcroy and Van Quelin.[1] Subsequent analyses have been made.[2-5] The most recent one was that reported by Ridley and Brown, in 1930.[5c]

Fleming,[6] in 1922, demonstrated that tears had the property of lyzing certain saprophytic cocci. He showed that this was an enzyme-like substance which he named lysozyme. This substance has been found in nasal mucus, sputum, various tissue extracts, and egg white. The ready availability of egg white provided a convenient source of material. Therefore, chemical studies of lysozyme have dealt with this egg-white substance which is considered the typical lysozyme.[7] It has been shown to be a basic protein containing 16-percent nitrogen and 2- to 3-percent sulfur. It is of small molecular size and has a molecular weight of 14,000 to 17,000.[8]

Available evidence suggests that the "lysozyme" from various tissues and secretions of the body are essentially similar to egg-white lysozyme.[7c, 9, 10] Roberts and coworkers[7c] found that lysozymes of egg white and of cat's saliva were both basic and had similar solubility and sedimentation constants. However, the two agents were antigenically distinct.

Thompson[11] concluded from a review of the literature that lysozymes from various sources are similar in chemical constitution and properties, and that differences in chemical makeup sufficient to produce antigenic differentiation do not negate the essential identity of these enzymes. It should be understood that the egg-white lysozymes used in these above studies were not crystalline although of fairly high purity.

The present study was undertaken in an effort to analyze human tears further with particular interest in the fraction containing lysozyme activity.[†] For fractionation of plasma proteins several methods have been employed such as salt fractionation, ultracentrifugation, and electrophoresis.

Although salting-out methods have been useful, it has been stated that these fractions do not fulfill the criteria necessary to establish them as chemical individuals.[12] It has been suggested that many of the fractions isolated by this method might have been altered by the severity of the treatment used.[13] Ultracentrifuge or gravity methods of separation have been helpful but contributed only little toward the progress in isolation of components.

The moving boundary method of electrophoresis has been employed recently with considerable success.[14, 15] This technique has proven of great importance especially for the estimation of the components of many proteins that at one time had been considered as being homogeneous. Tiselius emphasizes that electrophoresis is a very mild agent of separation and thus is likely to produce a constituent nearly unaltered from its natural state. However, the components found do not necessarily represent chemical individuals.

Previous analyses of proteins in the human tears have been based on salting-out procedures. Ridley and Brown, in 1930,[5c] determined the amount of protein soluble in 50-percent $(NH_4)_2SO_4$ which they called albumin. The remainder or insoluble protein was designated globulin.

Electrophoretic analyses of tears have not been recorded, although such analyses have been made on the vitreous humor and on ground-up lenses of cattle by Hesselvik,[16] and crystalline egg-white lysozyme has been

similarly analyzed by Alderton, Ward and Fevold.[8]

EXPERIMENTAL PROCEDURE

Tears were collected from the normal eyes of 215 volunteers (430 eyes). Sterile drawn-glass pipettes were used. Approximately 0.1 ml. were taken from each eye of every individual. Benzyl bromide was used frequently as a lacrimating agent. Earlier analysis of lysozyme activity showed that over 0.1 ml. of tears could be taken from an eye following benzyl bromide stimulation without a detectable reduction in lysozyme

TABLE 1

COMPOSITION OF NORMAL HUMAN TEARS

Fraction	Mg/1 ml.	Percentage
Original tears	18.7	100.0
Nondialyzable	9.1	48.6
NaCl	4.9	26.2
Dialyzable other than NaCl	4.7	25.1

content.[17] At different times, two batches of 14 ml. of tears and one of 13 ml. were obtained.

A. ANALYTICAL METHODS

1. Total solids. Total solids were found by placing 1 ml. of normal human tears in a weighing bottle and the water removed by evaporation at 105°C. It was then heated further for 1 hour at 105°C., cooled in a desiccator and weighed. The residue weighed 18.7 mg.

2. Chloride content. An amount, 2.288 mg., of the dried tears were removed from the bottle in which the total solid determination was made and the chloride content was determined gravimetrically. The yield was 16.0 percent of chloride or 26.6 percent of NaCl. Table 1 presents the results.

3. Dialysis. Tears were separated into dialyzable and nondialyzable fractions. Ten ml. of distilled water were added to 1.5 ml. of

clear tears. This solution was placed in cellophane tubing and dialyzed at 5°C. against 15 changes of 10-ml. volumes of distilled water. The dialysates were pooled. The final three dialysates gave negative tests for the chloride ion using silver nitrate. The dialysate and the nondialyzable material were dried from the frozen state. The yield of dialysate was 14 mg. or 55 percent; the yield of nondialyzable material was 11.5 mg. or 45 percent. A small amount of material adhered to the walls of the bottles which accounted for the slight loss, since 1.5 ml. of tears should have yielded 1.5 × 18.7 or 28 mg. and only 14.0 + 11.5 or 25.6 mg. were recovered.

In another experiment 3.2 ml. of tears were dialyzed at 5°C. versus running distilled water for 24 hours. The solution was removed from the cellophane tubing and dried at 105°C.; this weighed 29.9 mg. representing 48.6 percent of nondialyzable material. This latter determination is probably more accurate than the first method (45 percent) since the method employed was more exact. Table 1 includes these data.

B. ELECTROPHORETIC ANALYSES

1. Separation. Fourteen ml. of these pooled normal human tears were centrifuged and filtered through paper in order to remove extraneous materials. The filtrate was then put into cellophane tubing and dialyzed for 72 hours against phosphate buffer, pH 7.9 and ionic strength 0.1. Electrophoretic analyses* were made in the usual manner.[14, 15] The current was 19 ma.; the potential gradient was 10.8 volts/cm. At a later date another sample of 14 ml. of pooled normal human tears was similarly studied and the same results obtained.

Four components were seen at pH 7.9. Three of these migrated toward the negative pole and were positively charged, the fourth component was negatively charged. Percentages and mobilities of each component were

* Apparatus manufactured by Klett Mfg. Co., New York.

determined. Chart 1 reproduces a diagrammatic representation of the descending side taken after 7,020 seconds, and Table 2 gives the results obtained. Component 1 was easily

DIAGRAMMATIC REPRODUCTION
TEARS 3-11-48 DESCENDING 7020 SECONDS
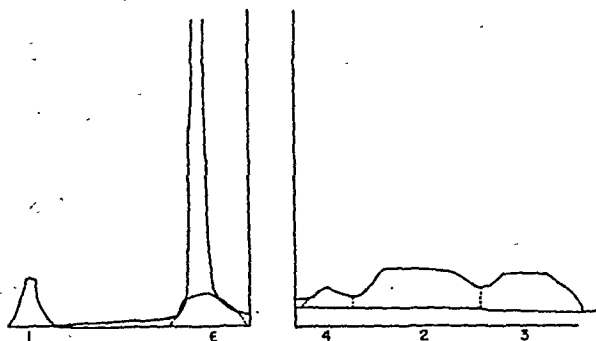
Chart 1 (Smolens, Leopold, and Parker). A diagrammatic representation of the descending side taken after 7,020 seconds.

isolated since it migrated in a direction opposite to that of Components 2, 3, and 4.

2. *Lysozyme activity of components.* In an effort to determine in which components the lysozyme activity resided, estimations were made of the ability of the pooled fresh tears, and of the components isolated electrophoretically to cause lysis of Micrococcus lysodeikticus. The method employed was that of Smolens and Charney.[18] Table 3 shows the results.

It was found that the original tears which had been dialyzed but not subjected to elec-

TABLE 2
RESULTS OF ELECTROPHORETIC ANALYSIS

Component	Percentage	Mobility $(u_d \times 10^5$ cm.^{2} volt^{-1} sec.$^{-1})$
1	15.1	−9.8
2	42.8	11.6
3	34.4	18.0
4	7.2	6.7

trophoresis and the combined Components 2, 3, and 4 which had been isolated electrophoretically lyzed the substrate in a very high and equal dilution. Component 1 had no activity. No effort was made to separate Components 2, 3, and 4 as the amount of the tears available was two small. No conclusion can be made as to whether all of the activity is contained in any single electrophoretic component. The evidence shows that the lysozyme active portions lie in Components 2, 3, and 4. Not one of these fractions had the same mobility as that found for crystalline egg-white lysozyme by Alderton, Ward, and Fevold.[8] It appears, therefore, that tears lysozyme differs, by electrophoretic analysis, from crystallized egg-white lysozyme.

C. AMMONIUM SULFATE FRACTIONATION.

1. *Separation. Ammonium sulfate* fractionation was attempted on 11 ml. recovered from the electrophoresis cell. An equal vol-

TABLE 3
LYSOZYME ACTIVITY OF TEAR FRACTIONS

Fraction	Final Dilution of Fraction ×1,000													
	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	1:1,024	1:2,048	1:4,096	1:8,192	1:16,380	1:32,760
Original tears	+*	+	+	+	+	+	+	+	+	±	0	0	0	
1 component	−	−	0	0	0	0	0	0	0	0	0	0	0	
2, 3, 4 components	+	+	+	+	+	+	+	+	+	+	±	0	0	
(NH₄)₂SO₄ ppt. pH 7.0	+	+	+	+	+	+	+	+	±	0	0	0	0	
(NH₄)₂SO₄ super. pH 7.0	+	+	+	+	+	+	+	+	+	±	0	0	0	
(NH₄)₂SO₄ ppt. pH 4.7	+	+	+	+	+	+	+	+	+	+	±	0	0	
(NH₄)₂SO₄ super. pH 4.7	+	+	+	+	+	+	+	+	+	+	±	0	0	
Lysozyme†	+	+	+	+	+	+	+	+	+	+	+	+	±	0

* + =Complete lysis.
± =Partial lysis.
0 =No lysis.
† Lysozyme =6 times recrystallized lysozyme from egg white.

ume of saturated ammonium sulfate was added. The pH of the mixture was 7.0. This was kept at 5°C. for 20 hours, centrifuged in the cold, and the supernate poured off. The sediment was washed twice with cold 50-percent ammonium sulfate and the two washings were combined with the supernate. Fifteen ml. of distilled water were used to dissolve the precipitate.

Both the supernate and the dissolved precipitate were put into cellophane tubing and dialyzed at 5°C. versus running distilled water until free of sulfate, phosphate, and chloride (about 54 hours). The yield for ammonium sulfate precipitate was 14.7 percent and the supernate yield was 85.3 percent.

Fifty-eight mg. of this were taken up in 7.5 ml. of 0.85-percent NaCl. This dissolved readily with very slight opalescence. $(NH_4)_2SO_4$ was added to 50-percent concentration. Since there was no buffer present, the pH of the mixture was 4.7. This was allowed to stand for three hours at 5°C. and centrifuged. The same procedure, as described above, was repeated. The yield of the precipitate was 41.0 percent and of the supernate 59 percent. There was a striking difference between the separation effected at the two pH levels. Repetition of the procedure gave almost identical results. At pH 7.0, the precipitate yield was 13.7 percent and the supernate 86.3 percent, and at pH 4.7, 41 percent and 59 percent, respectively.

From the salting-out procedure pH 4.7, the soluble fraction equals 59 percent. This agrees closely with the finding of Ridley and Brown.[5e] In their report they designated the soluble portion albumin as constituting 58.5 percent of the total. However, salt fractionation at pH 7.0 produced a markedly different result which resembled more closely those found by electrophoresis.

2. Nitrogen and phosphorus contents. Nitrogen determinations were made using the micro-Dumas method. Results were: Original undialyzed tears equal 7.1 percent; $(NH_4)_2SO_4$ supernate, pH 7.0, equals 13

percent and $(NH_4)_2SO_4$ precipitate equals 11.5 percent.

Phosphorus determinations were made on each of the two fractions using the method of King.[19] Negative results were obtained. From the result obtained in the positive P control it may be concluded that with the amount of sample used that less than 0.5 percent P is contained in the nondialyzable fraction of tears. This means that very little, if any, phospho- or nucleo-proteins are present in tears.

3. Molisch reaction. Tears which had been dialyzed gave a positive Molisch reaction indicating the presence of sugar. The 50 percent $(NH_4)_2SO_4$ supernate at pH 7.0 gave a very faint test using 2 mg. per ml.; whereas, the precipitate gave a much stronger reaction with a solution of 1 mg. per ml.

4. Lysozyme activity. Estimations were made of the ability of the ammonium sulfate fractions obtained at pH 7.0 and 4.7, to cause the lysis of M. lysodeikticus. The same method mentioned previously was employed.[17] It was found that, at pH 4.7, there was equal activity, but, at pH 7.0, the $(NH_4)_2SO_4$ precipitate contained only 25 percent of the activity of the supernate. Results are shown in Table 3.

5. Ultraviolet absorption spectra. None of the amino acids and only a few special proteins absorb light in the visible region. However, nearly all of the proteins and certain of the amino acids exhibit a strong specific absorption between 3,000 and 2,500 Angstrom units, in the ultraviolet region. The property of proteins to absorb ultraviolet light is most likely due to their content of aromatic amino acids, phenylalanine, tyrosine, and tryptophan. It is commonly accepted that the aromatic hydrocarbons are the only ones which exhibit band spectra. The ability of other amino acids to absorb light is slight in comparison to that of the aromatic amino acids.[20]

Ultraviolet absorption spectra were determined on pooled human tears and the results are shown in Chart 2. Maximum ab-

sorption occurred at 2,775 Angstrom units. The same figure obtained for the supernate isolated by 50-percent ammonium sulfate fractionation at pH 7.9 (Charts 2 and 3). This is most likely due to the tryptophan and or tyrosine content since the maxima for these amino acids are about 2,800 Angstrom units.[21]

Similar results have been obtained not only from the usual proteins but from virus and bacterial proteins.[22a-c]

demonstrates a specific antigenic dissimilarity.

DISCUSSION

The results show that the nondialyzable material in tears can be separated into at least four components by electrophoretic technique. The three components that migrated to the negative pole at pH 7.9 possessed all of the lysozyme activity. The mobilities of these components differed from those ascribed to crystalline egg-white lyso-
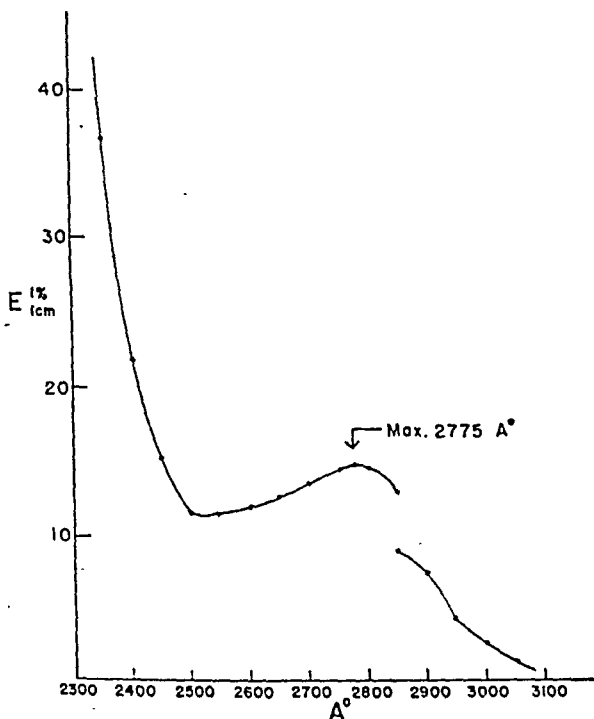
Chart 2 (Smolens, Leopold, and Parker). Ultraviolet absorption spectra were determined on pooled human tears.
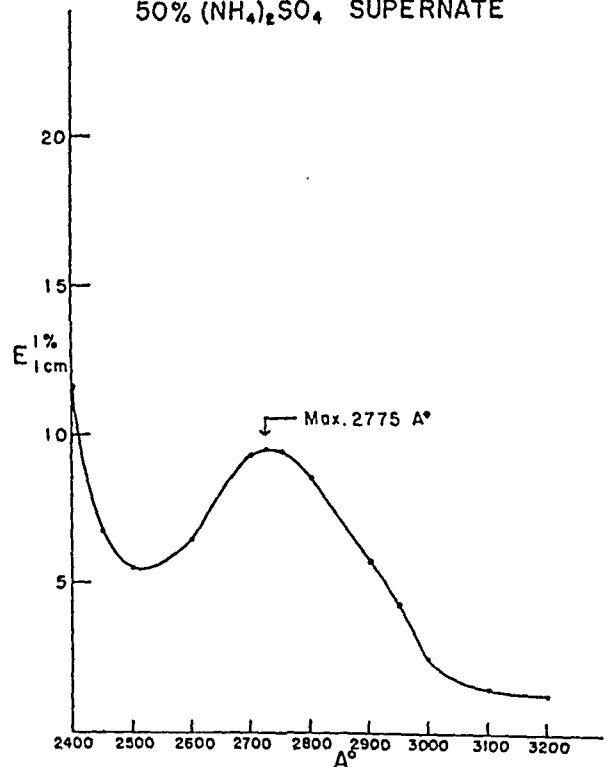
Chart 3 (Smolens, Leopold, and Parker). Ultraviolet absorption spectra were determined on pooled human tears.

D. INFLUENCE OF EGG-WHITE LYSOZYME ANTISERA

In order to demonstrate an antigenic difference of crystalline egg-white lysozyme and of tear lysozyme, the ability of each to lyze M. lysodeikticus, in the presence of rabbit antisera prepared versus crystalline egg-white lysozyme, was ascertained. It is evident from results shown in Table 4 that the antisera inhibits only the homologous and not the heterologous lysozyme which

zyme. Further, specific antisera prepared against crystalline egg-white lysozyme failed to inhibit the lytic activity of tears. These differences clearly demonstrate immunologic and chemical differences between egg-white and tear lysozymes. As has been shown previously,[18] this again points out that the ability of any material to lyze M. lysodeikticus is probably not to be ascribed to any specific entity.

It is also evident that the three compo-

nents have mobilities and isoelectric points that have not been described as occurring in human sera. This may mean that these substances are not present in human sera and that they are produced in the tear glands, or that these components exist in human sera in very low concentrations. It should be

hibit characteristic electrophoretic mobilities which are completely different from the tear components.

Electrophoretic analysis of calf thymus histone has been reported by Weissman and Graf[23] to give a value of $u_d = {}^+9.1$. Bloom, and others[24] have found a fraction B. an-

TABLE 4

INHIBITION EXPERIMENT DEMONSTRATING SPECIFICITY DIFFERENCE OF CRYSTALLINE
EGG-WHITE LYSOZYME AND TEAR FRACTION

Dilution	Time of Reading Hrs.	ml. Antiserum per Tube							
		0.1	0.05	0.025	0.0125	0.006	0.003	0.0015	0
1:80×10³ Egg white lysozyme	1½ 2½ 4	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
1:800×10³	1½ 2½ 4	0 0 0	0 0 0	0 0 0	+ + +	+ + +	+ + +	+ + +	+ + +
1:8000×10³	1½ 2½ 4	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0
1:80×10³ (NH₄)₂SO₄ pH 7.0 Supernate of tears	1½ 2½ 4	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +	+ + +
1:800×10³	1½ 2½ 4	± ± ±	± ± ±	± ± ±	± ± ±	± ± ±	± ± ±	± ± ±	0 ± ±
1:8000×10³	1½ 2½ 4	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0
Control (no lysozyme)	1½ 2½ 4	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0	0 0 0

+ = complete lysis (no inhibition).
± = partial lysis.
0 = no lysis (inhibition).
Note: Overnight readings showed that all of the tubes containing more than 0.003 ml. serum gave a ± reading. This was due to the lytic action of the serum.

possible to decide this by the use of immunologic methods. Since the lysozyme concentration of the tears is decreased with lacrimation, it is possible that the source of lysozyme resides in the bacterial flora normally present in the eye.

Ridley and Brown[50] have designated their (NH₄)₂SO₄ fractions as albumin and globulin following the classic nomenclature. These terms are untenable in view of the mobilities reported here. Albumins and globulins ex-

thracis that has a $u_d = {}^+8.0$ Both of these analyses were carried out at pH 5.5. These mobilities, which represent highly basic substances, are slower than those reported here for tear components. The discrepancy should be even more apparent if the difference in pH is taken into consideration. To date we have been unable to find in the literature any substance with similar electrophoretic mobility as those found in the tears.

It is of interest to note the difference in re-

sults obtained by 50 percent $(NH_4)_2SO_4$ fractionation at pH 4.7 and 7.0. Quantitatively our data at pH 4.7 closely corroborate the findings reported by Ridley and Brown.[50]

The salting out at pH 7.0 seems to produce fractions similar to those obtained electrophoretically, if yields and lytic activities are used as criteria. The decrease of precipitate with rise in pH suggests the presence of an acidic fraction. Seibert found analogous phenomena in her analysis of tuberculin preparations. She discovered that this can be contributed to contamination with nucleic acid and a polysaccharide.[25] The negative result obtained for P would rule out the presence of nucleic acid in any appreciable quantity in tears.

The positive Molisch test on the nondialyzable fraction indicates the presence of a sugar. It is interesting that both the dialyzed tears and the 50-percent $(NH_4)_2SO_4$ pH 7.0 precipitate give much stronger Molisch reactions than the supernate. This latter trace reaction may be due to contamination of small amounts of precipitate.

The possibility of an acidic polysaccharide is strengthened indirectly by the N values. A very high N content would be expected in tear fractions because of their basic isoelectric points. Contrary to this expectation low-N figures were given. If this were a simple protein a value of 16-percent N should be expected. However, the fraction found in tears contained only 12-to 13-percent N. This fraction must be either lacking or very low in N content as well as being acidic. Further experiments should clarify this point.

SUMMARY

1. Tears contain at least four components by electrophoretic analyses. One migrated to the positive pole and three to the negative pole.

2. Lysozyme activity resides in the three components that migrate to the negative pole.

3. Chemical and immunologic differences are demonstrated between tear components and crystalline egg-white lysozyme.

4. Ammonium sulfate fractionation of tears yielded two components in varying concentration depending on the pH at which the fractionation was performed.

5. The total solids in tears was 1.87 percent.

6. The chloride content of tears was 16-percent chloride or 26.2-percent sodium chloride.

7. Ultraviolet absorption showed a typical protein curve denoting the presence of aromatic amino acids.

8. The tears were divided into dialyzable and nondialyzable fractions. The yield of dialysate was 51.4 percent and the nondialyzable was 48.6 percent.

9. A positive Molisch reaction indicates the presence of a sugar.

Wyeth Institute of Applied Biochemistry (30).
1930 Chestnut Street (3).
Wills Hospital.

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DISCUSSION

DR. DAVID G. COGAN (Boston, Massachusetts) : Dr. Leopold's subject is on normal human tears, but I think it would be very interesting to know if he has made any determination of lysozyme concentration of tears under pathologic conditions.

DR. TRYGVE GUNDERSEN (Boston, Massachusetts) : It may be of interest at this time to draw attention to an apparent error in Duke-Elder's *Textbook of Ophthalmology*, v. 1, p. 639. In Table XXXII—Composition of Tears (in grams percent) Ridley-Brown (1930) are quoted as finding tear sugar 0.65.

Dr. John Talbot and I, in an analysis of approximately 10 tear samples, found this figure about 10 times too high. The error is apparently one of a decimal point.

DR. LEOPOLD (closing) : We have run lysozyme concentrations on normal and on pathologic tears. We have not done any chemical or electrophoretic analyses on pathologic tears because of the large amounts required. In order to get an analysis of one particular condition, you would have to get a great number of eyes; you must have at least 11 milliliters in order to run one electrophoretic analysis on our apparatus. For example, if one planned to investigate superficial punctate keratitis, one would have to get at least one tenth of a milliliter per eye. One hundred and ten eyes would be required in order to get enough for that analysis.

However, we have run lysozyme concentrations on superficial punctate keratitis and the resulting impression is that they are high in lysozyme content. At first Dr. Meyer in New York, who is also interested in this problem, believed that he was obtaining high values in the superficial punctate, but I believe when he used the new method of chemical analysis which does not depend on lysis of the Micrococcus lysodeikticus itself, he did not feel that the lysozme content was elevated in these eyes.

We have not reported the sugar content on total tears, but believe Dr. Gundersen is correct.

EFFECT OF BAL (2, 3 DIMERCAPTOPROPANOL) ON INTRAOCULAR COPPER*

Frank W. Newell, M.D., John A. D. Cooper, Ph.D., and
Chester J. Farmer, Ph.D.
Chicago, Illinois

BAL (2, 3 dimercaptopropanol) was developed early in the war by Peters, Stocken, Thompson,[1] and their associates as an agent to counteract the effects of arsenical war gases, particularly Lewisite (B-chlorovinyldichloroarsine). Subsequently its systemic effect as an antidote in heavy metal poisoning was described, and there have been reports concerning this action in mercury,[2] lead,[3] gold,[4] and arsenic[5] reactions. The antidotal effect is ascribed to the reaction of BAL with the heavy metal to form a stable, relatively nontoxic ring compound, in which the metal is not available for combination with the tissues and inactivation of sulfhydryl containing enzyme systems. Additionally there are indications that BAL may remove the heavy metal from the enzyme system even after combination.

This study was directed toward the possible detoxification of intraocular copper with BAL systemic administration of the intravenous salt which, according to McCance and Widdowson,[6] causes a 20-fold increase in urinary excretion of cooper. The severe chemical inflammation caused by intraocular copper has been known since the classical experiments of Leber[7] but the mechanisms are still poorly understood. Our studies concerning the effects of copper on the eye will be the subject of another paper and we shall largely concern ourselves here with studies with BAL.

Chemically, copper and BAL react quantitatively to form a heavy, bluish-green precipitate which settles rapidly out of solution. The precipitate is insoluble in alcohol, ether, hot and cold water, and concentrated hydrochloric acid. It is soluble in concentrated nitric acid with the liberation of hydrogen. On the basis of analogy with the reaction of BAL with mercury chloride, the copper compound formed probably has the structural formula:
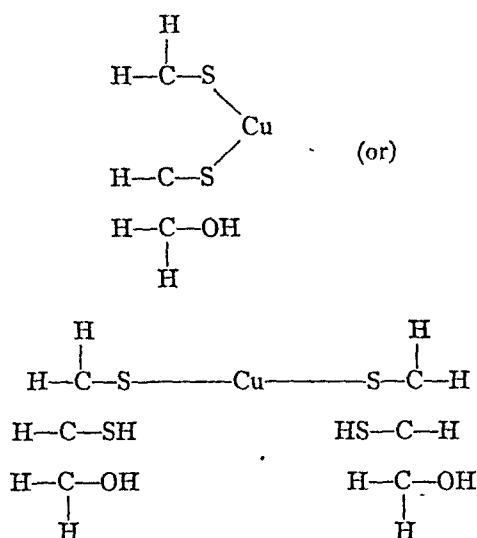
The reaction, as should be anticipated, occurs only with ionic copper and it was not possible to coat copper particles with BAL as metallic copper is insoluble in BAL solutions.

Experimental procedures

Male albino rabbits weighing 5 to 6 pounds were used throughout the study. Anesthesia was obtained with 10-percent sodium pentobarbital intravenously and 0.5-percent pontocaine topically.

Foreign material was placed in the anterior chamber with a Troncoso[8] introducer inserted through a small keratome incision at the limbus superiorly. Eserine was usually instilled in the conjunctival sac 30 minutes preoperatively to prevent iris prolapse.

Material was placed in the vitreous by

means of a specially constructed 14-gauge needle introduced into the eye through the pars plana superiorly. After the needle was in the eye and under direct observation through the pupil, the cooper or other material was forced into the vitreous with an obturator and the needle was withdrawn. There was a moderate loss of vitreous with this procedure but the eyes were white and apparently normal externally within 24 hours.

Injections of BAL into the anterior chamber were made with a 27-gauge needle introduced obliquely through the cornea to prevent loss of the injected material. Usually 0.15 cc. of aqueous was removed and a similar volume of fluid introduced through the same needle, care being taken not to touch the iris with the needle or entirely collapse the anterior chamber. BAL was injected into the vitreous through a 27-gauge needle inserted into the vitreous through the pars plana.

EFFECT OF BAL COPPER

Equimolar concentrations of BAL* and copper sulfate were mixed and the resulting precipitate filtered and repeatedly washed with distilled water. Immediately prior to use it was washed with alcohol and ether to sterilize and then introduced into either the anterior chamber or vitreous.

The precipitate was slowly absorbed from the anterior chamber and after a period of 60 to 90 days disappeared entirely without residue. Initially, a slight ciliary injection occurred and persisted for about 24 hours. It was attributed to the operative manipulation. At no time following this was there any evidence of inflammation provided the precipitate did not occlude the pupil. In the latter instance, a severe inflammatory reaction with secondary glaucoma ensued, an effect attributed to mechanical occlusion of the pupil. When the pupil was not occluded,

the precipitate caused a minimal reaction and disappeared at a rate that varied directly with the amount injected.

Histologic study of these eyes showed but slight evidence of inflammatory reaction. The cornea, lens, and posterior segment were free of the precipitate which was scattered through the iris and ciliary body. The angle contained some rather large particles but was open. The iris showed the most marked deposit of the copper salt in the area in contact and there was some endothelial proliferation here. Other copper was deep in the stroma with some round-cell infiltration but the inflammatory reaction was practically absent (fig. 1).

The precipitate was well tolerated by the vitreous and did not produce an inflammation if it did not come in contact with the retina. It remained glistening in the vitreous for periods as long as 60 days without change in appearance, size, or position.

Histologic study of these eyes indicated that in most the injection was through the anterior retina rather than the pars plana. The copper salt caused no cellular reaction and the retina in bulk and section showed no abnormality (fig. 2).

OCULAR TOLERANCE TO BAL

Studies were directed toward the determination of ocular tolerance to BAL when applied topically and when injected into either the vitreous or anterior chamber. Hughes,[9] Mann, Pirie, and Pullinger,[10] and Leopold and Adler[11] accurately determined the tolerance when topically applied in a variety of animals including man. Our findings did not vary from these investigators except that we found that BAL in the Fuqua base of Hughes was irritating on repeated application. Concentrations of BAL up to 20 percent in either aqueous or ointment bases were well tolerated by the cornea.

Leopold and Steele[12] showed that a therapeutic concentration of BAL following topical application penetrated the cornea. Their work was not repeated because the formation
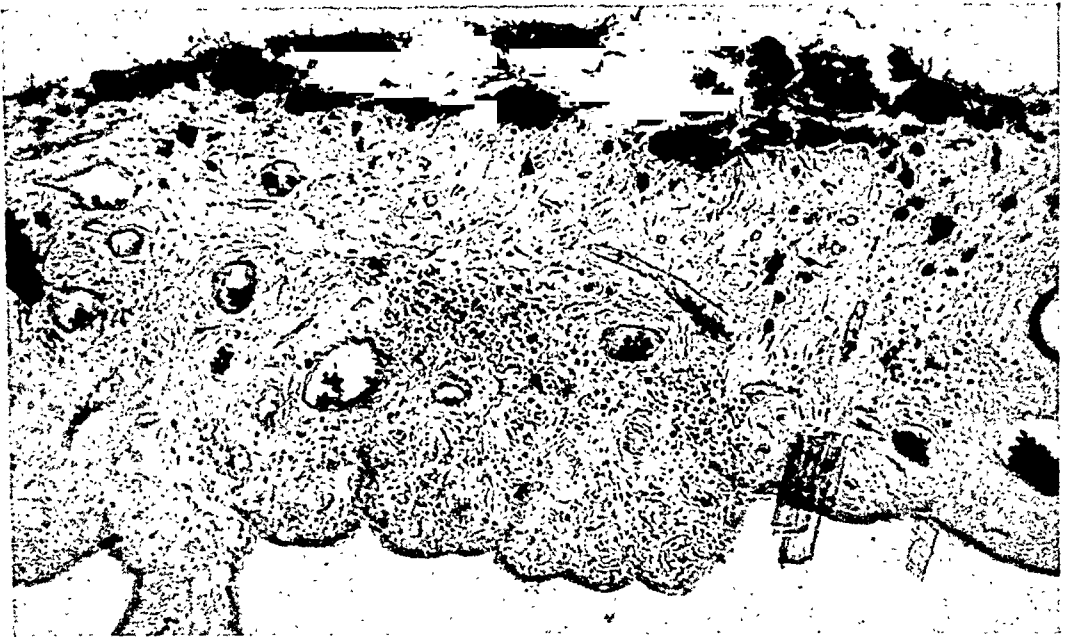
Fig. 1 (Newell, Cooper, and Farmer). Salt of BAL and copper sulfate scattered through the iris after 40 days. The inflammatory reaction is minimal.

of the precipitate of BAL-copper in the anterior chamber was evidence of the penetration through the cornea of BAL in eyes containing copper.

Considerable difficulty was experienced in finding a solution of BAL which could be injected into the anterior chamber without reaction. The solubility in water of various lots of BAL varied considerably and the toxicity varied from lot to lot. Injections of 1-percent BAL (by volume) caused a severe iritis with corneal infiltration and vascularization with permanent corneal scarring. Injection of 0.125-percent BAL in water was well tolerated provided the solution was freshly prepared and the operative manipulation was minimal.

EFFECT OF BAL ON COPPER IN THE ANTERIOR CHAMBER

Copper in the anterior chamber caused a remarkably constant reaction. Within 24 hours the foreign body was covered with leukocytes, the iris was diffusely injected, and there was an outpouring of fibrin into the anterior chamber. The acute phase lasted 7 to 8 days and subsided with the iris in-

Fig. 2 (Newell, Cooper, and Farmer). Salt of BAL and copper sulfate in vitreous 74 days after introduction. The retina is normal except at the wound of entrance of the needle used for introducing the salt.

jected only in the sector containing the foreign body. Approximately 4 to 5 days after introduction of the copper, a massive vascularization into the substantia propria commenced in the meridian nearest the foreign body and extended to a point just beyond the foreign body. At this time the leukocytic covering of the copper diminished and the foreign body became more metallic in appearance, although it was not visible.

Recession of the blood vessels began one month after maximal corneal involvement and, with their retrogression, copper was deposited in the cornea in the area involved in the vascularization. The copper particle was adherent to the cornea and iris and remained there for months without any reaction in the iris. These eyes remained unchanged for months except that the copper particle became more and more superficial. No animal completely extruded the copper but it was a simple procedure to dissect it from the cornea.

Slitlamp examination showed the metallic area to be composed of highly refractile crystals in either the endothelium or Descemet's membrane. The metallic area was present only where there had been vascularization, although the blood vessels appeared to be superficial to the coppering. In some animals a crescentic area in Bowman's membrane developed, separated by a clear interval from the main mass deep in the cornea; the mechanism of this deposition is not clear but seems to be related to the distribution of new blood vessels in the cornea.

Ten-percent BAL in aquaphor ointment was applied topically 4 times daily to eyes with copper in the anterior chamber. The initial application was made 4 hours after insertion of the metal in the eye. The right eye only was treated; the left eye, with copper in a similar location, was used as a control.

The severity of the polymorphic cellular reaction to copper was definitely lessened by topical BAL as long as the therapy was maintained. Reaction followed, however, within 24 hours after therapy was discontinued but was less severe than in the control eye. The aqueous showed a bluish coloration surrounding the foreign body within 4 hours after treatment was begun; this was attributed to the formation of the bluish salt of BAL-copper.

The most outstanding reaction of topical application of BAL was the severe corneal damage occurring in eyes with copper in the anterior chamber. After 2 or 3 installations of the BAL ointment the cornea was cloudy and diffusely edematous with numerous punctate staining areas. Slitlamp examination showed marked edema of the epithelium with multiple abrasions and cellular infiltration of the substantia propria. Frequently the cornea was so cloudy that the iris and pupil could be seen only with difficulty. Initially it was thought that this reaction was due only to the BAL, but topical application of the same ointment to normal eyes was well tolerated.

Leopold[12] indicated that corneas injured with Lewisite were more sensitive to the toxic effects of BAL than the normal cornea. Continued application of BAL to eyes containing copper resulted eventually in perforation of the globe. Interruption of the treatment within 72 hours resulted in rapid corneal healing with minute scars in the substantia propria.

Intramuscular administration of 2.5 mg./ kilogram of 10-percent BAL in peanut oil to animals with copper in the anterior chamber delayed the leukocytic reaction. To maintain therapeutic blood levels, the drug had to be injected every 4 hours and, as soon as the therapy was discontinued, the typical effects of copper followed.

Injection of 0.125-percent BAL into the anterior chamber of eyes containing copper resulted in a diminution of the leukocytic reaction plus the usual blue color. Interest-

ingly, there was no corneal reaction as occurred with topical application of the drug. Again, the administration of BAL had to be continued to prevent the copper reactions which occurred as soon as the drug was stopped.

EFFECT OF BAL ON COPPER IN THE VITREOUS

The reaction of the eye to copper in the vitreous varied considerably but in general two basic reactions were found to occur. A fibrous tissue proliferation with organization of the vitreous was most typical, the severity proportional to the rate of oxidation (and hence the surface) of the copper and the distance of the copper from the retina. Thus, a small enough piece of copper located as far as possible from the retina did not cause any gross reaction. The characteristic chalcosis oculi, with bluish-green discoloration of the iris and vitreous followed by deterioration of the eye, occurred only in the presence of blood in the vitreous. Study is being directed toward the possibility of a different copper salt being formed in the presence of hemorrhage.

BAL administered topically and intramuscularly understandably had no effect on copper in the vitreous. Intravitreal injection of 0.125-percent BAL may have had a minimal effect on preventing the fibrous tissue reaction of copper. It was difficult, however, to evaluate accurately the result, since a small piece of copper aroused such a minimal reaction immediately that no treatment was indicated, while a large piece or pieces of copper resulted in severe fibrosis of the vitreous which intravitreal BAL did not effect. Experiments were not done on eyes containing both blood and copper because of the long period of development of chalcosis oculi.

DISCUSSION

There have been several attempts to eliminate the toxic effects of copper in the eye,

most of them more ingenious than practical. Removal of the offending substance is, of course, indicated whenever possible and there have been numerous cases reported of complete recession of all of the ocular effects of copper once the exciting particle was removed.

Fragments in the posterior segment, however, frequently cannot be removed without destroying the eye. For copper in this location, some investigators have attempted to coat the particle with a metal, such as gold, well tolerated by the eye, while others have attempted to create a ferrous alloy which could then be removed with a magnet. Meller[13] reported a beneficial action of topically applied sodium thiosulfate which reacts with copper to form an insoluble salt well tolerated by the eye.

This study has indicated the possibility of detoxifying intraocular copper by some dithio compound that must, however, have certain chemical and physical characteristics not possessed by BAL. Since it is necessary to administer the drug over long periods, it must be nontoxic, be effective with oral administration, and have a molecule of such size or structure that it passes into the eye from the blood stream. Preferably it should be highly disassociated so it may be administered by iontophoresis, and it should form a salt with copper which is not toxic to the eye and of small enough size to be passed into the systemic circulation and be excreted.

CONCLUSIONS

1. BAL and copper react quantitatively to form a salt which is well tolerated when injected into either the anterior chamber or vitreous.

2. Topical application of BAL to eyes containing copper in the anterior chamber diminished the inflammatory effect of copper but caused severe corneal damage, the mechanism of which is not understood. BAL injected into the anterior chamber did not

cause corneal damage but had to be repeated at frequent intervals to be effective.

3. The effect of BAL on copper in the vitreous was minimal regardless of the mode of administration.

303 East Chicago Avenue (11).

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DISCUSSION

DR. JAMES RICHARDSON (Chicago, Illinois): I would like to ask if intracorneal injections of the BAL copper-sulfate precipitate were used?

DR. JONAS S. FRIEDENWALD (Baltimore, Maryland): I am very much intrigued by the idea that has been suggested that some copper-binding substance could be taken orally over long periods to prevent the toxic concentration of copper ions in the eye. There are such substances.

The thio-ureas form very insoluble copper salts and some of the symptoms of chronic thio-urea poisoning exhibit the characteristic pattern of copper deficiency. We need a certain amount of copper for survival. Animals that are copper-deficient lose their hair pigmentation and become ill, and so forth, and Dr. Richter, who has studied the effects of chronic thio-urea poisoning, has found that the characteristic symptoms of that poisoning are similar to that of copper deficiency.

Even if one had a copper remover that acted orally, it would be a total copper remover and might produce harm elsewhere.

DR. NEWELL (closing): The precipitate of BAL and copper sulfate was not injected into the cornea. Parenthetically, copper in the cornea causes a severe reaction with marked infiltration within 24 hours and within the week the cornea is necrotic and the foreign body is extruded.

Dr. Friedenwald's suggestion of using the thio-ureas in detoxifying copper reminds me that Meller in 1938 used sodium thiosulfate orally, topically, and subconjunctivally to create an insoluble copper salt well tolerated by the animal eye. Clinically, however, his work was not borne out.

THE MOVEMENT OF MONOSACCHARIDES INTO AND OUT OF THE AQUEOUS HUMOR*

JOHN E. HARRIS, PH.D., AND LETA B. GEHRSITZ, M.S.
Portland, Oregon

Two theories of the mechanism of aqueous formation are currently debated. One school of thought supports the view that the aqueous is largely a dialysate which is modified to a certain extent by the metabolism of intraocular tissues and possibly by some secretory activity. The proponents of this theory hold that the main osmotic constituents of the aqueous, that is, sodium salts, enter the aqueous humor via a simple diffusion augmented by a slight hydrostatic force.[1] The other school of thought supports the view that the aqueous is largely a secretion.[2,3] This theory, therefore, proposes that the main osmotic constituents are secreted into the aqueous.

Interpretation of the observed fact that glucose and urea exist in relative deficit in the aqueous humor as compared with plasma water has been the source of dispute between the protagonists of these two views. Those who feel that the aqueous is largely a dialysate contend that this deviation from a true equilibrium can be explained on the basis of a utilization of glucose by tissues bathed by the aqueous and/or an alteration of this dialysate by some secondary membrane in the system. A possible secretion of these substances into and/or out of the aqueous may occur at this membrane.

On the other hand, those who feel that the aqueous is largely a secretion hold that the deficiency of glucose and urea can be accounted for by the osmotic work done on the system by the secretion of sodium salts. Under this view, urea and glucose may enter by simple diffusion, although the possibility of secretion of these substances is not excluded. Therefore, independent observations of the exact means by which glucose and urea enter and leave the aqueous, that is, by secretion or diffusion, and of the extent by which metabolic activity modifies the concentrations, will be of material value in a definition of the dynamic factors involved in aqueous formation.

This information cannot be obtained from a knowledge of the distribution of these compounds between the aqueous and plasma at the steady state.† Steady-state ratios only indicate whether work is required for their maintenance but do not permit conclusions

† The term "steady state" is preferred to "equilibrium" since the latter may be confused with "thermodynamic equilibrium." A thermodynamic equilibrium requires that the concentrations of the nonelectrolytes be the same in both aqueous and plasma water. A steady state, as applied to a dynamic system, denotes a system in which there is no change with time and in which the concentration ratio may be any value.

as to the mechanism involved. Moreover, one cannot generally conclude from studies of the rate of passage of a substance across an unaltered barrier whether this substance is being secreted or is passing by simple diffusion. However, glucose is unique in this respect; work with other animal membranes has indicated that from a comparison of the rates of movement of various monosaccharides one can determine whether glucose is being secreted by the barrier.

It has been shown that glucose and galactose move across the intestinal wall approximately 7 to 10 times faster than the pentoses, xylose and arabinose.[4] Similar differentials have been observed in the kidney tubule.[5] This preferential movement of the hexoses is probably due to secretion.[6] On the other hand, the rate of absorption of the hexoses from the peritoneal cavity is substantially the same as that of the pentoses; that is, the movement seems to be by simple diffusion across a capillary membrane.[7]

One may assume, therefore, that glucose and galactose are secreted by the membrane in question if their movement is strikingly more rapid than that of the pentoses. If the rates of penetration of hexoses and pentoses are substantially the same, the process may be considered to be a simple diffusion. The work here reported was undertaken to determine which of these alternatives applies in the movement of these substances into the aqueous humor.

If the utilization of a sugar by ocular tissues is the sole factor responsible for its aqueous deficit, the pentoses should be equally distributed between plasma and aqueous water at a steady state, since it is quite certain that ocular tissues do not utilize pentoses to any appreciable extent. Thus, a comparison of the steady-state ratios of pentoses and glucose should provide a test of the theory that the deficit of glucose is due to its utilization by intraocular tissues. Moreover, if the monosaccharides are neither secreted into nor out of the aqueous, the process responsible for any deviation of the pentose

steady-state ratios from unity might reasonably be assumed to alter the glucose ratio in the same direction.

Many reports have been published on the movement of various carbohydrates into the aqueous. Robertson and Williams[8] showed that following the injection of glucose, its concentration in the aqueous increases; but the aqueous-plasma ratios they determined never exceeded 50 percent. Kinsey and Grant[9] reported a similar movement of fructose, with a steady-state ratio of about 50 percent. Weld, Feindel, and Davson[10] studied the accumulation of xylose, glucose, sucrose, and raffinose (a trisaccharide) in the aqueous and concluded that molecular weight is the determining factor in the movement; however, no steady-state ratios were determined. On the other hand, Rosner and Bellows[11] reached the conclusion that sorbitol accumulates in the aqueous humor much more slowly than glucose, although the molecular weights and structures of the two are similar. Again no steady-state ratio was obtained.

CALCULATIONS

To compare quantitatively the rates of movement of two or more substances across a membrane, some coefficient relating the concentrations of the substances in aqueous and plasma to the rate of movement must be calculated. A mathematical expression of this relationship is given by the following fundamental equation.

(1)
$$\frac{dC_a}{dT} = k_1 C_p - k_2 C_a$$

where C_a = Concentration of substance in aqueous.
C_p = Concentration of substance in plasma.
k_1 = Coefficient of transfer from plasma to aqueous.
k_2 = Coefficient of transfer from aqueous to plasma.

At the steady state:
$$k_1 C_p = k_2 C_a$$

Let
$$\alpha = \frac{C_a}{C_p} = \text{steady state ratio}$$

Then
(2)
$$k_2 = \frac{k_1}{\alpha}$$

Thus

(3)
$$\frac{dC_a}{dT}=k_1\left(C_p-\frac{C_a}{\alpha}\right)$$

No commitments are made concerning the force driving the solute in either direction. The conclusion concerning this must be drawn from a comparison of k_1 and k_2 values of the various sugars.

If the concentration in the plasma remains constant, expression (3) can be integrated within limits of T_1 and T_2 and rearranged to:

(4)
$$k_1=\frac{\alpha}{T_2-T_1}\ln\left[\frac{\alpha C_p-C_{a1}}{\alpha C_p-C_{a2}}\right]$$

A slightly different expression is obtained if C_p is not constant but still varies as a straight-line function of time. In this case $C_p=u+vT$ where u and v are constants that must be determined graphically from each experiment. Substituting:

$$\frac{dC_a}{dT}=k_1\left(u+vT-\frac{C_a}{\alpha}\right)$$

This equation has the general solution:

(5)
$$C_a=\alpha u+\alpha vT-\frac{\alpha^2 v}{k_1}+cc^{-k_1T/\alpha}$$

where c is a constant of integration. Equation (5) has no exact solution for k_1 but, by using the values of u and v for each particular experiment and the aqueous levels determined at T_1 and T_2, a sufficiently accurate figure for k_1 can be obtained by means of Newton's approximation.

k_2 is calculated from expression (2).

k_1 and k_2 incorporate the ratio of the area of the blood-aqueous barrier to the volume of the aqueous. This ratio is assumed to be reasonably constant from animal to animal.

As noted by Palm,[12] consideration should also be given to the assumption that the diffusing substance distributes itself immediately and in equal concentration throughout the aqueous. Actually, a concentration gradient may be established in the aqueous fluid. In the presence of such a gradient, k_1 calculated from aqueous levels determined at 10 and 30 minutes would be lower than that

calculated from data obtained at 5 and 25 minutes. Only the values for 1-arabinose indicated with an asterisk in Table 3 were determined over the later time period. They are the lowest obtained for this particular sugar and suggest that a concentration gradient may be established within the aqueous fluid.

METHODS

Albino rabbits, lightly anesthetized with nembutal, were used in this study. Sedation was considered necessary since struggling and excitement of the animal during a critical stage raises the blood sugar and vitiates
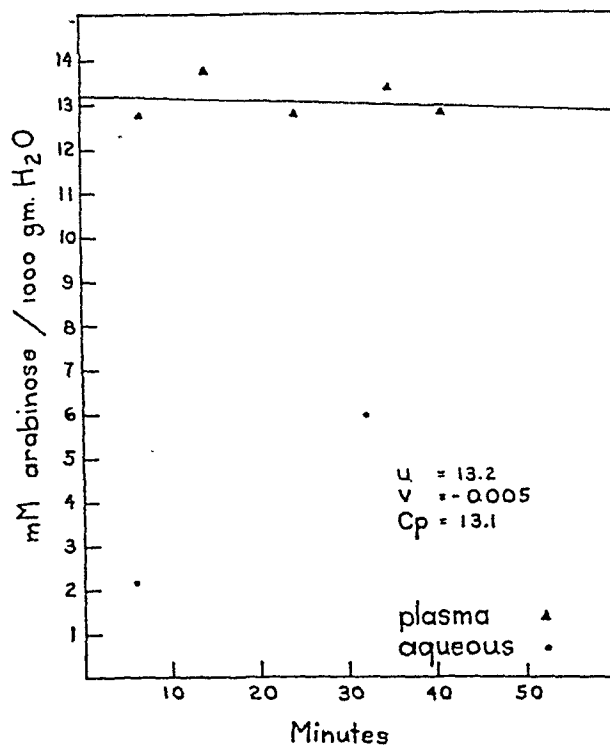
Fig. 1 (Harris and Gehrsitz). Sample data of one experiment from which the coefficients of transfer were calculated. The points represent the determined blood and aqueous levels. u and v are the constants determined graphically for this particular experiment, u being the ordinate intercept and v being the slope of the plasma concentration-time curve. C_p is the average plasma value and is used in the first approximation calculation of k_1 from Equation 4.

the results. The sugars, d-glucose, d-galactose, d-xylose, l-arabinose, and d-arabinose, were used. Each animal was given a subcutaneous injection followed by an intrave-

nous injection. The intravenous dose was 1 to 1.5 cc. per kilo of a 15-percent solution of the pentoses or an 18-percent solution of the hexoses. Five times this amount was given subcutaneously. By such a combination of injections, the plasma level of the sugar could be maintained as a straight-line function of time during the period of observation. Sample data from one experiment are graphically represented in figure 1.

Using heparin as an anticoagulant, periodic blood samples were taken from the

ous revealed that these filtrates contained no nonsugar reducing substances. Thus, the values reported are true sugar values. To determine absolute values for galactose and the pentoses, yeast fermentation was used on filtrates of these sugars.

Determination of the steady-state ratio of the various sugars presents a problem, since it is difficult, if not impossible, to maintain a constant level in the blood plasma for the hours necessary to achieve a steady state. Reformed aqueous is said to recover its glu-
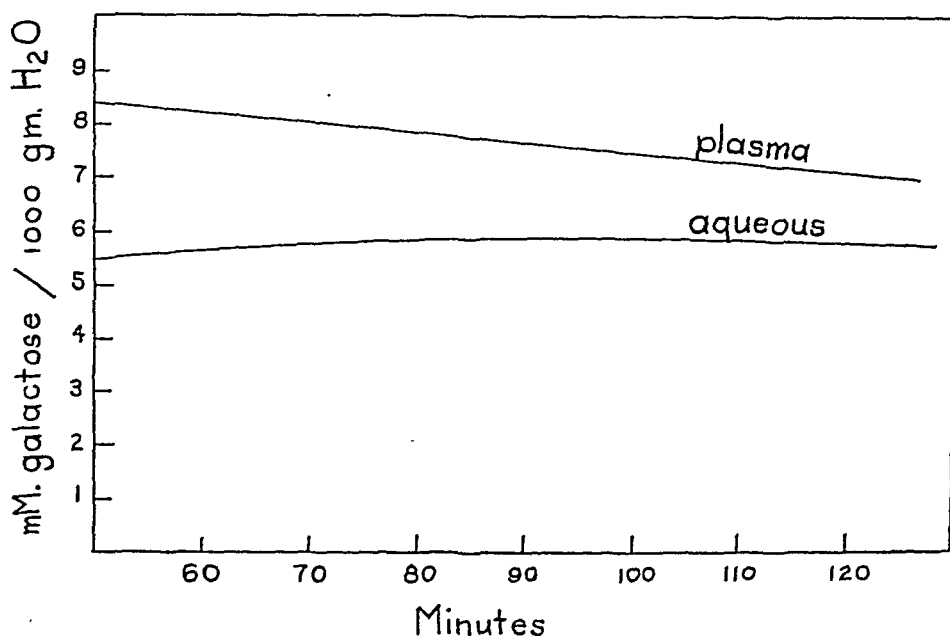
Fig. 2 (Harris and Gehrsitz). Graphic representation of the approach to the steady state of sugars diffusing into the aqueous where the plasma level is falling slowly. The curves mirror the trend of many experiments. In practice, the steady-state level was calculated by averaging determinations made at the inflection point.

marginal ear vein for analysis of the plasma sugar content. The value thus obtained was found to agree with that of arterial blood taken by heart puncture. A heart puncture was done at the end of each experiment for sugar and water determination. The first aqueous sample was generally taken 2 to 5 minutes after the intravenous injection; the second, 10 to 20 minutes later.

All sugars were determined by using the new reagent of Somogyi[13] on barium hydroxide-zinc sulfate filtrates. Yeast fermentation of sample filtrates of blood and aque-

cose level quite quickly.[14] In our hands, however, this did not prove a reliable method of determining the steady-state level. The ratio of the glucose content of the reformed aqueous to that of the plasma was found to vary inconsistently with that of the initial aqueous, even though periods as long as $1\frac{1}{2}$ hours had elapsed. In every case, the ratio was higher in the reformed than in the initial aqueous.

Examination of equation (1) shows that a steady state must be reached when $\dfrac{dC_a}{dT} = 0$.

The ratio of the blood level to the aqueous level at that point is the true steady-state ratio. Since the plasma sugar level cannot be maintained, the best alternative is to determine the peak or inflection point of the aqueous concentration during a period when the blood level is falling as a straight-line function of time. The ratio of the blood to the aqueous level at that point is the true steady state for the constituent in question.

Figure 2 shows an ideal graph of this relationship. It does not represent experimental data. A curve similar to this cannot be plotted for any one experiment because only two estimations of the aqueous concentration can be obtained. Moreover, the exact slope of the blood level cannot be duplicated in any two animals, or even in the same animal. Thus, the peak in aqueous concentration is not likely to occur at the same point on the time scale in any two experiments. For this reason, a composite curve of many animals cannot be constructed.

The average of a series of aqueous-plasma ratios determined at or near the peak was found to provide a reasonably exact approximation of the steady-state ratio. Experimentally, the peak for all sugars was demonstrated to be reached in about 85 to 105 minutes. The two aqueous samples were drawn 10 minutes apart during this time interval. The peak was considered to be reached if the aqueous levels did not vary more than 0.5 mM/kilo of water. Prior to the series, this figure was arbitrarily established from a consideration of the technical errors and the shape of the curve.

The time course of the plasma sugar level was determined for each experiment, starting 10 minutes before and extending through 10 minutes after the aqueous samples were withdrawn. If the plasma analyses would not fit a straight line, the experiment was discarded.

In actual practice, little difficulty was encountered in meeting these standards with xylose, arabinose, and galactose. Since the blood concentration of glucose had to be raised to a much higher level than that of the other sugars, the technical error contributed much more to the absolute difference. Nevertheless, the glucose steady state was determined in this same manner as a test of the validity of the assumptions and to insure experimental uniformity.

RESULTS

The steady-state values for the four sugars are given in Table 1 and are summarized in Table 2. The data indicate that the peak in aqueous concentration was approximated since the aqueous levels either fell or rose slightly or remained the same during the period of observation. The ratios for all sugars are below 1.0.

The values for k_1, the coefficient of transfer from plasma to aqueous, are given in Table 3. There is little difference between the rates of entrance of pentoses and hexoses. A closer parallel might be expected between d-xylose and l- and d-arabinose than was obtained. This difference may be due to the errors introduced by the assumptions made in the calculation of k_1. However, it may also be due to some restrictive influence at the barrier. Such a possibility was indicated by the work of Rosner and Bellows[11] on sorbitol.

The values for k_2, the coefficient of transfer out, are given in Table 4. Here again, no significant difference is shown between the movement of hexoses and pentoses.

DISCUSSION

In the introduction it was pointed out that where glucose and galactose are secreted across a membrane, their k values are 7 to 10 times greater than such values obtained when movement is by simple diffusion. The results show that the k_1 values for the hexoses and pentoses studied are essentially the same; consequently, glucose is not secreted into the aqueous. A similar evaluation of k_2 values indicates that glucose is not secreted out of the aqueous. It is concluded, therefore, that

TABLE 1

STEADY-STATE RATIOS

	d-Glucose					d-Galactose				
Ani-mal No.	Time—Minutes		Conc. in aqueous mM/1,000 gm. H_2O		$\dfrac{C_a}{C_p}$	Ani-mal No.	Time—Minutes		Conc. in aqueous mM/1,000 gm. H_2O		$\dfrac{C_a}{C_p}$
	Sample 1	Sample 2	Sample 1	Sample 2			Sample 1	Sample 2	Sample 1	Sample 2	
496	81:30	91:30	13.3	13.1	0.76 0.78	475	75:00	90:00	6.5	6.4	0.69 0.75
494	85:15	95:15	9.6	9.6	0.91 0.91	487	81:00	90:30	5.2	4.9	0.77 0.77
488	85:15	96:00	18.3	18.3	0.86 0.90	481	90:45	106:15	6.1	5.9	0.71 0.76
483	86:30	96:30	14.0	14.4	0.77 0.81	483	95:15	105:45	4.6	4.8	0.71 0.76
490	90:00	100:00	11.0	11.0	0.85 0.88	498	95:15	105:45	6.9	6.7	0.82 0.83
492	90:00	100:15	13.8	14.7	0.76 0.86	499	95:15	106:00	6.5	6.4	0.63 0.64
						488	100:30	111:45	4.7	5.1	0.77 0.88
	d-Xylose						l-Arabinose				
492	84:45	95:15	4.7	4.9	0.78 0.85	493	85:15	95:00	6.1	6.3	0.68 0.75
482	85:15	95:30	4.3	4.1	0.76 0.80	484	85:15	95:30	4.7	4.5	0.73 0.75
481	85:15	96:15	5.2	5.0	0.73 0.77	487	85:15	97:45	6.9	7.0	0.67 0.73
491	85.30	95:45	5.8	5.5	0.87 0.89	490	85:45	96:15	7.2	7.1	0.74 0.81
497	85:45	96:00	5.6	5.5	0.74 0.78	483	86:30	96:30	4.7	5.0	0.65 0.75
490	95:15	105:15	5.3	4.8	0.85 0.81	489	90:30	101:30	5.2	5.1	0.64 0.69
	d-Arabinose										
490	85:00	95:00	5.6	6.1	0.52 0.58						
486	85:00	95:15	3.7	4.1	0.47 0.56						
489	85:30	96:00	5.2	5.1	0.57 0.58						
487	85:45	95:45	4.5	4.5	0.49 0.52						

glucose enters and leaves the aqueous by a process of diffusion, not secretion.

As stated previously, if the metabolism of sugars were the only cause of deficit in the aqueous, the steady-state ratio of the pentoses would be expected to be one, and that of glucose below one. All sugars studied reach a steady-state ratio significantly below 1.0. This proves conclusively that the glucose deficit normally found is not due solely to its utilization by the lens and retina.* Indeed, it is surprising that the steady-state value for glucose is higher than that of other sugars. Since glucose is utilized by intraocular tissues, a lower value would reasonably be expected, all other things be-

TABLE 2
SUMMARY OF MEAN STEADY-STATE RATIOS

Sugar	Number of Animals	Mean	Standard Deviation
d-Glucose	6	0.84	±0.06
d-Galactose	7	0.75	±0.08
d-Xylose	6	0.80	±0.05
l-Arabinose	6	0.72	±0.04
d-Arabinose	4	0.54	

Two possibilities remain whereby a substance such as glucose, which is secreted neither into nor out of the aqueous, may exist in a relative deficit not accounted for by metabolic utilization. The first is that sufficient energy may be applied by the hydrostatic pressure in the capillaries to account

TABLE 3
COEFFICIENT OF TRANSFER (k_1) FROM PLASMA TO AQUEOUS

d-Glucose	d-Galactose	d-Xylose	l-Arabinose	d-Arabinose
2.9×10^{-2}	4.2×10^{-2}	4.5×10^{-2}	2.1×10^{-2}	2.3×10^{-2}
2.9	3.1	4.3	2.0	1.7
2.1	2.9	4.2	2.0	1.5
2.0	2.5	3.8	1.8	1.0
1.9	2.4	3.0	1.6	
1.6	2.1	2.7	1.5	
1.4		1.8	*1.3	
		1.5	*0.9	
Mean 2.1×10^{-2}	2.9×10^{-2}	3.2×10^{-2}	1.7×10^{-2}	1.6×10^{-2}
S.D. $\pm 0.6 \times 10^{-2}$	$\pm 0.7 \times 10^{-2}$	$\pm 1.2 \times 10^{-2}$	$\pm 0.4 \times 10^{-2}$	

* Time interval between intravenous injection and first aqueous sample—11 and 13 minutes, respectively

ing equal. The high glucose steady-state value may be due to the fact that the blood and aqueous concentrations of this substance must be raised higher than other sugars to determine the steady-state ratio by the method employed.

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*Since completion of our studies we have received a copy of a recent paper by Davson and Duke-Elder[15] who reported studies similar in some respects to our own. These authors found little difference in the rate of uptake of glucose, xylose, galactose, and 3-methyl-glucose in the cat. Our data conforms to this. Good agreement is shown between their steady-state value for glucose in the rabbit and that reported here. However, these authors did not measure the steady-state ratio for other sugars. From their studies, they concluded that the relative deficit of glucose can be explained on the basis of metabolic removal by the lens and retina. This view is incompatible with our findings in the rabbit.

for the deficit. This possibility was considered by Duke-Elder and Davson[16] and by Friedenwald,[3] but was found to be incompatible with the known pressure gradients.

The other possibility, suggested by Kinsey and Grant,[2] is that sufficient osmotic work can be done by some normal constituent of the aqueous to account for this deficit of

TABLE 4
COEFFICIENT OF TRANSFER (k_2) FROM AQUEOUS TO PLASMA

Sugar	k_2
d-Glucose	2.5×10^{-2}
d-Galactose	3.9×10^{-2}
d-Xylose	4.0×10^{-2}
l-Arabinose	2.4×10^{-2}
d-Arabinose	2.9×10^{-2}

nonelectrolytes. These authors envisage a through and through flow of aqueous driven by a secretion of sodium, the flow resulting from the osmotic influence of the secreted salts. The glucose deficit at the steady state is considered to be due to the relatively low rate of diffusion of this substance into the aqueous stream. Or, as Friedenwald[3] phrased it, "the least work toward establishing that steady state would occur if fluid relatively hypotonic in nonelectrolytes were 'transported." However, the secretion of sodium is not a necessary feature of this scheme if other means of doing osmotic work can be found.

If the aqueous humor is taken as the system, then the secretion of some substance into the aqueous involves work done on the system, and the deficit of nonelectrolytes results from work done by the system. If the system conforms to the second law of thermodynamics, then the work done on the system in the secretion of the substance must be equal to or exceed that done by the system in the formation of a glucose deficient fluid.* The work done on or by the system can be calculated from the equation:

$$w = nRT \ln \frac{C_1}{C_2}.$$

Calculations using this equation show that the work done by the system in the formation of a liter of aqueous with a glucose concentration of 80 mg. percent and an aqueous-plasma ratio of 0.8 is approximately 0.6 calories. A urea deficit, at physiologic concentrations, requires approximately one half this amount of work.

In a similar manner, the work done on the system in the secretion of a substance can be calculated if its concentration in aqueous and plasma is known.

Since the sodium analyses reported in the

literature do not show a consistent deviation from the Donnan equilibrium, that is, a true thermodynamic equilibrium, it is not possible to calculate the work theoretically done in its secretion, assuming for these purposes that it is secreted. However, using 1.0 calories as the minimum work that must be done, calculations indicate that the concentration of sodium chloride in the aqueous would be 1 mM/kilo of water in excess of a Donnan equilibrium if this substance were to satisfy the work requirements. This difference is too slight to be detected with regularity by the chemical methods that have been employed. Therefore, the possibility that a secretion of sodium may account for the glucose and urea deficit can be neither dismissed nor affirmed. Since there is no conclusive proof that sodium is secreted into the aqueous, it is advisable to evaluate other possible sources for osmotic work.

There is good evidence that ascorbic acid is secreted into the aqueous.[17] The work done on the system in the formation of a liter of aqueous with an ascorbic-acid concentration of 20 mg. percent and an aqueous-plasma ratio of 20 is calculated to be 2.0 calories. Therefore, the work necessary for the formation of a glucose deficient fluid is amply provided by the secretion of ascorbic acid into the aqueous, assuming all other substances enter by simple diffusion. Likewise, sufficient work is available to account for a urea deficit.

The fact that the work requirements are met in the rabbit if ascorbic acid is the sole substance secreted into the aqueous is not proof that the mechanism postulated is actually operating. There are other considerations.

First, since the concentration of ascorbic acid is not sufficient to account for the reported hyperosmotic pressure of the aqueous over plasma, other sources of osmotic work should be sought. For example, the formation of lactic acid from glucose by intraocular tissues, since it results in an increased osmotic activity, may aid in the

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* Since the work done on the system results in an increase in free energy of the system and the work done by the system results in a decrease, the work values will be opposite in sign. However, for our purpose, a comparison of the numerical values themselves is sufficient.

elaboration of an aqueous with a glucose and urea deficit in the manner suggested for ascorbic acid.

Second, although the low glucose and urea steady-state ratios have been the most consistently reported, osmotic work might reasonably be done on other aqueous constituents, for example, sodium salts. Yet, if the same amount of osmotic work that is performed on glucose was applied to the dilution of sodium salts, the resultant deviation from a true equilibrium would lie within the limits of error of the analytical methods that have been used.*

Finally, a thermodynamic balance which indicates that the secretion of ascorbic acid, perhaps supplemented by lactic-acid production, meets the necessary work requirements is only the first step in the proof that aqueous formation can be explained on this basis.

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* Within the limits of the work available, the steady-state ratio of a substance must also be influenced by its rate of diffusion into the aqueous. Thus, a substance which enters rapidly, such as ethyl alcohol,[12] would reasonably show the high steady-state ratio that has been reported, that is, approaching unity.

SUMMARY

A measure of the coefficient of transfer of d-glucose, d-galactose, d-xylose, l-arabinose, and d-arabinose into and out of the aqueous humor has been made in the rabbit. These coefficients have been shown to be substantially the same for the pentoses and hexoses. This indicates that glucose is neither secreted into nor out of the aqueous humor of the rabbit.

The steady-state ratios of all sugars studied was found to be substantially lower than 1.0 in the rabbit. The relative deficit of glucose in the aqueous of the rabbit cannot be accounted for solely on the basis of metabolic depletion.

The data obtained, using the rabbit, can be explained if ascorbic acid is considered to be the sole substance secreted into the aqueous. The production of lactic acid by intraocular tissues may be an additional source of osmotic work. The possibility of a secretion of sodium salts is not precluded.

Marquam Hill Road.

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DISCUSSION

DR. V. EVERETT KINSEY (Boston, Massachusetts) : I would like to point out, as I did to Dr. Harris last night, that I do not feel that it is possible to conclude whether glucose is secreted or diffused from the kind of data he obtained, although I do agree with his conclusion that it is diffused. I will try to point out in the following paper the additional kind of data which are necessary before conclusions can be drawn as to whether a substance enters the anterior chamber by secretion or diffusion.

DR. JONAS S. FRIEDENWALD (Baltimore, Maryland) : As I follow Dr. Harris's argument, it seems to me he assumes there is no intraocular utilization of glucose. I would like to ask him whether that is true. If there were intraocular utilization of glucose, then more glucose would have to go in than his equations account for, and the disparity between the glucose transport and the pentose transport would have to appear.

DR. HARRIS (closing) : Dr. Kinsey's objection, as he voiced it to me last night, is to our original premise that a comparison of the rates of transfer of various monosaccharides gives a basis for concluding whether glucose is secreted across some blood-aqueous barrier. The basis for this premise is included in the text of the paper. Across certain animal membranes, notably the intestine, the rate of transfer of glucose and galactose is much greater than that of the pentoses. This differential is eliminated by such metabolic poisons as sodium fluoride and phlorizin, indicating that the preferential

movement of glucose is due to some metabolic function of the membrane. Phosphorylation of glucose appears to be an essential part of this active transfer.

On the other hand, where the movement is by strict diffusion, as in solution or across a simple membrane such as the peritoneum, the hexoses and pentoses move at substantially the same rate, the pentoses having a slightly greater diffusion constant. It seems reasonable to conclude, therefore, that the movement is by diffusion if the rates of entrance are similar. Certainly, the burden of proof would rest with him who would interpret the data differently.

In answer to Dr. Friedenwald's question, we have not meant to infer that there is no intraocular utilization of glucose. Our kinetic results would be influenced by the intraocular metabolism of glucose if the rate of metabolism is proportional to the concentration in the aqueous. They would not mirror any intraocular utilization if it is constant and, thus, independent of the concentration in the ranges employed.

Since the latter is more likely, it is not surprising that our kinetic results do not demonstrate consumption of glucose by intraocular tissues. Parenthetically, it should be noted that the same considerations apply to a secretion at a blood-aqueous barrier.

One might expect the steady-state ratios to be demonstrably lower for glucose than for substances which are metabolically inert, such as xylose. This was not found and there are several possible explanations. One

important factor may be the concentrations employed in the experimental procedures. Glucose concentrations were maintained at a higher level than those of the other sugars.

Then, too, it may be that the metabolic activity of the intraocular tissues does not alter the concentration of glucose in the aqueous that one obtains for analysis by corneal puncture in the rabbit.

In this connection, the data presented in a recent paper by Davson and Duke-Elder are interesting. Studying the glucose distribution in the aphakic and normal eye of the cat and rabbit, they reported that, in the cat, the aqueous-glucose concentration was invariably higher in the aphakic than in the normal eye. On the other hand, in the rabbit, the glucose concentration was consistently the same or lower in the aqueous of the aphakic eye than in the normal eye.

The diffusion of glucose across the iris must certainly be considered a possibility. All that we can reasonably say is that, as we measured it by withdrawing fluid from the anterior chamber, we found no evidence that the deficit of glucose normally present in the aqueous of the rabbit can be explained on the basis of intraocular utilization. It may well be that there is a species difference between the cat and rabbit which extends beyond the ability to concentrate ascorbic acid.

THE RATE OF FLOW OF AQUEOUS HUMOR*

I. THE RATE OF DISAPPEARANCE OF PARA-AMINOHIPPURIC ACID, RADIOACTIVE RAYOPAKE, AND RADIOACTIVE DIODRAST FROM THE AQUEOUS HUMOR OF RABBITS

ERNST BÁRÁNY,[†] M.D.
Uppsala, Sweden
AND
V. EVERETT KINSEY,[‡] PH.D.
Boston, Massachusetts

The present papers will be concerned with methods for measuring the rate of flow of aqueous and the physiologic implication of flow. The time relations governing the entrance and exit of substances in the aqueous and the distribution ratios of substances between aqueous and blood are significantly affected by the rate of flow and cannot be understood without due regard to it (Kinsey and Grant[1]).

Since the eye is a physical system where the intraocular pressure is determined by the balance between the production and removal of aqueous, a knowledge of flow, and especially of its dependence on intraocular pressure, is of prime importance for an understanding of normal and abnormal intraocular pressure.

Finally, it is possible that the flow of aqueous in itself is of importance for the lens, since convection currents are probably more efficient than diffusion in moving material up to and away from the surface of the lens (Bárány[2]).

Determinations of the rate of aqueous flow using cannulation of the anterior chamber during the period of measurement cannot give physiologic values. Measurements aimed at establishing the rate of flow in eyes not altered by the procedures employed have to be done with indirect methods, by deriva-

tion from the time-concentration curve of a test substance in the aqueous.

This seems to have been attempted for the first time by Abe and Komura[3] who used fluorescein as a test substance and carried out the experiments on atropinized rabbits' eyes. The value they obtained shows a systematic error because of inadequate mathematical treatment.

Kinsey and Grant[1] derived the rate of flow of aqueous for the rabbit from curves representing the rate of accumulation of various substances in the aqueous. In these studies data from several animals were pooled and certain assumptions regarding the mode of entrance of the substances were made; for example, electrolytes were assumed to enter by secretion and not to be able to pass the blood-aqueous barrier by diffusion; nonelectrolytes were assumed to diffuse through the blood-aqueous barrier.

While their data were generally consistent with these assumptions, an independent redetermination of the rate of flow is indicated. The purpose of the present study is to make such a determination and to draw certain inferences from the flow rate thus obtained, regarding the mode of entrance of such physiologically important ions as sodium and chloride.

For convenience in presentation, the material has been divided into two parts. The first, the present paper, will be concerned with the rate of disappearance from the aqueous and the steady-state distribution ratio aqueous to plasma of several substances of graded molecular weight. The second will deal with the use of these data in computing the rate of flow of aqueous and the inferences regarding the mode of entrance of substances of physiologic importance.

METHODS

The rate of disappearance of a test substance from the anterior chamber would of itself constitute a measure of the rate of flow of aqueous, provided that (1) the substance was not replaced from the blood, (2) it

could leave the anterior chamber only by flow, and (3) it left the filtering angle at the same rate as other constituents of the aqueous humor. Under these conditions, when a certain fraction of the aqueous is removed from the anterior chamber by flow per unit of time, the same fraction of the total amount of test substance would disappear. While it is not practical to fulfill all of these ideal conditions, an experiment can be set up in which the deviations are slight. The experiments were designed in such a way as to provide such conditions.

The deviations from the ideal experimental arrangement are imposed primarily by the necessity of getting the substance into the eye under physiologic conditions. The most physiologic way to introduce the substance is by means of the blood stream. This leads to difficulties, however, since the object of the study is to determine the rate of disappearance from the aqueous of the substance under conditions of essentially no replacement from the blood. It is desirable to arrange the experiment so that once the substance is brought into the blood stream, and from there into the aqueous, it is rapidly removed from the blood again.

In the present study, this was accomplished by giving the test substance intravenously and selecting as test substances organic compounds which are actively excreted by the kidneys at maximal rate.

The ultimate goal of having the blood stream practically free of the substance while there still was a measurable amount in the aqueous was not reached, but the blood concentrations during the test period were so low that a small mathematical correction based on knowledge of the steady-state distribution ratios (aqueous concentration/plasma concentration) of the observed values was sufficient to take account of the presence of test substance in the blood.

The requirement that the substance leave the aqueous primarily by flow but still not be held back preferentially at the filtering angle was met by selecting materials of in-

termediate molecular weight. All of the desirable properties were encompassed in the following three substances: (1) para-aminohippuric acid (molecular weight, 194); (2) Rayopake, 2 Methyl-4-6 diketo-5-iodotetrahydropyridone-N-acetic acid (m.w., 308); and (3) Diodrast, 3, 5 diiodo-4-pyridone-N-acetic acid (m.w., 405).

The excretion of para-aminohippuric acid and Diodrast by the kidney approaches the theoretical maximum of total clearance of the blood by a single passage at low blood concentrations (Smith and others[4]). Rayopake is also rapidly excreted by the kidney. All three compounds have low toxicity and are only slightly adsorbed by the plasma proteins.

According to Hecht[5] the iodine compounds are unlikely to undergo any change in the body. Para-aminohippuric acid can be conjugated presumably by the liver, but it is extremely unlikely that this occurs also in the eye. While para-aminohippuric acid is readily estimated chemically, the current chemical methods for iodine are not accurate enough to determine the small amounts of the organic iodine compounds encountered in the experimental conditions here described.

In the experiments concerned with the rate of disappearance of the test substances, the aqueous samples contain only about one millionth of the amount of substance administered to the animal. Accordingly, Diodrast and Rayopake were synthesized using radioactive iodine, and the compounds were determined by measuring the radioactivity present.

Unanesthetized male albino rabbits, weighing between 1.6 and 2.6 kg., were used in all the experiments. They were kept on a stock diet and given water at pleasure. No effort was made to increase their kidney blood flow by forcing fluids. At least 10 days were allowed to elapse between repeated paracenteses in the same animal; such eyes were checked with the slitlamp. Animals whose eyes showed hyperemic iris, synech-

ias, aqueous flare, or other signs of inflammation were discarded. Small lens opacities caused by accidental injury to the lens at previous punctures were tolerated, however. A large proportion of the animals injected with each substance had never been used before. No difference in behavior between the eyes of these animals and eyes thought to be completely recovered from previous punctures was detected.

In the experiments in which the rate of disappearance of para-aminohippuric acid was to be determined, an isotonic solution of the sodium salt was injected intravenously. The dose was 0.75 to 1.5 gm. and the time for injection was 5 to 7 minutes. No acute toxic effects, except a slight drowsiness, were observed in the rabbits.

In those experiments with the same substance in which the ratio of the concentration in the aqueous to that in the plasma under steady-state conditions was to be determined in intact animals, an intravenous injection immediately followed by an intraperitoneal one was given at the start, and intraperitoneal injections were repeated at 20-minute intervals for 3 to 4 hours.

In three instances steady-state ratios were determined over a period of 7 to 8 hours in animals whose kidneys had been tied off under nembutal anesthesia the evening before. The animals were awake before injection of para-aminohippuric acid. In these animals, too, repeated intraperitoneal injections were needed to keep up the plasma level of the test compound.

The rate of disappearance of the iodine compounds Rayopake and Diodrast was measured approximately 120 minutes after intravenous injection of 0.25 to 0.5 millicurie of radioactivity. The latter was contained in about 0.5 gm. of substance, which was dissolved in 10 ml. of water. The solution was adjusted to pH 7.0.

The steady-state values were all obtained in animals with ligated kidneys, operated the evening before under a short-acting barbiturate, alurate. About 0.1 millicurie was given

intravenously immediately after the operation, and next day when the animals were awake and still little affected by the nephrectomy, the aqueous and blood samples were taken. At this time the activity in the plasma was found to be declining slowly so that the results could be used for steady-state distribution ratios with small correction.

Micropipettes previously described by Kinsey[6] were used for removing aqueous. The first aqueous and first blood samples were taken about 2 hours after intravenous injection of the substance; the second aqueous and second blood samples were taken 1 hour later. Since the pontocaine which was used as a topical anesthetic produced a color with the reagents used in the determination of para-aminohippuric acid, these eyes were thoroughly rinsed and blotted before withdrawing aqueous. Blood was taken by heart puncture in heparinized syringes.

Para-aminohippuric acid was determined by the method outlined by Smith and others,[4] which consists of deproteinating in alkaline solution, and diazotization followed by colorimetry. This method was followed exactly except that the quantities of reagents used in carrying out analyses in aqueous humor were reduced proportionately to give the maximum color in the minimum volume (1.5 ml.) which could be read in the colorimeter used. The color produced is stable and Beer's law is obeyed up to concentrations of 5 mg. percent. Replicates of samples containing 1.5 mg. percent of p-aminohippuric acid agreed within ± 1 percent. Control samples of aqueous humor and plasma gave no color when tested.

The two organic iodine compounds, Rayopake and Diodrast, were synthesized from their organic precursors and radioactive I^{131}. The substances were determined by measuring the radioactivity in dried samples of aqueous humor and whole plasma by means of a thin-wall beta counter and the usual planchent technique. Correction for self-absorption in the plasma samples was not necessary, since only ratios between samples of the same kind are used in the calculations.

Tonometry calibrated for rabbits' eyes was performed in some experiments to determine whether the injection of the large volume of fluid containing the p-aminohippuric acid had any effect on intraocular pressure. The intraocular pressures did not differ significantly from normal. The reproducibility of the method is described elsewhere (Bárány[7]).

MATHEMATICAL TREATMENT

The experiments provide information about the concentration of the test substance in the aqueous humor and also in the plasma at two different times after injection. The object of the mathematical treatment is to derive the rate of disappearance as it would have been if the plasma concentration had been zero during the whole test period. Should this have been the case it can be safely assumed that the aqueous concentration would be expressed by a simple exponential function. In this instance the relation between the concentration in two aqueous samples interspaced by the time interval t_1 is given by:

$$(1) \qquad \frac{C_{Aq_2}}{C_{Aq_1}} = e^{-k_{out} \cdot t_1}$$

where C_{Aq_1} and C_{Aq_2} are the aqueous concentration at the beginning and end of the interval t_1, and k_{out} is the rate of disappearance. When time is measured in minutes, k_{out} is of the order of magnitude of 0.01. It is perhaps more convenient to speak of the half-life of the substance in the aqueous $t_{1/2}$, which is $0.693/k_{out}$.

The exponential relation (1) results from a differential equation which indicates that the rate of change of concentration is proportional to the concentration present in the aqueous, the volume being constant. The equation is:

$$\frac{dC_{Aq}}{dt} = -k_{out} \cdot C_{Aq}$$

When there is some of the substance cir-

culating in the plasma, the equation should contain a term indicating the possibility of entrance of substance from the blood stream. Assuming that the rate of entrance is proportional to the concentration in the plasma, for which experimental evidence will be given later in this paper, the differential equation becomes:

$$(2) \qquad \frac{dC_{Aq}}{dt} = k_{in} \cdot C_{pl} - k_{out} \cdot C_{Aq}$$

where k_{in} is the rate constant for entrance, and C_{pl} the plasma concentration.

After the first hour following injection, the plasma concentration was found to fall along a nearly exponential curve. This is described by:

$$(3) \qquad C_{pl} = C_{pl_0} \cdot e^{-k_{pl} \cdot t}$$

where C_{pl_1} and C_{pl} are the initial and momentary plasma concentrations, respectively, and k_{pl} is a rate constant for disappearance of the substance from the plasma. By inserting this expression in Equation (2) and solving the differential equation, the following expression is arrived at for the ratio of the concentration in the second aqueous sample to that of the first:

$$(4) \qquad \frac{C_{Aq_2}}{C_{Aq_1}} = e^{-k_{out} \cdot t_1} \left(1 + k_{in} \cdot \frac{C_{pl_1}}{C_{Aq_1}} \cdot \frac{1 - e^{-(k_{pl} - k_{out}) t_1}}{k_{pl} - k_{out}} \right)$$

When the second term in the large parenthesis is zero, Equation (4) degenerates into Equation (1). The large parenthesis thus represents the effect of the presence of the test substance in the blood.

In expression (4), t_1, C_{Aq_1}, C_{Aq_2}, and C_{pl_1} are given directly by the experiment. K_{pl} is derived from t_1 and the two plasma concentrations by means of Equation (3). This leaves both k_{in} and k_{out} unknown so that it is necessary to obtain supplementary data to solve for either. It will be shown that data can be obtained by finding a value for the ratio k_{in}/k_{out} in independent experiments. That this ratio is identical with the steady-state ratio of the concentration in the aqueous to that in the plasma can be seen from

the following. At steady state, there is no change in aqueous concentration. Hence Equation (2) becomes:

$$0 = k_{in} \cdot C_{pl\ st.\ state} - k_{out} \cdot C_{Aq\ st.\ state}.$$

It follows that:

$$k_{in} = k_{out} \cdot \frac{C_{Aq\ st.\ state}}{C_{pl\ st.\ state}} = k_{out} \cdot R$$

where R is the steady-state distribution ratio aqueous/plasma.

To solve k_{out} in (4), k_{in} is expressed as $k_{out} \cdot R$, and a mean value of R, obtained from a separate series of experiments, is used. The solution of k_{out} is then arrived at by successive approximations. In solving the equation much time is saved by preparing graphs of the function.

$$\frac{1 - e^{-(k_{pl} - k_{out}) \cdot t_1}}{k_{pl} - k_{out}}$$

While the procedure followed involves the use of animals different from those in which attempts were made to determine k_{out} values, the factor R occurs only in a correction term, the average effect of which was 10 percent of the finally derived value of k_{out} for para-aminohippuric acid and 7 percent for Rayopake. The error introduced by using a steady-state ratio derived from a supplementary group of animals is therefore negligible so far as the mean values of k_{out} for these substances are concerned. For Diodrast, the correction amounted to an average of 29 percent. Less reliance should be placed, therefore, on the results obtained with this substance.

The experimental determination of the distribution ratio R involves certain mathematical adjustments to take into account the fluctuations in plasma concentration and to make possible the estimation of the steady-state concentration ratio from experiments in which the time was too short for steady state actually to be reached. Repeated plasma samples were taken and the plasma concentration curve was divided into intervals, within which it was assumed that the plasma concen-

tration changed linearly with time. Under this assumption the following formula can be derived:

$$
(5) \quad
\begin{aligned}
C_{Aq_n} = &\, C_{Aq_{n-1}} \cdot e^{-k_{out}t_n} \\
&+ R \left(C_{pl_{n-1}} - \frac{S_{pl_n}}{k_{out}} \right) (1 - e^{-k_{out}t_n}) + R S_{pl_n} \cdot t_n
\end{aligned}
$$

where C_{Aq_n} is the calculated aqueous concentration at the end of the nth interval

$C_{Aq_{n-1}}$ is the calculated aqueous concentration at the beginning of the nth interval

$C_{pl_{n-1}}$ is the calculated plasma concentration at the beginning of the nth interval

t_n is the length of the nth interval

S_{pl_n} is the slope of the plasma curve during the nth interval

k_{out} is the rate of disappearance of the substance from the aqueous

and R is the distribution ratio to be determined.

In applying Equation (5), a start is made with the first interval, where of course the assumption of linear change in plasma concentration is unrealistic. Because of the first exponential term, however, the influence of a distant enough interval on the end result is small. The expected aqueous concentrations are then calculated at the end of each interval, step by step, until the point in time is reached where the actual aqueous samples were taken. The calculated values, which will be expressed as multiples of R are then compared with the observed values for aqueous concentration and R is obtained.

For the computation of R a value of k_{out} has to be known. On the other hand, knowledge of R is necessary for computation of the exact value of k_{out}. The influence of R on k_{out}, and vice versa, is small, however, if the experiment is conducted properly so that the necessary corrections are not large. Then the rough value of k_{out} from Equation (1) can be used in the computation of R with only a small error. This almost correct value of R can then be used to give a nearly correct value of k_{out} which in its turn can be used for an even better value of R, and so forth. In our experiments successive approxima-

tions of this type were not necessary because of the smallness of, the corrections. Even in the case of Diodrast a change from the rough k_{out} obtained from Equation (1) to the corrected k_{out} changed the value of R by less than 2 percent of its total.

RESULTS

Figure 1 is a composite from several experiments with para-aminohippuric acid. It shows the concentration of this substance in
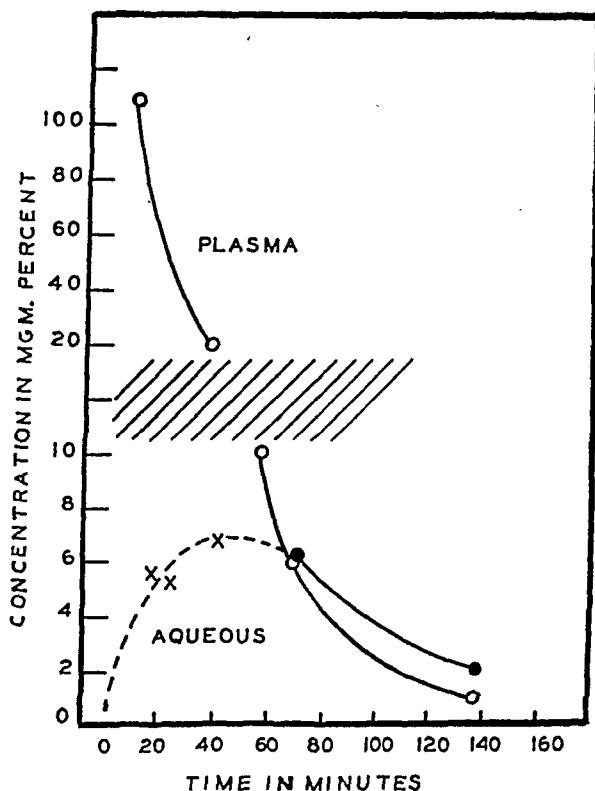
Fig. 1 (Bárány and Kinsey). Concentration of para-aminohippuric acid in the aqueous humor and plasma at various times following intravenous injection.

plasma and aqueous at various periods following intravenous injection. The break in the scale was necessary because of the extremely high concentration of the para-aminohippuric acid in the plasma compared with that in the aqueous during the initial part of the experiment. After sufficient time the concentration in the plasma is so reduced by renal excretion that the aqueous concentration is higher. It is noteworthy, although

not visible in this curve, that after a certain interval the aqueous concentration starts to decrease while the plasma concentration still is above it.

Figure 2 shows the results of five typical experiments plotted on a logarithmic concentration scale. The short lines to the right connect the aqueous concentrations of the right and left eye which were sampled about 60 minutes apart. It is seen that the slopes of the aqueous curves are very similar, indicating similar rates of disappearance.

Table 1 shows relevant data pertaining to 23 experiments in which the rate of disappearance of para-aminohippuric acid was determined. From column 8 it may be seen that

ence shows that the distribution is fairly symmetrical.

It may be seen from the case numbers that in the few experiments in which the same
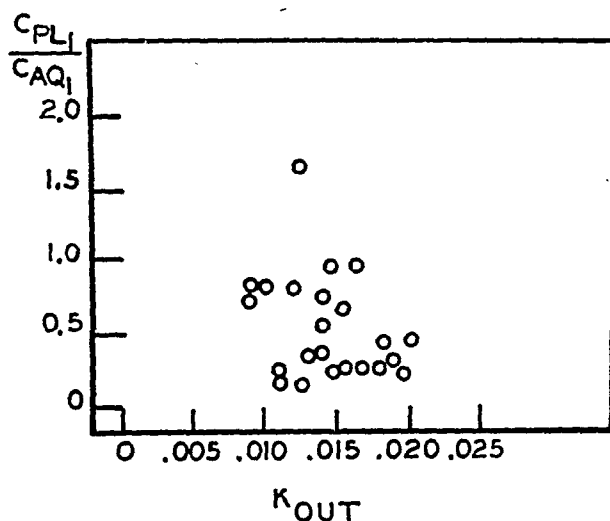
Fig. 3 (Bárány and Kinsey). The ratio of the concentration of para-aminohippuric acid in the first plasma to that in the first aqueous samples as a function of the rate of disappearance (k_{out}) in 23 rabbits.

animal was used twice, the values obtained differ considerably. Each experiment has consequently been used as a statistical unit.

The table also illustrates (compare columns 7 and 8) the magnitude of the correction necessary to take account of the presence of test substance in the plasma. To show that the correction is adequate, a scattergram was prepared (figure 3) by plotting the ratio of the concentration in the first plasma to that in the first aqueous as ordinate against the corrected value for k_{out} as abscissa.

Figure 3 shows that the majority of points form a symmetrical cluster, the corrected rate of disappearance being independent of the plasma concentration at the beginning of the test run. If the uncorrected rates were plotted instead, the cluster would be skewed with its top displaced to the left.

There was no noticeable difference in the half-life of para-aminohippuric acid between light and heavy rabbits and between rabbits used for the first time and those which had been subjected to paracentesis some time

Fig. 2 (Bárány and Kinsey). Logarithm of the concentration of para-aminohippuric acid in the plasma and aqueous of six rabbits at various times after injection.

the mean rate of disappearance is 0.0148. The median rate is 0.0143. These values correspond to a half-life of 47 and 48.5 minutes, respectively. The close correspond-

TABLE 1

The rate of disappearance of para-aminohippuric acid from the aqueous humor of rabbits

1	2	3	4	5	6	7	8	9
Case	C_{pl_1} (mg. %)	C_{Aq_1} (mg. %)	C_{Aq_2}	Time (Min.)	k_{PL}	k_{out} (uncorrected)	k_{out} (corrected)	$t_{\frac{1}{2}}$ (min.) (corrected)
1	1.70	1.77	0.82	59	0.0267	0.0131	0.0151	46.0
1	1.07	1.92	0.893	62	0.0094	0.0123	0.0140	49.3
2	1.9	2.32	1.20	60	0.0198	0.0110	0.0125	55.4
17	0.92	1.28	0.565	63	0.0289	0.0130	0.0143	48.5
23	1.80	2.42	1.47	60	0.0231	0.0083	0.0092	75.5
25	0.80	1.83	0.64	60	0.0231	0.0175	0.0188	36.9
25	0.31	1.27	0.522	63	0.0064	0.0141	0.0151	45.9
19	0.562	1.24	0.40	60	0.0198	0.0189	0.0205	33.8
19	0.26	1.48	0.77	60	0.0071	0.0109	0.0114	60.8
24	0.64	1.66	0.735	60	0.0231	0.0136	0.0143	48.6
11	0.35	1.53	0.534	60	0.0239	0.0176	0.0183	37.9
4	1.28	1.89	0.81	60	0.0210	0.0141	0.0158	43.0
22	5.8	3.55	1.92	60	0.0239	0.0103	0.0130	53.2
41	5.4	5.60	2.24	63	0.0247	0.0145	0.0168	41.0
49	2.6	2.98	1.77	61	0.0224	0.0086	0.0098	70.6
49	0.71	2.78	1.14	60.5	0.0071	0.0147	0.0157	44.2
30	0.22	0.602	0.28	63	0.0085	0.0122	0.0133	52.1
43	0.87	1.051	0.64	55	0.0173	0.0090	0.0104	66.9
46	0.35	1.17	0.468	58.5	0.0110	0.0157	0.0168	41.3
48	0.18	1.33	0.615	61	0.0094	0.0126	0.0129	53.9
36	0.20	0.662	0.228	60.5	0.0084	0.0176	0.0192	36.1
34	0.20	0.872	0.279	60.5	0.0084	0.0188	0.0200	34.7
40	0.15	0.675	0.348	59.5	0.0069	0.0111	0.0116	59.7
					Average	0.0135	0.0148	47.0
					Median	0.0135	0.0143	48.5

C_{pl_1} is the plasma concentration at the time the aqueous, with concentration C_{Aq_1}, was removed from the first eye. C_{Aq_2} is the concentration in the aqueous of the second eye t_1 minutes later. K_{pl} is the rate constant for disappearance from the blood stream and k_{out} the rough rate constant for disappearance from the aqueous, assuming the blood free from test substance. K_{out}, corrected, is mathematically corrected for presence of test substance in the plasma and $h_{1/2}$ is the half-life corresponding to the corrected rate of disappearance.

earlier. This does not prove that the half-life is independent of, for example, size of eye; it only shows that the unavoidable variability associated with the experiments overshadows minor differences.

In one group of experiments the first aqueous was removed as early as 70 minutes after the intravenous injection and in another as late as 210 minutes. The object of this variation of the standard experiment was to determine whether the half-life might be significantly affected by para-aminohippuric acid coming from or going to the lens and vitreous humor. Thus, it would be expected that since the concentration in the aqueous would build up faster than in the vitreous and lens, the substance would leave the aqueous for these structures during the

earlier intervals following injection; whereas, it would move from them to the aqueous at later times when the concentration of para-aminohippuric acid in the aqueous is falling. No shift in disappearance rate which could be attributed to effects of this kind was discernible, however.

The results of the same type of experiments with the two iodine compounds, Rayopake and Diodrast, are shown in Table 2. Their median rates of disappearance are 0.0125 and 0.0122, respectively. In these experiments every rabbit appears only once in connection with each substance. Approximately half of the animals used with each substance were used for the first time. Figure 4-A and B shows scattergrams of the rate of disappearance as a function of the

plasma/aqueous concentration ratio at the beginning of the experiment, illustrating in the same way as Figure 3 the adequacy of the correction applied for presence of the test substance in the blood.

The scatter of the values obtained with all three test substances may appear high. It must be borne in mind, however, that in addition to the unavoidable errors of volumetry and analysis and the variability between animals, there is a specific source of variability in every experiment where a rate curve is determined by sampling of the two eyes.

It is assumed that the two eyes are identical, but this is not necessarily so. When one eye differs from the other in almost any respect, the result on the rate of disappearance as obtained in experiment can be either an increase or a decrease, even if the respect in which the eyes differ has nothing to do with the parameter studied. Because of this possibility of erratic values, the medians probably more accurately represent the rates of disappearance than do the arithmetic means. As it happens, they differ very little in the present experiments.

The corrections for presence of test sub-

TABLE 2

THE RATE OF DISAPPEARANCE OF RAYOPAKE AND DIODRAST FROM THE AQUEOUS HUMOR OF RABBITS

Rayopake k_{out} (corrected)	Diodrast k_{out} (corrected)
0.0125	0.0147
0.0123	0.0160
0.0156	0.0112
0.0073	0.0110
0.0114	0.0127
0.0125	0.0147
0.0129	0.0108
0.0066	0.0089
0.0100	0.0155
0.0086	0.0070
0.0088	0.0029
0.0174	0.0120
0.0133	0.0177
0.0130	0.0083
0.0183	0.0148
0.0128	0.0194
0.0106	0.0122
0.0168	0.0089
0.0052	
0.0149	Mean 0.0122±0.0010
0.0168	Median 0.0122
0.0146	
0.0180	
0.0108	
0.0182	
0.0106	
0.0104	

Average 0.0126±0.0007
Median 0.0125
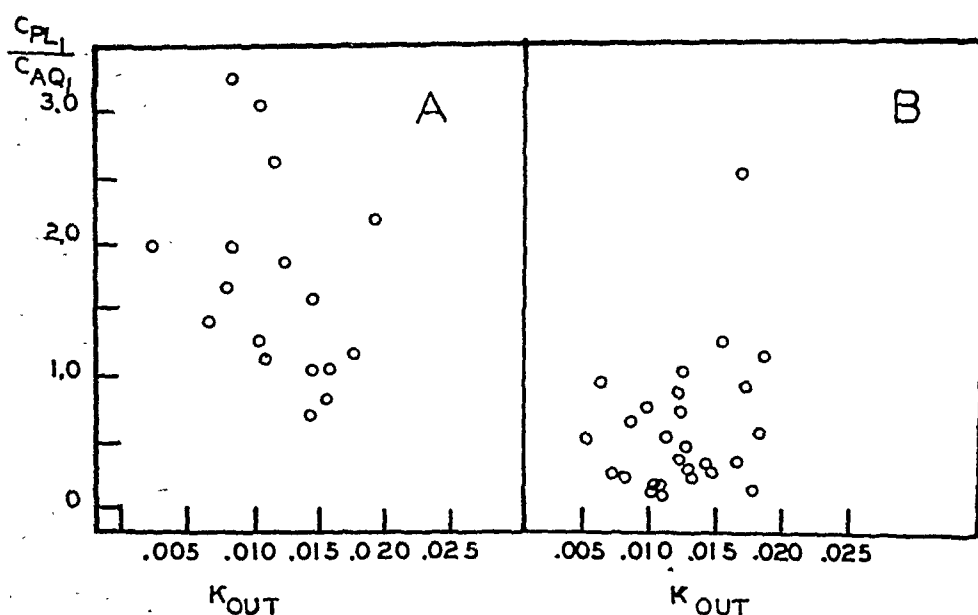
Fig. 4 (Bárány and Kinsey). The ratio of the concentration of Diodrast (A) and Rayopake (B) in the first plasma to that in the first aqueous samples as a function of the rate of disappearance (k_{out}) in 18 and 27 rabbits, respectively.

stance in the blood were made by means of the values for the ratio between the concentration of a substance in the aqueous and that in the plasma when steady state has been reached. These values will also be used in the following paper for calculation of the rate of flow of aqueous.

Figure 5 shows three experiments in in-
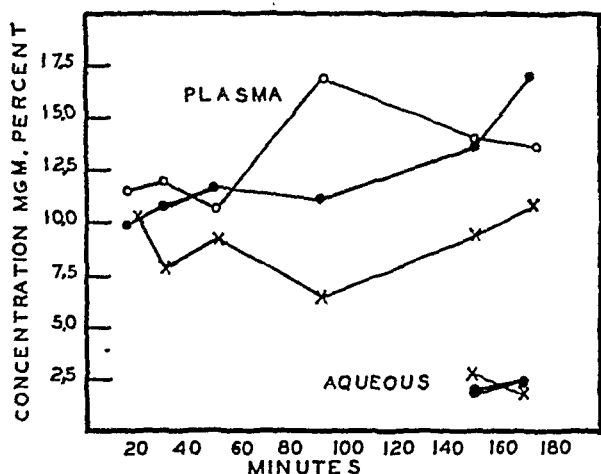
Fig. 5 (Bárány and Kinsey). The concentration of para-aminohippuric acid in the aqueous humor and plasma of rabbits at various periods following multiple injections.

tact rabbits where the plasma concentration of para-aminohippuric acid was upheld by an initial intravenous injection of 75 mg. immediately followed by an intraperitoneal in-

jection of 300 mg., and then by intraperitoneal injection of 125 mg. every 20 minutes. The difficulties in obtaining a constant plasma level by a schedule of this kind are great, it being considerably easier when the kidneys are tied. This is especially true for Rayopake and Diodrast.

In animals with tied kidneys the Rayopake concentration drops only slowly after the first few hours. In one typical experiment in which 6 animals with tied kidneys had been injected with Rayopake 15 hours earlier, the plasma concentration dropped only 8 percent of its value over a period of 200 minutes. In a corresponding experiment with Diodrast, a fall of about 13 percent was observed.

TABLE 4

STEADY-STATE DISTRIBUTION RATIO OF RAYOPAKE

Dose			
5.6 mg.		50 mg.	
O.S.	O.D.	O.S.	O.D.
0.095	0.089	0.078	0.104
0.100	0.098	0.127	0.120
0.108	0.102	0.127	0.119
0.130	0.132	—	0.123
		0.131	0.145
		0.186	0.167
Mean	0.107	0.130	
Median	0.101	0.127	
	Grand mean	0.120	
	Grand median	0.120	

TABLE 3

STEADY-STATE DISTRIBUTION RATIO OF PARA-AMINOHIPPURIC ACID

Normal Rabbits		Rabbits with Tied Kidneys	
O.S.	O.D.	O.S.	O.D.
0.17	0.13	eye tonometrized	0.18
0.14	0.15		0.14
0.23	0.17		0.13
0.18	0.19		—
0.39	0.21		—
0.16	0.19		—
Mean	0.19	Grand mean	0.18
Median	0.17	Grand median	0.17

TABLE 5

STEADY-STATE DISTRIBUTION RATIO OF DIODRAST

O.S.	O.D.
0.078	0.070
0.104	0.095
0.105	0.101
0.142	0.142
0.146	0.151
0.152	0.159
0.179	0.196
0.209	(0.252)*
Mean	0.143
Median	0.144

* The value in parentheses was from an unusually small aqueous sample with large measuring and counting error.

Tables 3, 4, and 5 show the results of the steady-state experiments with the three test substances. The correction formula given in the mathematical section was employed in all instances.

Table 3, giving the para-aminohippuric acid values, shows that kidney ligation experiments lead to distribution ratios within the normal range. This was to be expected. The left eyes of the nephrectomized animals were tonometrized and the tonometer readings were normal.

Table 4 gives the Rayopake values, all obtained with ligated kidneys. The table shows that the amount of actual test substance in the aqueous can be varied as $1:9$ without significantly changing the distribution ratio. This observation is of importance because it justifies the use of linear expressions for the rates of entrance and exit of the substance from the aqueous. If nonlinear relations prevailed here, the distribution ratio would not be constant over a wide range of plasma concentrations.

Diffusion and flow both can be expected to give rise to linear expressions, but for secretion this is not necessarily true. Kinsey[8] has demonstrated the large variation of the distribution ratio for ascorbic acid with varying plasma levels. The proof of linearity for Rayopake is considered to be extendable to the two other substances, too; although, strictly speaking, special experiments would have been required to prove this. Since the method of analysis did not permit the determination of the other two substances at low enough concentrations, the experiments were not carried out.

Surveying the steady-state values in Tables 3, 4, and 5 the relatively good check between the two eyes, as compared with the significant variation between animals, is noticeable. The large variability between different animals makes comparisons between the values obtained for the three substances difficult. One would have expected Diodrast, which has the highest molecular weight, to

have the lowest distribution ratio. That this was not found may be due to random variation. On the other hand, it is possible that the Diodrast molecule is so large that it is held back to some extent at the filtering angle. This would increase the steady-state concentration.

The method used here to determine rate of disappearance of a substance from the aqueous is very similar to that used by Abe and Komura. These authors, too, watched the disappearance of their test substance from aqueous some time after an intravenous injection. They made no correction for the presence of test substance in the blood, however, but assumed that as soon as the fluorescein concentration in the aqueous had dropped to lower than one fortieth of that in the plasma, there was no passage of fluorescein into the aqueous any longer. Their figure, one fortieth, was supposed to be the fraction of fluorescein freely diffusible. The rates of disappearance observed by these authors thus are systematically too low. Moreover, since they worked with atropinized eyes a comparison with our values has no point.

SUMMARY

In order to obtain a value for the rate of flow of aqueous, the rates of disappearance from the aqueous of three test substances which could be expected to leave the aqueous mainly by flow were measured. The test substances were para-aminohippuric acid, Rayopake, and Diodrast. They are able to enter the aqueous from the blood stream. They are excreted by the kidneys at maximal rate, so that the plasma concentration after an intravenous injection shows a very sharp drop. Some time after the injection, therefore, the substances disappear from the aqueous at a rate which is only to a small extent influenced by simultaneous replacement from the blood. A mathematical treatment taking this replacement into account was worked out. The rates of disappearance

(k_{out}), as they would have been found if the blood stream were free of test substance, were para-aminohippuric acid, 0.0143; Rayopake, 0.0125; and Diodrast, 0.0122.

The steady-state distribution ratio aqueous/plasma was measured, using a mathematical correction taking fluctuations of plasma level of the test substance into account. The median distribution ratios were para-aminohippuric acid, 0.17; Rayopake, 0.12; and Diodrast 0.14.

The distribution ratio for Rayopake was independent of large variations in the concentration of the substance, showing that essentially linear conditions prevail with respect to exit and entrance of this substance.

Bangardsgatan 9.

243 Charles Street (14).

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THE RATE OF FLOW OF AQUEOUS HUMOR*

II. Derivation of Rate of Flow and Its Physiologic Significance

V. Everett Kinsey,[†] Ph.D.

Boston, Massachusetts

AND

Ernst Bárány,[‡] M.D.

Uppsala, Sweden

In the preceding paper,[1] the authors reported values, in rabbits, for the rate of disappearance of three test substances from the anterior chamber and the ratio of their concentrations in the aqueous humor[§] to those in the plasma under steady-state conditions. The object of the present paper is to utilize these data to derive the rate of flow of aqueous humor and in turn to use the derived value for determining how various substances, including sodium and chloride, enter the anterior chamber.

One of the postulates of the theory of intraocular fluid dynamics advanced by Kinsey and Grant[2] is that all nonmetabolized substances in the aqueous humor leave by flow, and may, in addition, leave by diffusion. Thus, the rates of disappearance are thought to consist of a rate of flow, and also, in the case of some substances, a rate of diffusion. An exact value for the rate of flow of aqueous humor cannot be derived, therefore, from the rate of disappearance of a single test substance without knowing whether the substance can diffuse out of the anterior chamber.

Information of this kind, however, is equivalent to knowing how the substance enters the anterior chamber. There are two main possibilities. If the substance is capable of entering the anterior chamber only as a result of a secretory process, and not

by diffusion, it can leave only by flow. The rate of disappearance and rate of flow will then be the same, assuming, as the authors do, that no secretion out of the eye occurs, and that the substance is not metabolized.

The other possibility is that the substance is capable of entering the anterior chamber entirely, or in part, by diffusion. Then it is also capable of leaving it by diffusion. In this instance some of the loss out of the anterior chamber will occur as a result of diffusion, and the rate of disappearance will be made up of a rate of diffusion, as well as a rate of flow, as stated above.

The rate of flow in this instance is less than the rate of disappearance. Thus, knowledge of the rate of disappearance of the test substance permits calculation of a maximum and minimum value for rate of flow corresponding to entrance by secretion[||] only, or by diffusion only, respectively. When both secretion and diffusion occur, intermediate values for rate of flow are obtained.

In order to obtain the rate of flow, we attempted to circumvent the lack of knowledge of how most compounds enter the anterior chamber by determining the rate of disappearance of substances of relatively high molecular weights. Through the use of such substances, the contribution of diffusion, if any, to the loss from the aqueous humor can be expected to be small, and consequently the limits between which the actual flow rate

|| Secretion is used in the broad sense of unidirectional transfer of substances into the anterior chamber as a result of an expenditure of energy. The source of the energy and the site of any secretory activity, more than to say that they must lie toward the ciliary body from the anterior chamber, do not enter the argument at this point.

lies would be narrow. In addition to the large size, the substances selected were of graded molecular weights, it being thought that still more exact information concerning the rate of flow might be obtained by extrapolation, in the event that the rate of disappearance was found to decrease progressively with increase in molecular weight. Inherent in the argument, of course, is the assumption that the test substances are not preferentially prevented from leaving the anterior chamber by flow.

The rate of flow of aqueous humor within the limits referred to above can readily be derived from the rate of disappearance of a test substance by use of equations formulated by Kinsey and Grant[2] to describe entrance and exit of constituents from the anterior chamber when these enter either by diffusion or secretion. The relations may be more apparent from the equation representing the rate of disappearance and rate of entrance by any means, as used by Palm[3] and employed by Bárány and Kinsey.[1] The latter is:

$$(1) \qquad \frac{dC_{Aq}}{dt} = k_{in}C_{pl} - k_{out}C_{Aq}$$

where C_{Aq} and C_{Pl} are the concentration in the aqueous humor and plasma, respectively; k_{in} is the rate of entrance and k_{out} the rate of disappearance. At steady state, when the rate of change of C_{Aq} equals zero, this gives

$$(1a) \qquad \frac{k_{in}}{k_{out}} = \left(\frac{C_{Aq}}{C_{pl}}\right)_{Steady\ state} = R$$

whence:

$$(1b) \qquad k_{in} = Rk_{out}$$

where R is the steady-state distribution ratio aqueous/plasma. When entrance occurs by secretion:

$$(2)^* \qquad k_{in} = k_{secr.}$$

and

$$k_{out} = k_{flow}$$

---

* The subscripts used by Kinsey and Grant[2] have been changed as follows: In (2) k_2 to $k_{secr.}$; in (3) k' to k_{flow} and k_2 to $k_{diff.}$. The subscript abbreviations diff. and secr. refer to diffusion and secretion, respectively.

where $k_{secr.}$ is the rate of entrance by secretion and k_{flow} the rate of loss by flow.

When entrance occurs by diffusion:

$$k_{in} = k_{diff.}$$

but

$$(3) \qquad k_{out} = k_{diff.} + k_{flow}$$

where $k_{diff.}$ is the rate of entrance and exit by diffusion. Steady state then is:

$$(4) \qquad \frac{k_{diff.}}{k_{diff.} + k_{flow}} = \left(\frac{C_{Aq}}{C_{pl}}\right)_{Steady\ State} = R$$

which gives

$$(5) \qquad k_{flow} = k_{out}(1 - R).$$

Since it was proposed to calculate the rate of flow of aqueous humor from the rate of disappearance of a test substance on the basis of the concepts already set forth and represented mathematically by the above equations, and since the validity of Equation (4) and the differential equation from which it has been derived have been questioned, some discussion of these concepts seems warranted.

Duke-Elder and Davson[4] disagree with the concept described by Kinsey and Grant's Equation (4) above. The latter represents entrance into the anterior chamber by diffusion and exit by flow. They state that energy would have to be supplied if fluid lost by flow were not replaced by fluid having the same concentration of the substance in question as found in the blood. They argue that, since, under the conditions of dialysis and ultrafiltration, there would be, at best, only small amounts of energy available, the situation must be described by their Equation (5) which, with symbols changed to conform with those used elsewhere in this paper, is reproduced below.

$$\frac{dC_{Aq}}{dt} = k_{diff.}(C_{pl} - C_{Aq}) - k_{flow} \cdot C_{Aq} + k_{flow}C_{pl}$$

from which the following is obtained

$$\frac{k_{diff.} + k_{flow}}{k_{diff.} + k_{flow}} = \left(\frac{C_{Aq}}{C_{pl}}\right)_{Steady\ State} = R = 1.0$$

Under these conditions they point out that the ratio of the concentration in the

aqueous humor to that in the plasma at steady state must always be unity. The objection to their argument is that their equation describes a situation in which there is a unidirectional force moving constituents of aqueous humor through the membrane under steady-state conditions, namely flow of fluid through the membrane. Since this is *not* dialysis, by definition, it represents a situation different from that which Kinsey and Grant were considering, and therefore is not relevant to the argument that flow, in the presence of dialysis, could account for steady-state ratios below 1.0. It is clear that energy would have to be supplied to keep the aqueous humor flowing, but it does not follow that the diffusion equation of Kinsey and Grant is erroneous. The equation given by the latter workers simply describes what would happen to a substance diffusing into the anterior chamber in the presence of flow out of the anterior chamber. The source of energy required to maintain this flow does not enter the problem at this stage.

Since it is apparent that the separation of water from its solutes would require energy (indeed more energy than can be provided by the filtering blood pressure), it follows that if the constituents of aqueous humor entered only by diffusion, that is, when no excess energy is supplied, there could be only an insignificant flow.

Thus, if no energy is supplied one is at a loss to explain the low distribution ratio of such substances as urea and levulose, which was the original objective of testing the consequences of the flow hypothesis, not to speak of the very low ratios observed with the test substances used by the present investigators.

Subsequent criticism of Equation (4) is of a different kind. It is contained in the statement by Davson[5] that "this equation has been shown to involve a simple mathematical error which completely invalidates it. . . ." He cites the above-mentioned paper of Duke-Elder and Davson[4] as a reference. There is, however, no mention in the paper

by Duke-Elder and Davson of a "simple mathematical error."

Furthermore, reference is made in [5] only to the paper of Duke-Elder and Davson and not to a paper of Kinsey and Grant[6] in which rebuttal is made to the former's disagreement with the concepts involved, giving the reader who is unfamiliar with the literature on the subject the erroneous impression that the whole original concept is now an admitted mistake because of an error in mathematics. The paper referred to by Davson contains no reference to the specific rules of mathematics which are violated and we maintain that Equation (4) is mathematically sound.

Without specific assumption of secretion, Palm[3] proposes the following more general expression intended to take into account the possibility that the fluid which replaces that lost by flow contains the substance in a fraction α of the concentration found in the plasma. His equation, with altered subscripts, is:

$$(6) \quad \frac{dC_{Aq}}{dt} = k_{diff.}(C_{pl} - C_{Aq}) + \alpha k_{flow} C_{pl} - k_{flow} \cdot C_{Aq}$$

where, according to Palm, α denotes the ratio of the rates of passage of the substance and water through the membrane. Under these conditions the distribution ratio becomes

$$(7) \quad \frac{k_{diff.} + \alpha k_{flow}}{k_{diff.} + k_{flow}} = \left(\frac{C_{Aq}}{C_{pl}}\right)_{Steady\ State} = R$$

whence

$$(8) \quad k_{flow} = k_{out}\left(\frac{1-R}{1-\alpha}\right).$$

Inspection of Equation (8) shows that when α is >1, R must also be >1, and thus the concentration in the aqueous humor would be greater than in the plasma, which is opposed to the original assumption of entrance by diffusion. When α is <1 it cannot exceed R and it can equal R only when there is no diffusion. Since there is no way of evaluating α the derivation of k_{flow} from k_{out} has been carried out on the assumption that $\alpha = 0$. If α were considered to have

TABLE 1

THE MEDIAN RATES OF DISAPPEARANCE AND RATIOS OF CONCENTRATION IN THE AQUEOUS
HUMOR TO THAT IN THE PLASMA WATER

Test Substance	Mol. Wt.	No. of Expts.	k_{out}	$\left(\dfrac{C_{Aq}}{C_{Pl}}\right) = R^*$ steady state
Para-aminohippuric acid	194	23	$.0143 \pm .0007$[†]	0.21
Rayopake	308	27	$.0125 \pm .0007$	0.12
Diodrast	405	18	$.0122 \pm .0010$	0.16

* The ratios are calculated on a kg. of water basis assuming the water content of the plasma to be 93 percent, and adjusted to take into account the fraction of the substance bound to plasma protein. The latter correction was based on dialysis experiments. The fraction bound was 23 percent, 4 percent, and 17 percent, respectively, for para-aminohippuric acid, Rayopake, and Diodrast. (Six experiments with each in cellophane bags.)

† The standard errors are those for the means.

some positive value, the lower limit of the rate of flow would become raised, that is, would approach that given on the assumption of entrance by secretion, and the limits between which k_{flow} must lie become narrower. Thus, the limits for flow obtained by the calculations which follow are too wide, and are therefore conservative.

The median rates of disappearance (k_{out}) and ratios of concentration in the aqueous humor to that in the plasma water at steady state for the three test substances—para-aminohippuric acid, Rayopake, and Diodrast —are given in Table 1.

The rate of flow can be calculated from the k_{out} values assuming entrance into the anterior chamber by either secretion or diffusion. When the substances are assumed to enter by secretion, k_{out} and k_{flow} are the same, so that no calculation is required to obtain the upper limit for the rate of flow. When entrance is assumed to occur by diffusion, the calculation is carried out with

TABLE 2

EXTREME LIMITS FOR k_{flow}

| Test Substance | Assumed Entrance By: | |
| | Secretion | Diffusion |
	k_{flow}	k_{flow}
Para-aminohippuric acid	0.0143	0.0113
Rayopake	0.0125	0.0110
Diodrast	0.0122	0.0102

Equation (5). This gives the lower limit for the rate of flow. The results are tabulated in Table 2.

The extreme limits for k_{flow}, as shown in Table 2, are 0.0102 and 0.0143 as derived from the rate of disappearance of Diodrast, assuming entrance by diffusion, and para-aminohippuric acid, assuming entrance by secretion, respectively. The values for k_{flow}, assuming that all of the substances enter by diffusion, vary only between 0.0102 and 0.0113. Consideration of all of the evidence would suggest that k_{flow} in rabbits must be very close to 0.011. This means that 1.1 percent of the total volume of aqueous humor in the anterior chamber leaves by flow every minute. For an average anterior chamber having a volume of 250 cubic mm., this corresponds to 2.75 cu.mm./min.

Because of the through and through circulation in the eye (flow), all constituents of the aqueous humor which are not preferentially held back at the filtering angle must disappear from the anterior chamber with at least this basal rate. If they are able to exchange between blood and aqueous humor in the anterior chamber by other means, their rates of disappearance will be higher than the basal rate, that is, the rate of exchange by diffusion will be added to the flow rate (equation 4) (see also fig. 4). Information concerning the magnitude of the rate of flow in conjunction with a value for the rate of disappearance of a substance can, there-

fore, be used to draw inferences regarding the role of diffusion in the entrance of the substance into the anterior chamber. The following discussion (based on this type of reasoning) will be concerned with conclusions which can be drawn concerning the mode of entrance of the chief electrolytes of the aqueous humor, sodium and chloride, and certain other substances.

In previous studies, Kinsey and Grant[7] found that the half-life of sodium in the anterior chamber of rabbits was approximately 50 minutes, which corresponds to a k_{oyt} of 0.0140. In making their calculations they assumed a steady-state distribution ratio for sodium of 0.90. We have determined experimentally the steady-state ratio for sodium in rabbits by injecting radioactive sodium (Na24) and, 13 hours later, determining the relative concentration in the anterior chamber and plasma. The data for the steady-state values are shown in Table 3.

Table 3 shows that the median value for the steady-state ratio of sodium is 0.93. Using this value and the data reported previously by Kinsey and Grant,[7] the rate of disappearance of sodium in the anterior chamber was determined by plotting the logarithm of the difference between the observed value and that reached at steady state against time, once the sodium level in the blood had become constant (fig. 1). This method of treating the data is based on the fact that, in the case of isotopes, at steady state, the rate of accumulation of one isotope is a measure of the rate of disappearance of
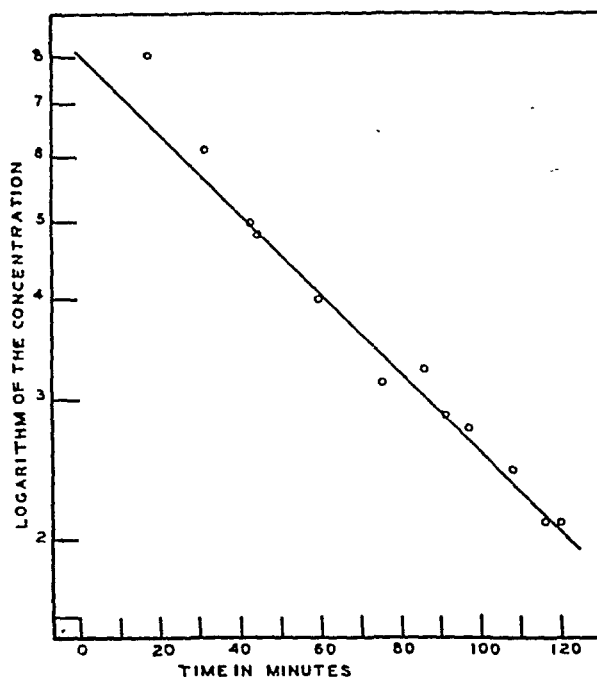
Fig. 1 (Kinsey and Bárány). Disappearance of sodium from the aqueous humor of the rabbit eye.

the other isotope present. In the present instance, the rate of accumulation of trace amounts of Na24 was measured, assuming that the body does not differentiate between Na24 and the normally present isotope Na23; this is equivalent to measuring the rate of disappearance of the latter ion.

Figure 1 shows that the experimental values obtained at times earlier than 40 minutes fall above the line. The initial rapid rise in concentration of radioactive sodium in the anterior chamber may be due to insufficient stirring of the aqueous humor so that loss of the tracer sodium by flow is at first abnormally low with the result that the concentration of radioactive sodium in the aqueous humor increases too rapidly at first, and gives the appearance of a short half-life. Palm[3] was the first to point this out. More-

TABLE 3

THE RATIO OF THE CONCENTRATION OF SODIUM IN THE AQUEOUS HUMOR TO THAT IN THE PLASMA WATER* AT STEADY STATE

	Eye	
	O.S.	O.D.
	0.84	0.89
	0.93	—
	0.99	0.94
	0.88	0.95
	1.14	0.94
	0.93	0.95
	0.96	0.975
	0.87	0.89
	0.925	0.925
Mean	0.94	0.935
Mean O.U.	0.94	
Median O.U.	0.93	

* The water content of plasma was assumed to be 93 percent by volume.

over, it will be seen from the figure that, although the concentration is rising too rapidly, the actual concentrations are too low. This may be explained simply by the fact that the blood levels have not yet reached their steady state. The half-life of sodium, once constant rate has been reached, is. 61 minutes. This corresponds to a k_{out} value for sodium of 0.0113.

The difference between the k_{out} values as given above, namely, 0.0113 and that found previously, namely, 0.0140, is due partly to

TABLE 4

COMPARISON OF RATE OF FLOW AND RATE OF DISAPPEARANCE

Organic Test Substance Assumed to Enter By:	Aver., Weighted for No. of Determinations, Para-aminohippuric Acid, Rayopake, and Diodrast	Sodium
	k_{flow}	k_{out}
Diffusion	0.0109	0.0108
Secretion	0.0130	

the use by Kinsey and Grant[2] of a steady-state distribution ratio of 0.90 instead of 0.93, and partly to utilizing the experimental points obtained at earlier times when the concentration was changing too rapidly.

To obtain further data on the rate of disappearance of sodium from the anterior chamber of rabbits, five additional experiments were carried out. The injections of radioactive sodium were given intraperitoneally, and blood and samples of aqueous humor from one eye, and then the other, were taken at approximately 45 and 100 minutes. The plasma levels used to calculate the half-lives were the mean of the two plasma concentrations at the moment of aqueous-humor withdrawal which was timed to occur after the plasma concentration of radioactive sodium was essentially constant. The rates of disappearance calculated from these experiments are represented by the k_{out} values 0.0119, 0.0115, 0.0099, 0.0099, and 0.0087. This represents an average k_{out}

value of 0.0104 with an average for all the sodium results of 0.0108.

The value for the rate of disappearance of sodium can now be compared with the rate of disappearance which must be imposed by flow on all constituents of aqueous humor, excepting, of course, any held back at the filtering angle, for example, protein. As previously indicated, because of the lack of knowledge of the exact mode of entrance of the three organic test substances, there is some uncertainty as to the exact value of the rate of flow. Accordingly, the average values for k_{flow}, assuming entrance either by diffusion or secretion, will be used in making the comparison. The data are presented in Table 4.

The close correspondence between the rate of disappearance of sodium and rate of flow, as obtained by the three test substances on the basis of assumed entrance by either diffusion or secretion, is evident from the data given in Table 4. A quantitative estimate for the rate of loss by diffusion ($k_{diff.}$) for sodium can be calculated by insertion of the experimental values into Equation (4). $K_{diff.}$ for sodium is found to equal -0.0001 or -0.0022 for assumed entrance of the organic ions by diffusion or secretion, respectively. The almost precise agreement between the rate of disappearance of sodium (k_{out}) and the rate of flow (on the assumption that the organic test substances entered by diffusion), is fortuitous, considering the magnitude of the individual variations in rate constants.

For the same reason the definitely negative value for loss by diffusion of sodium, assuming entrance of the test substances by secretion, does not necessarily preclude the possibility that the test substances enter by this means, even if it favors the idea that the test substances enter by diffusion. The experiments show unequivocally, however, that *any loss of sodium from the aqueous humor by diffusion must be so small as to be within the experimental errors involved, and very much smaller than the loss by flow.*

Thus for sodium:

$$k_{diff.} \ll k_{flow.}$$

The question now arises as to what inferences can be drawn from these results with regard to the rate and mode of *entrance* of sodium. It might be thought that if but a small proportion of the total amount of a substance leaves the aqueous humor by diffusion, as is the case for sodium, the substance could not enter solely by diffusion and the conclusion could be drawn immediately that the substance must enter by an active process. That this is not the case, however, can be seen from the following consideration.

If there were only a small concentration of the substance in the aqueous humor so that the total *quantity* of substance lost by flow each minute would be small, the substance might well be replaced from the blood by diffusion, provided the plasma concentration, and thus the driving concentration difference, were sufficiently large, even if the diffusibility were low. Thus, entrance by only diffusion is compatible with exit predominantly by flow, but then the steady-state distribution ratio aqueous/plasma will be low. The organic test substances used in the present experiments are probable examples.

In the case of sodium, however, the concentration in the aqueous humor is nearly the same as in the plasma, and the driving concentration difference is consequently small, too small in fact, to account for the loss by flow. Moreover, since the diffusibility through the membrane is low, as shown above, complete replacement of the lost sodium by diffusion is not possible; sodium must, therefore, enter the aqueous humor predominantly by some other process. The same reasoning expressed in symbols:

According to Equation (1b)

$$k_{in} = R k_{out}.$$

for sodium R is 0.93, thus

$$k_{in} = 0.93 \cdot k_{out}.$$

Since 0.93 is near unity and we have

shown above that $k_{diff.} \ll k_{out}$ for sodium, it follows that $k_{diff.} \ll k_{in}$ too. Thus, diffusion can at most play a minor part in the entrance of sodium into the aqueous humor.

The discussion of flow up to now has been based on comparison between values obtained in different groups of animals. To eliminate this difference, the authors carried out a smaller number of experiments in which the rate of disappearance of Rayopake or Diodrast from the anterior chamber and the rate of accumulation of radioactive sodium in this chamber were determined simultaneously in the same animal.

For this purpose rabbits were selected which were as dissimilar as possible. Some animals had never been used before, several had been injected with radioactive compounds previously, several were large (3 to 3½ kg.), and several were small (1.2 to 1.4 kg.).

Separate assay of the sodium and iodine compounds in the aqueous humor and plasma samples was accomplished by measuring the radioactivity through sufficient absorbing material to eliminate all but an insignificant part of the radiations arising from the iodine, and then remeasuring the activity, without filters, a week later when the radiations from the sodium had decayed to an insignificant portion. After correction for radioactive decay, the first measurement indicates the amount of sodium, and the second measurement the amount of the iodine compound, which is present. The sodium was injected 60 minutes after the iodine compound, the first sample was withdrawn 40 minutes later, and the second sample one hour after the first sample.

The resulting values of k_{flow}, calculated on the basis of assumed entrance by diffusion or secretion of the organic ion, and the k_{out} values for sodium are shown plotted as scattergrams in Figures 2 and 3, respectively. The lines illustrate what would be theoretically perfect correlation. With one notable exception the data show a reasonable correlation between the k_{flow} values calcu-

lated from the Rayopake (open circles), and Diodrast (filled circles), and the k_{out} values for sodium.

Presumably because the animals in this group were so variable, there was a considerable spread between the results obtained with individual animals, particularly in the

Fig. 2 (Kinsey and Bárány). Rate of disappearance of sodium and rate of flow as determined simultaneously with Rayopake or Diodrast assuming entrance of the organic compounds by diffusion.

case of k_{out} values for sodium. There is a tendency for the k_{out} values for the sodium to be slightly higher than the k_{flow} values for the organic ions. This difference is of questionable significance, but could be explained on the assumption that a small proportion of the sodium diffuses out of the anterior chamber.

On principle, the same method of reasoning which has been applied for sodium holds for any substance, once the rate of flow is known. The reasoning can be simplified by plotting the general relation between the steady-state distribution ratio R and the rate of disappearance k_{out} for any substance assumed to enter the anterior chamber only by diffusion.

This relation can be shown graphically by substituting the value 0.011 for k_{flow} in Equation (4) and plotting the steady-state ratio R against k_{out}. Equation (4) contains the inherent assumption that the re-

placement fluid is free from the particular solute in question.

Although, as stated earlier in this paper, it is not possible to evaluate exactly the fractional term α introduced by Palm to take account of solute entering along with water, one can make the assumption that α is equal
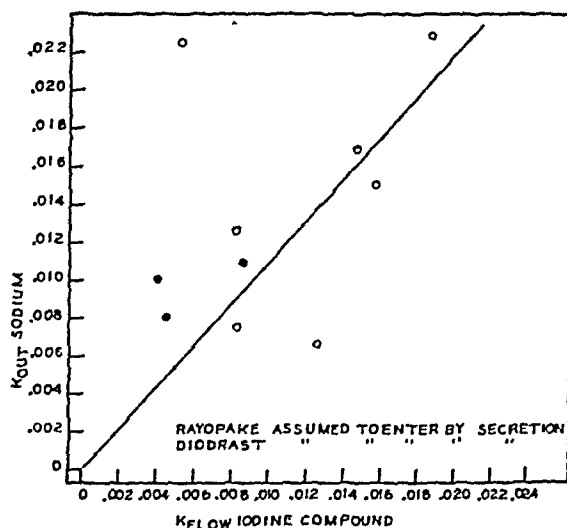
Fig. 3 (Kinsey and Bárány). Rate of disappearance of sodium and rate of flow as determined simultaneously with Rayopake or Diodrast assuming entrance of the organic compounds by secretion.

to the ratio of the rates of passage by diffusion of the substance and water through that part of the blood-aqueous barrier concerned with diffusion into the anterior chamber. This might well be a reasonable approximation to the true value of α.

Accordingly, this value, that is, $k_{diff.\ solute}/k_{diff.\ H_2O}$, where $k_{diff.\ H_2O}$ is approximately 0.20 (see Kinsey and co-workers[8]), was set equal to α and k_{flow} equal to 0.011 in Equations (7) and (8) with the following result:

$$(9) \qquad R = \frac{1.055 \cdot k_{out} - 0.0116}{k_{out}}.$$

The broken and solid curved lines of Figure 4 represent a plot of Equations (4) and (9), respectively. The perpendicular broken line graphically represents the circumstance in which the substance enters by secretion and leaves only by flow, Equation

(2). In this instance, it is clear that the rate of disappearance will not exceed that given by the rate of flow, irrespective of the steady-state ratio. For convenience the units of the abscissa are expressed as both k_{out} values and as half-lives.

The distance to the left of the perpendicular line of Figure 4 shows graphically the rate of disappearance imposed by flow on all substances not held back preferentially

crosses shown on Figure 4 represent the experimental values found by the authors for the rate of disappearance of the three organic substances tested.

The lines of Figure 4 represent the general situation describing both entrance and exit from the anterior chamber irrespective of whether a substance enters by secretion or any other active process alone and leaves only by flow, or enters by diffusion alone
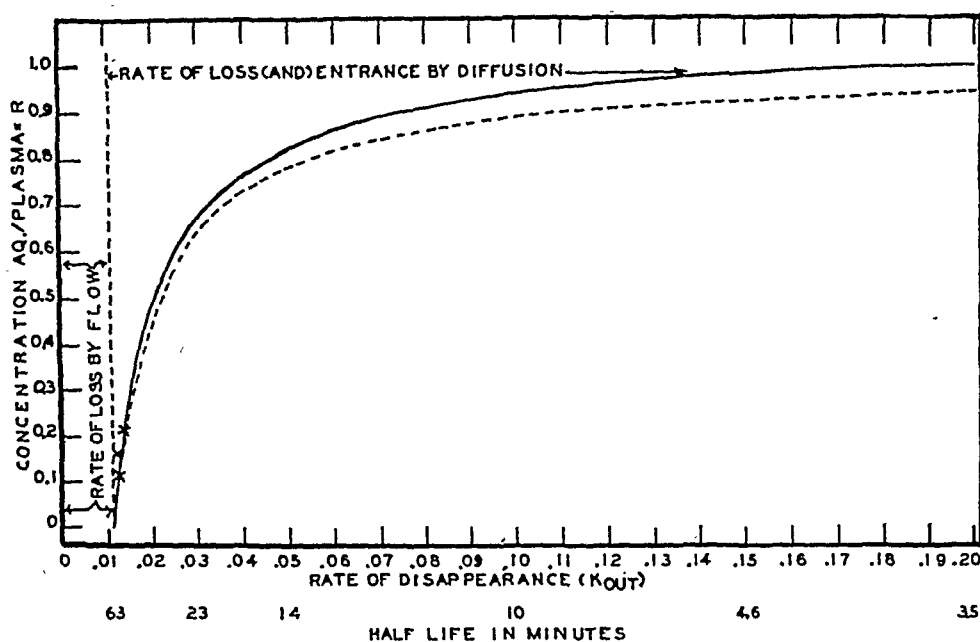
Fig. 4 (Kinsey and Bárány). The relation between steady-state distribution ratio R and the rate of disappearance k_{out} for any substance assumed to enter the anterior chamber either by diffusion (curved lines) or secretion (broken perpendicular line). (For difference between solid and broken curved lines see text.)

at the angle, and the distance to the right of the line shows the contribution of diffusion to the rate of disappearance. Obviously, a comparison of the magnitude of the distances to the left and right of the line shows the comparative contribution of flow and diffusion to the rate of disappearance. Since diffusion is a two-way process, the distance to the right of the line also represents the rate constant for entrance by diffusion for any particular substance. The distance between the solid curved line and the broken curved line represents the magnitude of the entrance due to bulk filtration as indicated by the alpha term previously referred to. The three

and leaves by diffusion and flow.

Reference to the graph, therefore, permits deductions to be drawn conveniently concerning the mode of entrance of any non-metabolized substance whose rate of disappearance and steady-state distribution ratio are known. If it enters exclusively by secretion or diffusion, its point will fall near to or upon one or the other line. If it enters by both mechanisms, its point will fall somewhere in the field between the two lines. Figure 5 is a graphic construction showing how in this general case the various rate constants can be found once R and k_{out} for a substance are known. The construction is

valid only if the active transport mechanism is linear, so that one can write:

$$k_{in} = k_{diff.} + k_{secr};$$

The situation with respect to sodium has been discussed above. Now it can be considered again as an illustration of the use of Figure 4. Sodium has a steady-state value of 0.93 and a rate of disappearance of 0.0108. The only point on the graphs corresponding to these values appears along the secretion line indicating that sodium must enter the anterior chamber solely by secretion and

Fig. 5 (Kinsey and Bárány). Graphic method of determining mode of entrance and exit from the anterior chamber given the steady-state distribution ratio and the rate of accumulation in the anterior chamber.

therefore leave solely by flow. In order for it to enter by diffusion and have a steady-state ratio of 0.93, it would have to disappear with a rate of approximately 0.10, or half of that of water, instead of the observed rate of one tenth of this amount.

Kinsey and Grant[7] have shown that the half-life of chloride cannot be very different from that of sodium, and Kinsey[9] has found that in rabbits it has a steady-state distribution ratio of 1.0. Therefore, it follows that

chloride too cannot enter to any significant extent by diffusion, but enters primarily, if not exclusively, by a secretory process at about the same rate as sodium. Similar results are obtained for thiocyanate, the half-life of which was determined by Kinsey and Grant. The values for phosphate (Palm[10]), together with our present values for the rate of flow, show that phosphate too must enter mainly by secretion. Palm states, in effect, that if phosphate is secreted into the aqueous humor and removed by flow, k_{flow} has to be 0.01 to fit his data. On the other hand, if phosphate entered by diffusion, k_{flow} would have to be 0.005. Since our value of k_{flow} is 0.011 it is obvious that his values show that phosphate enters the anterior chamber by secretion.

From the conclusions drawn thus far it may seem that the mode of reasoning adopted leads to the conclusion that all substances, except water, enter the anterior chamber by secretion. That this is not the case may be seen from consideration of ethyl alcohol. Palm[3] has investigated the rate of accumulation of ethyl alcohol in the aqueous humor and found it to be approximately one half of that of water, that is, k_{in} equals 0.10. Since the steady-state value for alcohol was found to be about 1.0, k_{out} must be of the order of 0.10. Figure 4 shows that ethyl alcohol must enter mainly by diffusion. From the figure, the predicted steady-state distribution ratio would be approximately 0.95, a value compatible with Palm's results. Because of lack of mixing in the aqueous humor, and for other reasons throughly discussed in Palm's paper, assignment of precise values for the rate constants of substances entering the anterior chamber as rapidly as ethyl alcohol is not possible. It is sufficient to point out here that ethyl alcohol enters the anterior chamber primarily by diffusion, the mode of entrance which is assumed by Palm.

In rabbits, ascorbic acid has a steady-state distribution ratio of approximately 15, at

physiologic plasma concentrations.[11] We have found (in unpublished work,) that the rate of disappearance from the anterior chamber of rabbits is approximately 0.01.

In this instance the enormously large concentration in the aqueous humor compared with that in the plasma is presumptive evidence of secretion, although Mueller and Buschke[12] have postulated that the ascorbic acid in the aqueous humor comes from the reduction of dehydroascorbic acid by the lens. If ascorbic acid enters the aqueous humor as such from the blood, and is freely diffusible in the aqueous humor, reference to the figure indicates that it must do so mainly by secretion. If it is formed from a precursor, as Mueller and Buschke suggest, its rate of disappearance shows that it leaves entirely by flow—a secondary assumption of the theory of Mueller and Buschke. It is not possible from the present data to choose between the alternatives that ascorbic acid is secreted as such or that it is formed from dehydroascorbic acid.

As stated earlier in this paper, it was in part to explain the steady-state values of urea and levulose that Kinsey and Grant formulated the postulates embodied in Figure 4. Many observers have investigated the steady-state ratio of concentrations for urea; the most recent value, based on 13 rabbits, given by Kinsey and Robison[13] is 0.88. Bárány and Ross[14] have found a ratio of 0.75 in a series of 10 rabbits. Using the average of these values the steady-state distribution ratio is 0.82. Accordingly, if urea were to enter by diffusion, as originally assumed by Kinsey and Grant, it would have to disappear from the anterior chamber with a k_{out} equal to approximately 0.050, or have a half-life of approximately 14 minutes. Recent experiments by Kinsey in a small number of rabbits (4) have given a half-life of approximately 17 minutes, $k_{out} = 0.04$. In view of the small number of available rate experiments the observed half-life is compatible with that derived under diffusion assump-

tions, and it may be concluded that a large proportion of urea must enter by diffusion.

In summary, within the limits of accuracy imposed by experimental variables and variations between animals, the inorganic ions sodium, chloride, thiocyanate, and phosphate enter the anterior chamber predominantly by secretion; whereas, the nonelectrolytes, ethyl alcohol and urea, both enter the anterior chamber primarily, if not exclusively, by diffusion. For the large organic ions used as test substances this question must be left open. The same is true for ascorbic acid because of its special properties. All these substances leave by flow, and those entering by diffusion must in addition leave by diffusion. These conclusions in regard to nonelectrolytes and inorganic ions are the same as those reached previously by Kinsey and Grant, but, because of the relatively precise knowledge of the rate of flow, they can now be considered as established quantitatively within the limits given above.

It is to be noted, however, that the two nonelectrolytes shown to enter mainly by diffusion are known to penetrate cell walls with special ease. It may be that the high rate of entrance by diffusion masks any simultaneous but slower entrance by the same mechanism that transports the various ions. If the mechanism is highly unspecific, it might transport certain nonelectrolytes too.

This leads to the question as to the nature of the mechanism for transporting solutes into the aqueous humor. A detailed discussion of this subject is beyond the scope of this paper; however, several limitations to the application of the findings presented here to the mechanism problem should be stressed. Analyses made on samples of aqueous humor provide information primarily, if not exclusively, on aqueous humor as it exists in the anterior chamber, since the contribution of aqueous humor from the posterior chamber to samples withdrawn for analysis must be small indeed. In so far as the substance analyzed, for instance water or

urea, diffuses into the anterior chamber across the iris-blood barrier, such analytical information immediately enables one to draw inferences with regard to the mechanism by which the substance is transferred from blood to aqueous humor.

For substances like sodium and chloride, on the other hand, which we have shown do not diffuse appreciably into or out of the anterior chamber from the iris (so must pass from the posterior to anterior chamber through the narrow space between iris and lens), it is only possible to state that they enter the anterior chamber by an active process.

Since there is a continuous flow of fluid from the posterior to the anterior chamber, this flow of fluid is probably the active and unidirectional mechanism by means of which the substances are transported into the anterior chamber, and which, in the sense of the term as used here, has been called secretion. If this be true, the limiting factor for the rate of entrance of many solutes into the anterior chamber may not be the transport from plasma to aqueous humor in the posterior chamber through the ciliary epithelium, but the rate at which they are carried into the anterior chamber by a flow of water.

Since the flow of water requires energy for its maintenance, clearly it is essential that some substance or substances, but not necessarily either sodium and/or chloride (which might diffuse back and forth between the plasma and aqueous humor in the posterior chamber), be actively transferred into the posterior chamber from the plasma. Perhaps the simplest means of obtaining a hypertonic aqueous humor would be the production of bicarbonate in excess of that found in the plasma as a result of metabolism of the ciliary epithelium, a possibility consistent with recent experiments by Kinsey[15] who has shown that in the rabbit there is a relatively large excess of total CO_2 in the aqueous humor compared with that in the plasma, averaging, in 7 cases, 6.3 and 12.0

millimoles higher than the venous and arterial blood, respectively.

SUMMARY

The rate of flow of aqueous humor in rabbit eyes has been derived within narrow limits from the rate of disappearance from the anterior chamber of three test substances, para-aminohippuric acid, Rayopake, and Diodrast, and from the ratio of the concentration of these substances in the aqueous humor to that in the plasma water under steady-state conditions.

By assuming that all three test substances enter either by diffusion or secretion, respectively, the limits for rate of flow were found to be 1.07 to 1.30 percent of the volume of the anterior chamber per minute. From all of the evidence available the best value for rate of flow was considered to be 1.1 percent per minute which is equivalent to about 2.75 cubic mm. of aqueous humor per minute.

The average rate of disappearance of sodium was found to be 1.08 percent per minute, which corresponds almost precisely with the minimum rate of disappearance imposed by flow on all aqueous humor constituents not preferentially held back at the filtering angle of the eye. The ratio of the concentration of sodium in the anterior chamber to that in the plasma water at steady state was found to be 0.93. From these figures it was inferred that sodium must leave the anterior chamber almost entirely by flow and enter the anterior chamber predominantly by a unidirectional active process (secretion).*

The general relation between the steady-state distribution ratio aqueous humor/plasma and rate of disappearance for any nonmetabolized substance entering either by diffusion or secretion or both, was expressed graphically using the experimentally established value for the rate of flow. By reference to the graph, deductions can be made readily concerning the mode of entrance into

* See footnote page 189.

the anterior chamber for all substances whose steady-state ratios and rates of accumulation are known.

It was concluded that within the limits of error of the available data, sodium, chloride, thiocyanate, phosphate, and probably ascorbic acid enter the anterior chamber predominantly as a result of a secretory process and leave predominantly by flow; whereas, ethyl alcohol and urea enter predominantly by diffusion and leave both by flow and by diffusion.

243 Charles Street (14).
Bangardsgatan 9.

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DISCUSSION

DR. DAVID G. COGAN (Boston, Massachusetts): Such an outstanding paper ought, I think, have some discussion. I am not the one to open it but in order for us to arrive at a simple general rule, I would like to ask Dr. Kinsey if it is correct to state that all substances which are ionized appear to be secreted while those which are not ionized seem to obey laws of diffusion. Moreover, has not much of the confusion in the past regarding the formation of the aqueous been due to the consideration of the aqueous humor as a whole rather than to its various constituents? Dr. Kinsey and Dr. Bárány have shown that there are at least two means by which substances enter the anterior chamber from the blood.

DR. JOHN E. HARRIS (Portland, Oregon): I would like to ask Dr. Kinsey whether his studies of the kinetics of entrance of the compounds, which his analyses show are secreted into the aqueous, have enabled him to determine the order of the reaction. We have been perplexed by this

problem. In the development of the mathematical expressions which we used in the analysis of our data, we pointed out that, where the movement in any one direction is considered to be by strict diffusion, the rate of the movement is proportional to the concentration. The proportionality constant is the "k" of our expressions and the "$k_{diff.}$" of Dr. Kinsey's expressions. The kinetics of this type of movement will be that of a first-order reaction, and the k values calculated will be the same over the entire range of concentrations, all other things being equal.

On the other hand, if a substance moved by secretion it might be expected that the rate of movement would be proportional to the product of the concentration and some function of the cell. On the face of it, this is a second-order reaction, but the kinetics of the movement would depend upon the nature of the cellular function and would be difficult to predict.

If the limiting factor were the concentration of the substance to be secreted, the kinetics would be that of a first-order reaction and the movement would be proportional to the concentration. At the other extreme, where the limiting factor is the cellular function, the movement would be totally independent of the concentration. In any event, where the function of the cell is included in the calculated proportionality constant, as it is in Dr. Kinsey's "$k_{secr.}$" one would expect that the k value as calculated would not be the same over a wide range of concentrations. Unfortunately, there are so many other variables in the in vivo, plasma-anterior chamber system, that it is difficult to establish this relationship, and I was wondering what luck Dr. Kinsey has had in its evaluation.

DR. KINSEY: Dr. Harris has raised an important question, and one which we have indeed considered in evaluating our "k" factors. In our experiments in which sodium was the test ion it will be recalled that we used radioactive sodium. This method enables one to trace the passage of sodium from the blood to the aqueous humor without appreciably changing the concentration of sodium in the blood. In this way one avoids any limitation in transfer rate associated with cellular function.

In earlier work with ascorbic acid, I did encounter just the type of limiting factor of which Dr. Harris speaks. In this instance, when the concentration of ascorbic acid in the plasma exceeds 3 mg. percent, there appears to be no further increase in the rate of transfer of this compound into the anterior chamber (Kinsey, V. E: Transfer of ascorbic acid and related compounds across the blood-aqueous barrier. Am. J. Ophth., 30:1262, 1947).

I agree with Dr. Harris that the proportionality constant "k" for a substance which diffuses would not be influenced by the relative concentration in the plasma compared with that in the aqueous humor.

DR. KINSEY (closing): I would like to thank Dr. Cogan for his kind remarks and say that as a simple rule our findings to date indicate that water and all nonelectrolytes appear to enter the anterior chamber of the eye by diffusion; whereas, the electrolytes enter the anterior chamber by an energetic process which we have defined as secretion.

I would agree with Dr. Cogan's statement that much of the confusion regarding the formation of aqueous humor has arisen from the consideration that the aqueous humor is formed as a whole. Further confusion arises too, I believe, from considering that aqueous humor is formed in but one place in the eye; whereas, our results indicate that nonelectrolytes and water enter the eye both from the iris and probably from the ciliary body. The electrolytes, on the other hand, enter the eye exclusively somewhere posterior to the iris, probably the ciliary body.

THE STEADY STATE OF CORNEAL HYDRATION*

T. D. DUANE, M.D.

Iowa City, Iowa

It is desirable to know the percentage of water present in the corneas of experimental animals since, in contrast to the relatively inert mass of stroma, water is the continuum in which most of the chemical reactions occur in this area. Furthermore as Fischer[1-4] has demonstrated, the transparency of the cornea varies with the water content. Krause[5] has warned that the percentage of corneal hydration obtained by experimental measurement varies with "age, species, and method of manipulation of the tissue."

There is little uniformity in the literature concerning the percentage hydration of either the cornea[6] or sclera.[7] This study was undertaken, therefore, to determine statistically the water content in the bovine, rabbit, and cat cornea and to compare the value with that found in the sclera of the same species. The results indicate that within a given species the water content of the cornea is an extremely constant value.

METHODS

Bovine eyes. The corneas and scleras were obtained from animals of both sexes varying from 1 to 6 years in age. The animals were killed by a bullet shot through the brain. The carotid arteries and jugular veins were then incised, and the animals were permitted to bleed to death.[†] The eyes were enucleated while the animals were still in the convulsions of extremis, and the corneas were dissected from the enucleated globe before the animals had actually expired. The corneas were dissected within a few seconds, employing a forceps and scissors and a minimum amount of manipulation. They were carefully blotted with fine-grade filter paper and were transferred to previously tared weighing bottles which were closed with greased glass stoppers. These bottles plus the contained samples were weighed within an hour of the time of enucleation, and the difference in weight represented the wet weight of the tissue. The grease was then removed from the ground-edge surfaces, and the open bottles and tissues were exposed to 115°C. for 48 hours. The bottles were then re-weighed with and without the tissue, the difference representing the dry weight.

The scleral samples were carefully dissected free from adnexa after both corneas had been removed. They were sealed and weighed in the same manner as described for the corneas.

No attempt was made to obtain total weights of the cornea or the sclera. All weights recorded herein are of representative samples of these two tissues. The weighings were made to the nearest 0.1 mg.

Rabbit. The same procedures were employed in the rabbit experiments except that these animals were killed by injecting 10 cc. of air intravenously.

Cat. The first series of cat eyes was removed from animals which had been subjected to ether anesthesia for periods of 1 to 3 hours. Another group of corneas was obtained from unanesthetized cats killed with intravenous air emboli. These latter corneas were removed from the eye in situ after death. The same weighing procedure was followed as described above for the other species. In the experiments on rabbits and cats middle-aged animals of both sexes were used.

RESULTS

The data are summarized in Table 1. From the table it can be seen that corneal hydration of a given species does not vary to a great extent from animal to animal. In

TABLE 1

CORNEAL AND SCLERAL HYDRATION IN EXPERIMENTAL ANIMALS

Species	Cornea			Sclera		
	No.	% Hydration	S.D.	No.	% Hydration	S.D.
Bovine	25	77.77	0.63	25	68.07	1.90
Rabbit	25	77.67	1.15	25	68.30	2.81
Cat—etherized	38	75.39	1.73	37	67.69	4.92
air-injection	27	76.40	1.62	—	—	—

all instances the standard deviation for the corneal tissue is less than one half of that for the sclera.

DISCUSSION

It is difficult to obtain reliable samples of sclera because of the closely bound chorioid and ciliary body on one side and episclera and inserting muscle tendons on the other. Furthermore, the peculiar anatomy of the ciliary body in the carnivora[8] precludes the possibility of obtaining uniform specimens of the sclera from random sampling of the available sclera. This may account for the relatively high standard deviation in the hydration of cat sclera as shown in Table 1.

In a given species the mean corneal hydration is an extremely constant value from a biologic point of view. This suggests that there is some controlling mechanism operating to keep the water content at a constant level.

Cogan and Kinsey[9] showed that the semipermeable membranes on the anterior and posterior surfaces of the cornea maintain a constant circulation through this region and keep the tissue in a "dehydrated state." This terminology may be confusing unless one appreciates that the "dehydration" is expressed in terms of possible hydration. In

TABLE 2

CORNEAL AND SCLERAL HYDRATION (BOVINE EYES)

Cornea Wet Wt. (mg.)	Cornea Dry Wt. (mg.)	Cornea % H_2O	Sclera Wet Wt. (mg.)	Sclera Dry Wt. (mg.)	Sclera % H_2O
401.4	90.0	77.6	26.6	9.6	63.9
373.1	87.0	76.7	22.7	8.4	64.0
378.6	85.1	77.6	42.8	15.1	64.6
358.8	81.5	77.3	65.4	21.2	67.5
389.6	88.3	77.3	103.6	32.1	68.4
407.7	91.3	77.6	151.1	44.6	70.6
610.8	109.2	82.1	283.6	88.5	69.2
462.6	101.3	78.0	175.4	52.6	70.0
427.5	92.6	78.4	282.5	90.6	68.0
443.5	95.0	78.6	209.0	64.0	69.4
428.2	90.7	78.8	397.8	115.0	71.0
441.4	93.1	78.9	226.5	70.6	69.8
520.6	112.9	78.3	172.8	59.0	65.9
528.4	115.4	78.1	273.2	86.9	68.2
443.3	102.0	77.0	198.5	63.7	67.9
432.5	97.1	77.5	95.5	30.9	67.6
446.9	104.3	76.9	256.1	82.8	67.8
494.4	113.4	77.0	220.8	70.3	68.2
381.2	83.5	78.1	155.1	47.3	69.6
368.1	83.2	77.4	162.4	53.5	68.1
497.6	108.9	77.1	304.1	93.5	69.4
498.1	109.0	77.3	274.7	88.3	67.9
538.4	118.6	78.0	736.3	230.9	68.6
595.6	127.6	78.6	762.8	227.6	70.1
473.5	106.5	77.5	441.2	149.4	66.1
Mean		77.77			68.07
S.D.		0.63			1.90

TABLE 3

CORNEAL AND SCLERAL HYDRATION (RABBIT EYES)

Cornea Wet Wt. (mg.)	Cornea Dry Wt. (mg.)	Cornea % H_2O	Sclera Wet Wt. (mg.)	Sclera Dry Wt. (mg.)	Sclera % H_2O
70.1	16.2	76.9	40.1	14.4	64.2
71.4	16.1	77.2	64.9	20.6	68.2
76.2	16.7	78.2	44.0	14.8	66.4
82.2	17.1	79.2	45.5	14.1	69.0
63.7	13.4	78.9	36.5	13.8	61.2
57.9	12.6	78.2	41.5	14.0	66.3
64.5	16.1	75.0	51.5	19.6	62.0
66.7	15.8	76.3	46.6	15.8	66.1
86.5	18.8	78.3	59.6	20.4	65.8
84.6	19.1	77.4	62.9	20.6	67.2
100.1	22.7	77.4	79.7	24.5	69.2
104.9	23.1	78.0	57.6	19.0	67.0
88.8	19.2	78.4	34.0	9.1	73.3
85.5	18.4	78.4	48.1	15.1	68.4
72.2	16.0	77.8	45.0	12.4	72.4
70.6	16.4	76.8	62.1	19.2	69.0
59.9	14.1	76.5	39.6	12.5	68.4
57.4	13.8	75.9	63.5	19.0	70.0
69.0	16.6	75.9	64.5	17.5	72.9
76.0	17.0	77.6	60.8	20.0	67.1
77.1	17.1	77.8	63.7	16.0	73.6
76.6	17.0	77.8	68.5	22.2	67.6
81.0	16.4	79.7	84.1	22.3	73.5
95.0	20.0	79.0	123.2	38.7	68.6
107.0	22.4	79.1	120.6	36.0	70.2
Mean		77.67			68.30
S.D.		1.15			2.81

TABLE 4

CORNEAL AND SCLERAL HYDRATION (CAT EYES (ETHERIZED))

Cornea Wet Wt. (mg.)	Cornea Dry Wt. (mg.)	Cornea % H_2O	Sclera Wet Wt. (mg.)	Sclera Dry Wt. (mg.)	Sclera % H_2O
173.9	46.6	73.2	49.4	17.5	64.6
179.6	48.0	73.3	33.2	13.5	59.4
152.9	45.7	70.1	25.0	11.4	54.5
169.7	46.9	72.4	24.9	8.7	65.0
216.0	53.3	75.4	42.0	14.3	66.0
225.8	55.6	75.4	54.0	16.5	68.4
151.5	39.3	74.1	61.4	17.9	70.9
173.9	41.6	76.0	76.8	20.3	73.5
159.6	36.6	76.3	70.9	20.8	70.7
159.0	36.0	77.4	60.4	18.0	70.1
186.0	44.6	76.0	77.6	18.6	76.0
180.2	42.3	76.6	47.4	17.2	63.6
121.9	29.8	75.6			
125.9	31.0	76.0	48.5	16.0	67.0
141.2	31.5	77.7	34.3	10.0	70.8
135.1	30.8	77.3	35.5	11.0	69.0
98.6	20.6	79.1	22.2	6.5	70.5
91.6	20.0	78.2	16.7	5.3	68.2
140.0	32.6	76.6	92.5	24.1	73.9
137.3	33.2	75.7	50.4	13.2	73.8
118.7	28.0	76.4	25.2	9.9	60.6
123.4	27.8	76.6	33.6	12.2	63.8
130.4	30.7	76.6	51.0	16.4	67.9
125.5	32.4	74.2	17.9	7.2	59.8
86.8	21.4	75.0	51.5	15.7	69.5
91.1	20.3	72.7	34.7	12.0	65.4
Mean		75.39			67.69
S.D.		1.73			4.92

TABLE 5

CORNEAL HYDRATION (CAT EYES (AIR EMBOLI))

Cornea Wet Wt. (mg.)	Cornea Dry Wt. (mg.)	Cornea % H$_2$O
68.7	14.6	78.8
72.9	18.1	75.2
73.3	15.9	78.3
176.7	41.7	76.3
206.1	48.8	76.4
157.3	36.9	76.6
177.9	42.5	76.1
164.5	40.5	75.4
167.7	33.4	80.0
174.1	41.1	76.5
152.3	39.6	74.1
171.6	36.5	78.7
152.8	38.2	75.0
153.2	38.0	75.3
169.2	37.4	77.9
195.6	48.5	75.3
170.3	44.4	74.0
211.8	48.0	77.3
190.0	46.0	75.8
164.9	37.5	77.8
210.6	50.4	76.1
183.8	49.6	73.0
181.8	42.7	76.5
198.4	45.1	77.3
232.1	48.6	78.1
218.2	53.2	75.7

| Mean | | 76.40 |
| S.D. | | 1.62 |

other words the cornea can swell to 300 to 400 percent of normal and the reason that this does not occur normally is because of the dehydration action of the semipermeable membranes. The present investigation supports Cogan and Kinsey's theory.

It is possible that these membranes act as governing mechanisms to control the maintenance of a very constant water content. This assures a normal transparency and uniform milieu in the tissue. Most of the changes which occur in the cornea following trauma to either surface are perhaps primarily due to the absence of these controls.

This explanation of corneal opacification has been partially postulated by Kronfeld[10]

and others but experimental substantiation has been lacking.

That the matter may be much more complex is indicated by the recent work of Hart[11, 12] who shows that many factors besides water content affect the transparency of the cornea and must be considered in any theory of normal corneal transparency.

There is a difference between the corneal hydration of the etherized and air-injected cats in this experiment. The dehydration which occurs in the living eye when the lids are open for a prolonged interval alters the data significantly. It is likely that even greater errors would occur if the enucleated eye or excised cornea were permitted to dehydrate. The tissues must be fresh to yield reliable data. The lack of information regarding these facts may account for some of the discrepancies which are recorded in the literature.[6, 7] Although the age extremes were not included in the study, it was observed that there is no variation in corneal hydration within the age spans investigated, nor was any variation found with the sex of the animals.

Finally the simplicity of the techniques involved in the determination of corneal and scleral hydration suggests that this study would be a suitable laboratory exercise for courses in basic ophthalmology.[13]

SUMMARY AND CONCLUSIONS

The corneal and scleral hydration of bovine, rabbit, and cat eyes has been determined and has been statistically analyzed. The uniformity of the corneal data as compared with the scleral data is interpreted as an indication of the controlling forces which are exerted by the corneal semipermeable membranes.

Medical Laboratories.

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DISCUSSION

DR. DAVID G. COGAN (Boston, Massachusetts): Dr. Duane has carefully chosen fresh specimens to determine the water content of normal cornea. This is of the utmost importance for a cornea will spontaneously imbibe water during the first few hours after enucleation and, if the specimen is not fresh, one obtains an abnormally high water content. Presumably the permeability of the endothelium is altered or the stromal fluid becomes more hypertonic through evaporation from the surface so there is no longer an osmotic gradient and semipermeable membrane separating the stroma from the aqueous.

The purpose of a maintained dehydrated state is presumably transparency. If the cornea is allowed to swell, it may become as opaque as the sclera and, on the other hand, if the sclera becomes dehydrated to an extent comparable to that of the normal cornea, it becomes transparent, but it is important to remember that turgescence should always be recorded as a function of the imbibitory power of the tissue and not of its absolute water content.

DR. DUANE (closing): I would like to thank Dr. Cogan for his remarks. I perhaps did overstress the fact of transparency factors when discussing the constancy of the corneal hydration. Of course, a great many other functions can be ascribed to the cornea and perhaps many just as important as the transparency effect.

We all know that the enzymes present in the epithelium layer and endothelium layer and possibly other mediums which are present in the stroma, such mediators as were suggested by Dr. Friedenwald in his talk this morning, all of those constituents require a rather constant environment for their optimal action and if the environment changes to any appreciable extent one way or another, these enzymes are not able to function as normally as they would under optimal conditions.

I am not exactly certain. We haven't investigated the fact of how much trauma or change in the semipermeable membranes in the epithelium and endothelium is required to produce a change in the transparency of the cornea.

I think that that might be an experiment which could at least be looked into. As I conceive it, slight metabolic changes of either of these layers produce what we recognize plainly, at least in the very early stages, with a slitlamp as an opacity. Bedewing of the various layers or slight opacity formation (transient opacities such as striate keratitis) might be ascribed to the loss of the protecting action of the two layers. I think it is quite likely that these opacities occur because of an inhibition of the protecting action of the semipermeable membranes or at least the metabolic enzymes and other controlling factors which are acting in those regions.

THE USE OF ISOLATED RETINAL TISSUE IN STUDIES OF THE METABOLISM OF THE CENTRAL NERVOUS SYSTEM*

W. A. ROBBIE, PH.D., AND P. J. LEINFELDER, M.D.

Iowa City, Iowa

Cellular respiration processes are extremely important for both the functioning and survival of the cerebral cortex and the retina and, if the supply of either oxygen or substrate is interrupted, unconsciousness follows quickly. Manometric studies on the metabolism of isolated brain have revealed something of the nature of the enzyme systems that are involved in oxidation, and of the effects of anesthetics and other pharmacologic agents. A comparison of the metabolism of the cerebral cortex and the retina may be of interest to the ophthalmologist because of interest both in the retina itself and in the information that retinal studies may give about the physiology of the central nervous system.

Physiologically, the retina resembles cerebral cortex in its high rate of oxygen consumption, its unusually high rate of both aerobic and anaerobic glycolysis,[1] its dependence upon glucose substrate, and the almost complete depression of respiration produced by heavy metal inhibitors.[2] Since the retina is derived from neuroectoderm, a morphologic similarity is to be expected, and this has been shown to be true up to the 45-mm. stage of embryologic development.[3] In the adult tissues, in spite of specialization of each, a similarity remains in the lamellar arrangement of nerve cells, synaptic, and nerve-fiber layers.

Isolated rat retina is a convenient tissue for use in manometric metabolism measurements. It is easily and quickly removed from the eye with relatively slight injury, and is thin enough to permit adequate oxygenation without slicing, even though air is the gas phase rather than 100-percent oxygen.

If the suspension medium is buffered and contains glucose and a properly balanced salt mixture, linear respiration may be obtained for a period of 5 to 7 hours. It is thus possible and convenient to measure respiration during a control, experimental, and recovery period on the same tissue. Since the rat retina does not break up while it is shaking in the manometer, it may be easily removed and weighed at the end of the experiment.

Experimental determination of respiration in isolated brain is complicated by the procedure of cutting thin slices of the tissue in order to insure adequate oxygenation. Since the nerve cells are extensively branched, it is evident that a slice of optimum thinness must have a high proportion of cells with cut processes. It is recognized that cutting a nerve process may cause degeneration of the cell body even though the cell is otherwise undisturbed. In an artificially prepared saline solution, there may be additional injury from diffusion into the cell of ions in a concentration different from the normal constitution. Certain experimental agents that do not penetrate the intact cell may likewise adversely and misleadingly affect the brain slice. The necessity for use of 100-percent oxygen also complicates certain determinations because of the oxygen-poisoning effect.

TECHNIQUE

The experiments described in the present paper were performed on albino rats. The animals were killed by breaking the neck, and either the eyes or the brain was removed immediately. In studies on cerebral cortex, the brain was sliced by means of a razor blade and a transparent plastic template.[4] The slices were weighed on a microtorsion balance before they were immersed in physi-

ologic saline solution. Retinas were removed by cutting around the globe just posterior to the ora serrata. The retinas were then lifted out and cut into halves to prevent folding.

The isolated tissues were suspended in phosphate-buffered saline solution at pH 7.35 containing 0.2-percent glucose.[5] Small Warburg manometer flasks containing a total volume of about 7 cc. were used for the oxygen consumption determinations. The center wells contained 10-percent KOH on filter paper. Temperature of the water bath was 37.2°C. Unless otherwise mentioned, experiments on retinas were performed with air as the gas phase and those on brain slices with 100-percent oxygen.

Retinal weights were determined after rinsing the tissues at the end of the experimental periods and drying them on weighed cover glasses at 110°C. The dry weights for the brain slices were calculated from the recorded wet weights by means of a wet-dry ratio obtained by drying sample tissue at 110°C.

In the histologic studies, brain tissue was prepared in the following manner: For the control sections, Figure 5 (left), the brain was removed immediately after the death of the animal, and slices of the cerebral cortex were cut and placed in 10-percent neutral formalin for fixation.

In other specimens studied, slices of tissue were placed in manometer flasks in the phosphate-glucose-saline solution. These flasks were then placed in the water bath and the respiration rate was recorded for one-half and 2½-hour intervals in order to verify the viability of the tissue. Following this, the tissue was removed from the flask and fixed. A similar procedure was used in experiments on the rat retina.

In addition, tissue slices and blocks from rat brain were stored in saline solution at 4°C. for intervals varying from 2 to 24 hours. At the end of the storage period, the brain tissue was placed in formalin for fixa-tion. Sections made from all preparations were stained with hematoxylin and eosin.

EXPERIMENTAL RESULTS AND DISCUSSION

Results of a number of experiments seem to indicate that in the tissues studied oxygen consumption is not dependent upon the integrity of the cell. Both cortex slices or chopped tissue made by cutting the cortex into small pieces respire at about the same level. Similarly, either intact retina or retina which has been cut into small pieces shows the same oxygen uptake for a period of at least one hour. However, if the tissues are ground up in a tissue grinder, then the respiration falls off considerably. It is possible that as long as the gross intracellular organization is not appreciably disturbed, the respiratory enzyme systems may function at a normal rate.

Figure 1 shows that when a properly buffered and balanced saline solution containing glucose is used, the respiration of the retina in air is maintained at a constant rate for as long as 7 hours. The lower curve in the figure shows the course of oxygen consumption when a retina is run in fluid containing no glucose. The rapid decline in respiration to almost the zero level is convincing evidence that the process being measured in the respirometers is glucose metabolism rather than any sort of autolytic degenerative change.

There is a pronounced difference in the course of oxygen consumption of the retina in air and in 100-percent oxygen. In air, the rate of respiration is constant during the observation period. In oxygen, the rate of respiration is higher at the start of the measurement period, but there is a marked falling off and, by the time the experiment has been run for a period of 7 hours, the oxygen consumption has decreased to 50 percent of that of the specimen in air. This is shown in Figure 1.

The curve for brain respiration is similar to that for retina in oxygen and it may be

that if it were possible to run cortex slices in air, the respiration would be more constant. This is not feasible since a tissue slice that is thin enough to permit adequate oxygenation at the center, with air as the gas phase, is almost impossible to prepare.

The steady rate of respiration of the retina in air perhaps more nearly resembles the situation in the living animal, since the oxygen tension within the eye can certainly

tex slices, the response of the injured cells to certain chemical factors may be considerably different than would be expected from normal tissue. It is well known that highly dissociated acids do not go through the normal cell membrane.

Figure 2 shows the results of an experiment with brain slices and retinas in which the tissues were exposed to a saline solution at pH 5.2 for a period of one hour, after
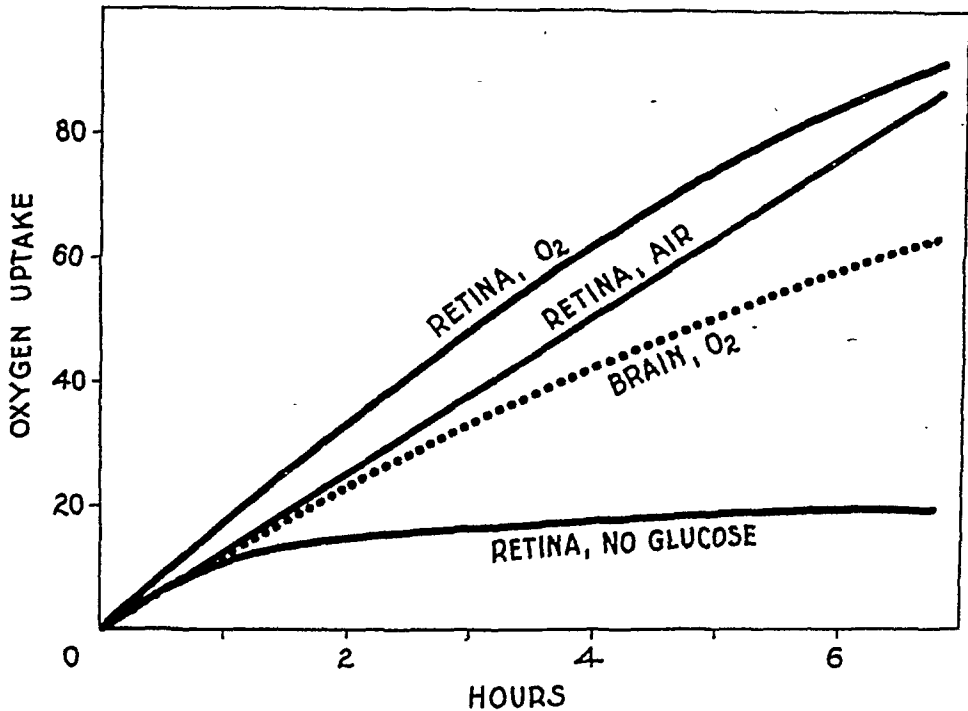
Fig. 1 (Robbie and Leinfelder). Oxygen consumption of isolated rat retinas in phosphate-buffered saline solution containing 0.2 percent glucose. Ordinate shows the mm.³ of O₂ consumed per mg. dry weight, and the abscissa the time in hours.

never approach that which exists in the flasks gassed with 100-percent oxygen. Whether the increase in oxygen consumption of the retina in oxygen at the start of the measurement period is actual respiration or simply oxidation of substrates that might not otherwise be utilized, is a question. The falling off in respiration at the end of the 6- or 7-hour period of measurement may possibly be an oxygen-poisoning effect.

Although the rate of respiration is perhaps not immediately affected by cutting the processes of the nerve cells in cerebral cor-

which the recovery oxygen consumption was measured. Although the retina has apparently not been damaged by this exposure to an acid environment, the cortex slices with their cut cells and processes show considerable injury, as evidenced by a marked decline in respiration. Kidney and liver slices also have been shown to recover almost completely after an hour's exposure to a medium at pH 5.[6]

Figure 3 shows the results of an experiment using 0.1M potassium chloride in the suspension fluid. In vivo, the potassium ion

penetrates the brain very slowly.[7] Yet the respiration of the brain slices is increased by almost 100 percent when a high concentration of potassium is included in the saline solution. (The sodium chloride concentration in these experiments was reduced to maintain an isotonic medium.)

The retina, on the other hand, shows, if anything, a slight decrease in oxygen consumption in the medium containing high potassium. Similar observations have been reported by Dickens.[5] This again indicates that potassium, whatever may be the nature of its stimulating action, apparently does get into the cortex cells which have been cut, but not into the retina cells.

The cytologic picture also gives evidence that the brain is much more injured during
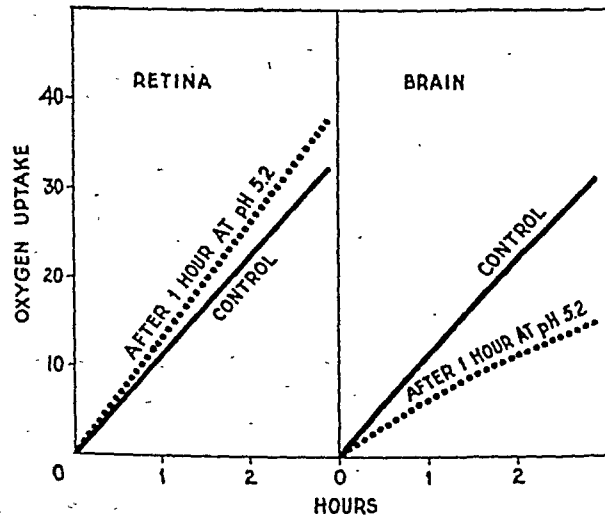
Fig. 2 (Robbie and Leinfelder). Recovery of retinas and cerebral cortex slices after one hour at pH 5.2. During the exposure period the tissues were shaken in manometer flasks in glucose-saline solution containing 0.01M. primary sodium phosphate. Ordinate shows oxygen uptake during recovery period in mm.[3] O_2 per mg. dry weight.

preparation for respiration measurement than the retina. Figure 4 shows sections from a control retina and one which had been run for 2½ hours in a manometer flask at 37.2°C. The ganglion cells and the other retinal cellular elements were similar in both the control and in the experimental tissues at the end of the experiment.

With brain tissue, on the other hand (fig. 5), edema was noted after one-half hour in the Warburg flasks, and the ganglion cells had begun to undergo chromatolytic change, as shown by the swelling of the
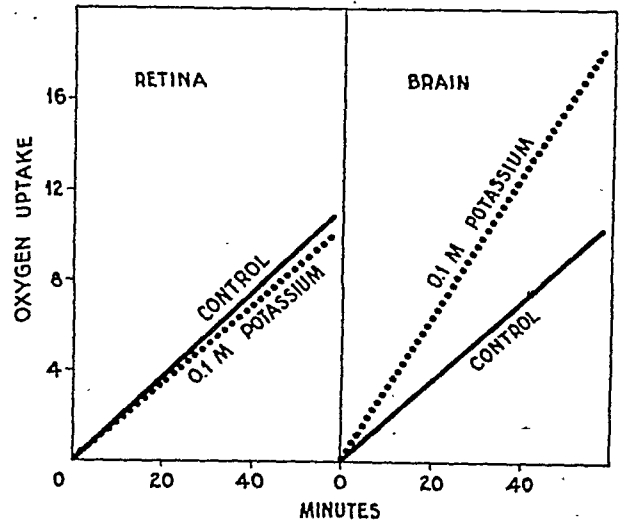
Fig. 3 (Robbie and Leinfelder). Effect of addition of 0.1M. KCl to phosphate-buffered saline solution on the respiration of retina and cerebral cortex slice. Ordinate: mm.[3] of O_2 per mg. dry weight.

cytoplasm and nuclei. In some instances, the ganglion cell nuclei were extremely vacuolated, indicating karyorrhexis. These changes were considerably exaggerated in a 2½-hour specimen and many of the ganglion cells had disappeared, while all of those remaining showed advanced chromatolysis. In some instances, glial clumping about the ganglion cells could be observed. A similar type of change was observed after two hours' storage at 4°C, and this became increasingly apparent after longer storage periods.

When the brain remains intact in the dead animal at room temperature for as long as 2½ hours, chromatolytic changes do not occur. However, if the brain is removed and tissue slices or blocks are prepared, evidence of cellular damage can be recognized within half an hour if the tissue is maintained at 37°C.; similar changes are apparent after two hours when the tissue is kept at 4°C. After greater periods of time, more severe
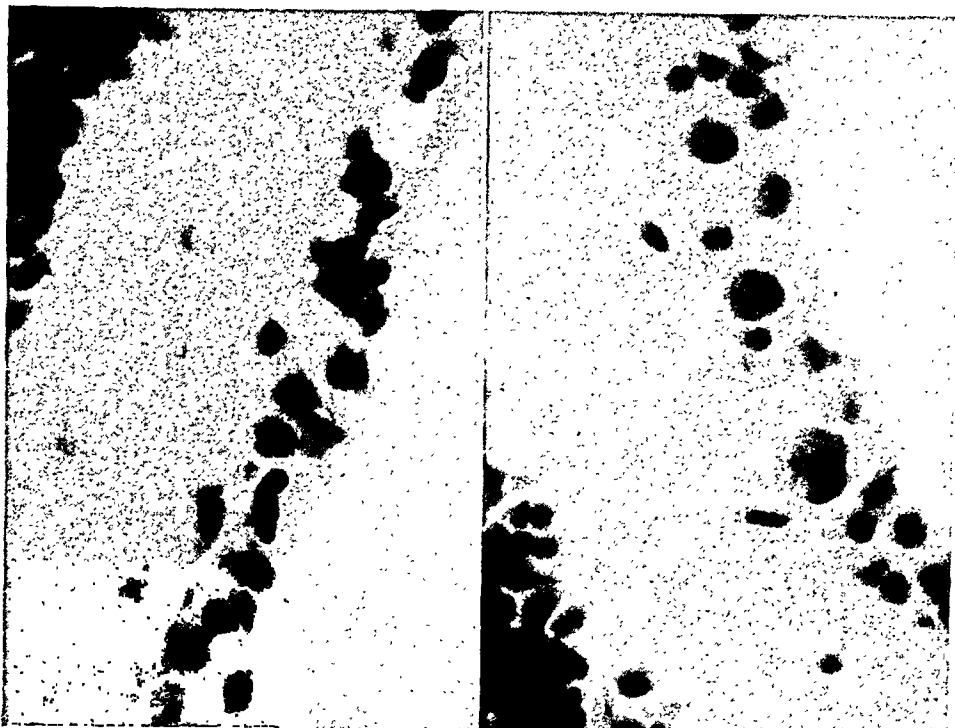
Fig. 4 (Robbie and Leinfelder). Photomicrographs of sections of rat retinas. (Left) Control section. (Right) Section of retina shaken for 2½ hours in manometer flask at 37.2°C.
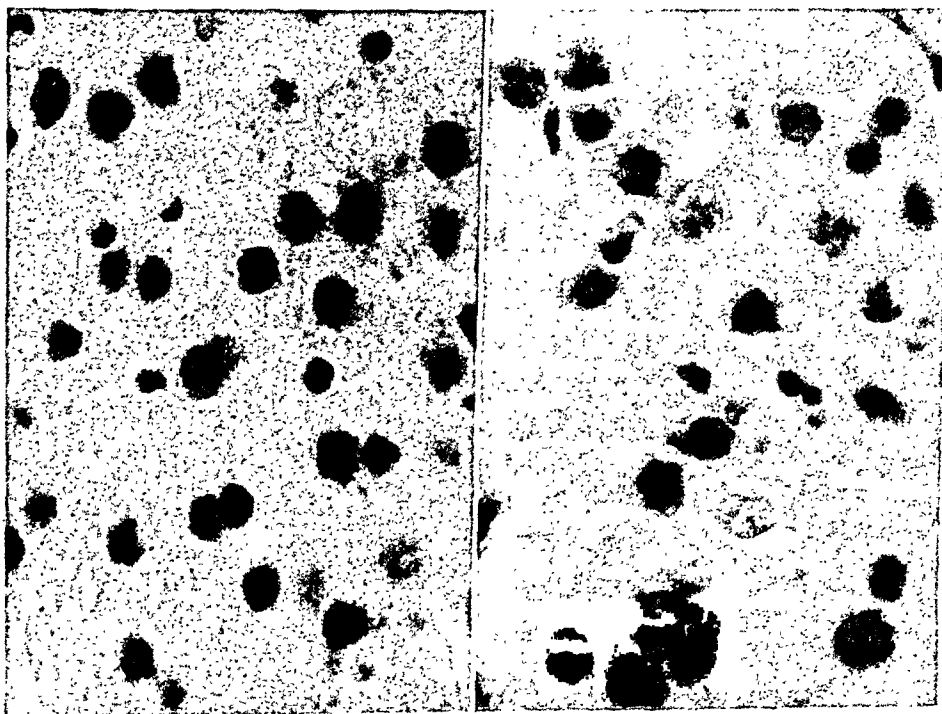
Fig. 5 (Robbie and Leinfelder). Sections of rat cerebral cortex slices. Control on left fixed immediately after death. Experimental tissue on right shaken for one-half hour in manometer flask before fixation.

chromatolytic phenomena are apparent.

These changes, which are identical with those occurring in encephalomalacia, appear to be the result of injury to the ganglion cells or their processes, and the chromatolytic response may occur directly as a result of the injury to the cells or indirectly because of the change in the intracellular chemical environment that occurs when the cut cells are placed in physiologic saline solution. (The concentrations of certain ions in protoplasm are quite different than those in blood plasma.)

In the preparation of retinal tissue, the ganglion cells themselves are not directly injured and only the axone is cut. This injury to the retinal ganglion cell axone occurs at some distance from the cell body, and is less severe trauma than that which occurs to the ganglion cells of the brain when tissue slices are prepared, for, in the latter case, both cell processes and the cells themselves are cut. With the brain slices, a much greater proportion of the cell cytoplasm is exposed to an abnormal chemical environment than in the retina when the main mass of the tissue has not been disrupted.

CONCLUSIONS

The structural and physiologic similarity between the cerebral cortex and the retina make it seem probable that the respiratory response of the retina is, in many ways, truly indicative of central nervous-system metabolism. Rat retinas are convenient to prepare and to use in manometric determinations, and the period of constant oxygen uptake is long enough to allow measurement of experimental treatment periods and recovery in the same tissue.

Injury to the cell membrane in cerebral cortex slices is evidenced by hydrogen ion effect and potassium stimulation of respiration, as well as by a rapid cytologic response to the injury. In studies involving an agent that normally does not penetrate the brain cell, results may be more representative if measurements are made on the retina rather than on a brain slice.

The toxic action of pure oxygen on the retina, and the similarity of the curves representing respiration in oxygen of the retina and the brain, also indicate that brain metabolism in 100-percent oxygen is probably not normal.

It is believed that studies of the retina may in some ways be more clearly indicative of central nervous-system metabolism than observations on brain slices, and it may be advisable to use the retina for comparison and control experiments.

University Hospitals.

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DISCUSSION

DR. T. D. DUANE (Iowa City, Iowa): Granit in Sweden, Adrian in England, Bronk, Hartline in the United States have shown that the retina is an ideal tissue upon which to study electrical phenomena in the body, action potential currents, secondary to stimulation, and so forth.

Dr. Robbie has just pointed out that the retina is an ideal tissue upon which to study metabolic activities of the central nervous system. It seems to me this is a typical example of the point which Dr. Friedenwald was making last night, that we are opening new vistas in research in ophthalmology, because the next obvious step is to make a correlation between electrical phenomena and metabolic phenomena.

In other words, it seems conceivable to me that one might injure the various portions of the retina, say the rods and cones, bipolars, or the ganglion cells, to see what effect that has upon the electrical phenomena in the electroretinogram, and then the retina could be removed and studied in vitro from the metabolic standpoint and I think some very interesting correlation might be made.

DR. P. J. LEINFELDER (Iowa City, Iowa): The portion of this paper that has been particularly interesting and spectacular to me is the portion dealing with the pathology in the nervous system. Unfortunately, the lantern slides do not show the great degree of chromatolysis that occurs in the ganglion cells of the brain.

You who have taken photomicrographs of brain tissue at 800 or 900 magnification know how difficult it is to show representative areas in a particular slide. However, the effects of slicing the brain tissue are real and occur with great rapidity for they can be clearly recognized one-half hour after sectioning. The paradox of the situation is this.

If we leave the brain intact in the animal for 2, 4, 6 hours, and then remove the calvarium, take out the brain, take a thin slice of it, and put it in fixative immediately, we obtain perfectly normal histologic appearances. However, if the brain tissue is sliced and then allowed to lie in saline buffer solution with glucose and oxygen available, the changes of chromatolysis take place. Such changes are not recognized in the retina up to 6 hours when the temperature is 37.5°C., nor up to 24 hours when the retinas are kept at 4°C.

The occurrence of these chromatolytic changes in nerve tissue which is assumed to be dead is a particularly interesting problem and one which has to be investigated in the light of what is taking place in the tissues as far as respiration, glycolysis, and utilization of substrate is concerned.

DR. DAVID G. COGAN (Boston, Massachusetts): I would like to ask Dr. Robbie if there is any contradiction in the apparent susceptibility of the retina to anoxemia, as judged by "black-outs," and the apparent resistance of the retina to oxygen lack as determined by studies in the Warburg apparatus.

DR. ROBBIE (closing): I would like to say that I have no way of knowing what effect the proteolytic enzymes may have on the histologic structure of the tissue. To Dr. Cogan's comment I may say that I think the two factors are possibly quite dissociable —oxygen consumption and the preservation of the visual functions. It is well known of course that the anoxic retina loses its power of perceiving light very rapidly, and anoxia for a period of 7 minutes in the intact eye leads to permanent blindness. Yet if we kill the animals and keep the dead bodies at 37°C. for a period of 45 minutes and then take the retinas out and measure them in the manometer flasks, the oxygen consumption is apparently normal. So it seems as if the limiting element in the system is something other than a chain of respiratory enzymes.

It may be that the ganglion cells themselves are particularly susceptible in some way morphologically or chemically.

To Dr. Duane's contribution, I would like to discourse somewhat on his use of the word "ideal." We do not believe that the retina is necessarily ideal for these purposes. For example, Dr. Friedenwald suggested to me that perhaps the pigment layer is important in retinal function. When we take the retina out of the eye and leave the pigment layer behind, we no longer have a completely normal retina, and perhaps we are disturbing the function in that way. Furthermore, when an animal is killed, unless the eye is fixed immediately, the rod and cone layer quickly becomes diffused in appearance. So the retinas we are studying probably do not have an intact rod and cone layer. What we are measuring is the metabolism of the surviving cells. Any conclusions regarding vision that involve the photochemistry of visual purple are perhaps not shown by these studies. The one point that I do wish to make is that possibly the retina is more representative of the normal central nervous system than the cerebral cortex slice, and at least it may be valuable to compare both types of tissues when the effect of a drug is being studied so that it may be possible to evaluate the factors of permeability and injury.

METABOLISM OF THE CRYSTALLINE LENS*

I. WATER CONTENT AND GROWTH RATE

LAWRENCE O. ELY, M.D.
Iowa City, Iowa

Water is quantitatively the major constituent found in the crystalline lens. Accurate interpretation of certain lenticular properties, namely, QO_2, is dependent upon a precise knowledge of the ratio of wet weight to dry weight. Bellows[1] presents a table summarizing the information in the literature concerning the water content of bovine lenses (Table 1), but it is of note that the cases cited by any one worker are too few in number to be of statistical significance except for Salit's[2] figure of 65.41-percent water for 1- to 4-year-old bovine lenses. However, Krause[3] gives a statistically reliable water content of 67 percent in 1-year-old bovine lenses, but he gives no indication of the changes occurring with growth.

Salit[2] found the water content of the rabbit lens to be 59.25 percent (the mean of only two cases), while Brückner[4] reports the water content as 62.7 percent (also the mean of two cases). No report on the age of the animals was made by either worker. Field and others[5] found a mean dry weight of 30.7 percent, which would indicate a water content of 69.3 percent.

Brückner[4] reported the water content of a lens from a 5-day-old cat as 74.5 percent. No other references on the water content of cat lenses have been found in the literature.

Therefore, it is important to make a more extensive study of the water content of the crystalline lens to correlate its relationship with the age of the animal in cattle, rabbits, and cats, three species commonly employed in experimental studies of the eye.

METHODS

The eyes were removed from the animals within a few minutes of their death.† All

† The cattle eyes were obtained through the courtesy of Gay's Locker Plant, Iowa City, Iowa, and Wilson Packing Company, Cedar Rapids, Iowa.

TABLE 1

WATER IN BOVINE LENSES

Age (years)	Number of Lenses	Author	Percent Water	Percent Water (weighted average)
1	6	Cahane	60.17	
	18	Bürger & Schlómka	68.70	66.70
	6	Jess	66.27	
	4	Salit	67.94	
1–4	49	Salit	65.41	
	10	Bürger & Schlomka	65.60	64.9
	16	Jess	64.65	
	6	Cahane	59.81	
5–9	12	Jess	63.99	64.4
	11	Bürger & Schlomka	64.9	
10–14	10	Jess	63.2	63.7
	10	Bürger & Schlomka	64.2	
15–17	8	Bürger & Schlomka	63.4	
	2	Jess	63.82	63.5
Unknown	?	Simon	65.76	
	4	Laptschinsky	63.51	

TABLE 2

RELATIONSHIP OF THE AGE OF BEEF TO THE TOTAL WEIGHT AND WATER CONTENT OF THE CRYSTALLINE LENS

Age (years)	No. of Lenses	Weight in Grams			Percent Water		Standard Deviation*
		Range (wet)	Mean (wet)	Mean (dry)	Range	Mean	
0–1	42	0.9036–1.4641	1.1781	0.3783	66.53–71.0	68.63	0.97
1–2	38	1.1878–1.7521	1.5984	0.5515	63.5 –68.1	65.6	1.24
3–4	32	1.6431–2.2417	1.9532	0.6991	61.9 –66.5	64.4	1.25
5–10	28	1.9645–2.7650	2.3042	0.8377	59.4 –65.0	63.7	1.56

* Standard deviation has been calculated from the formula, $\sigma = \sqrt{\dfrac{\overline{\Sigma x^2}}{N}}$

x = the deviation of individual cases from the mean.
N = total number of cases.

TABLE 3

RELATIONSHIP OF THE AGE OF RABBITS TO THE TOTAL WEIGHT AND WATER CONTENT OF THE CRYSTALLINE LENS

Age (weeks)	Animal	No. of Lenses	Weight in Grams			Percent Water		Standard Deviation
			Range (wet)	Mean (wet)	Mean (dry)	Range	Mean	
1–4	A*	18	0.1769–0.3621	0.2529	0.0800	67.2–70.3	68.7	1.1
	P†	12	0.2001–0.4136	0.2981	0.0975	68.3–70.1	69.0	1.96
8–16	A*	28	0.5187–0.6600	0.5899	0.2042	62.9–67.1	65.4	1.03
	P†	4	0.6347–0.6648	0.6465	0.2180	65.7–67.2	66.4	—
20–36	A*	10	0.5942–0.6723	0.6196	0.2250	62.8–64.5	63.7	0.6
38–46	A*	12	0.5985–0.6723	0.6341	0.2345	60.7–64.8	63.1	1.56

* A—albino rabbits.
† P—pigmented rabbits.

TABLE 4

RELATIONSHIP OF THE AGE OF CATS TO THE TOTAL WEIGHT AND WATER
CONTENT OF THE CRYSTALLINE LENS

Age (months)	No. of Lenses	Weight of Grams			Percent Water		Standard Deviation
		Range (wet)	Mean (wet)	Mean (dry)	Range	Mean	
2–4	22	0.2896–0.3946	0.3533	0.1153	65.6–68.6	67.2	0.88
5–12	24	0.4983–0.6214	0.5457	0.1939	62.3–65.8	64.6	0.95
13–24	32	0.6175–0.7582	0.6745	0.2556	59.5–63.9	62.2	1.28
25 and over	24	0.7048–0.7943	0.7371	0.2835	59.5–63.2	61.6	1.16

lenses were dissected from the eyes within a short time after death of the animal, and in no cases did this time exceed one hour. The lens was removed intracapsularly in the following manner.

all cut, special care being taken to avoid rupturing the capsule. As the lens was gently eased out of the patellar fossa, the ligamentum hyaloideocapsulare was cut if the vitreous was adherent to the posterior capsule.
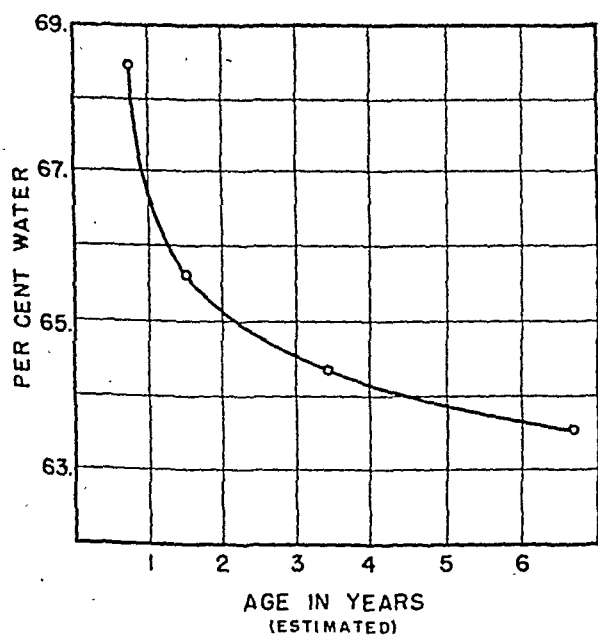
Fig. 1 (Ely). Relationship of age to water content of bovine lens.
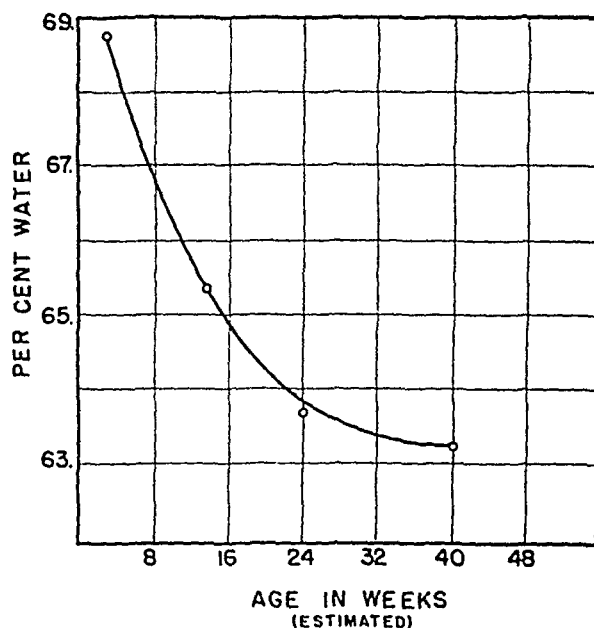
Fig. 2 (Ely). Relationship of age to water content of rabbit lens.

The cornea was removed and a total iridectomy was performed in order to expose the anterior surface of the lens and make visible the zonular fibers. These fibers were

After removal of the lens any adherent bits of vitreous were removed with forceps and scissors.

Each lens was weighed on a chainomatic balance and dried in an electric oven at 104°C. for 48 to 72 hours, or until the weight of the dry residue became constant on two successive weighings.

In these procedures two precautions should be noted: (1) The lens contains a certain proportion of water that is difficult

to remove by drying. Only by drying for 48 to 72 hours, or until the dry weight is constant, can this error be avoided. (2) The weight was noticed sometimes if the dried lenses were allowed to stand exposed to the air for several hours before weighing.
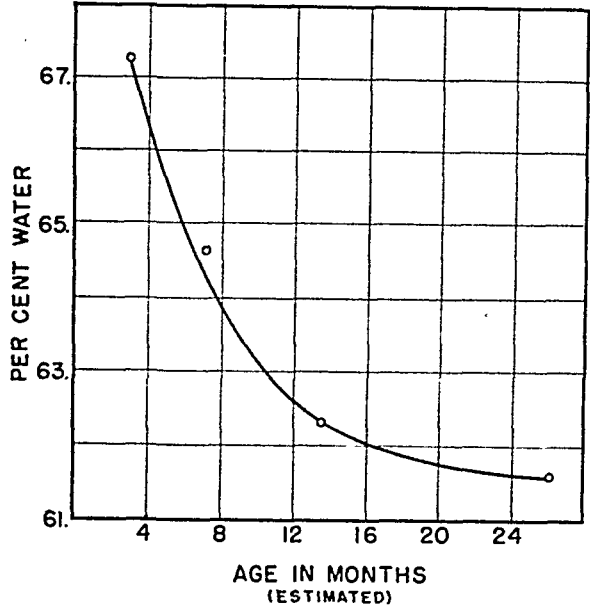
Fig. 3 (Ely). Relationship of age to water content of cat lens.
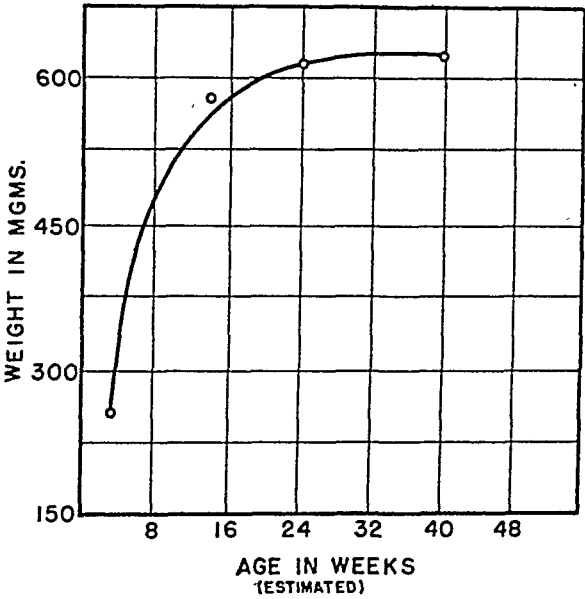
Fig. 5 (Ely). Growth rate of rabbit lens.
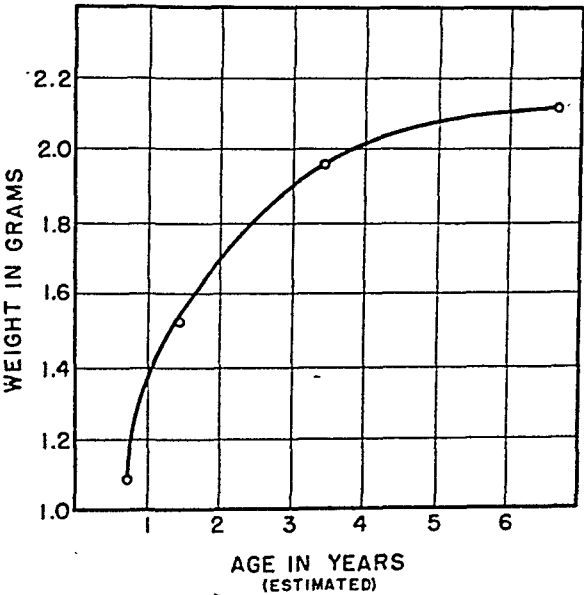
Fig. 4 (Ely). Growth rate of bovine lens.
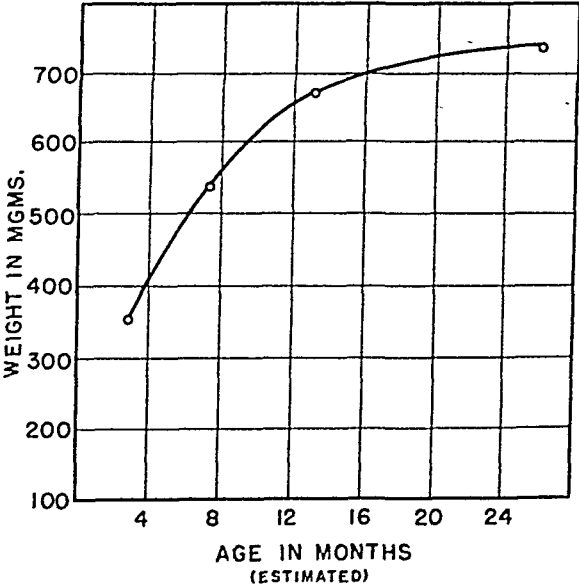
Fig. 6 (Ely). Growth rate of cat lens.

dried lens must be kept in a desiccator during the interval between drying and weighing, if this interval exceeds a few minutes, as the dried residue is somewhat hygroscopic. An increase of 5 to 10 percent in

RESULTS

A compilation of the results obtained is found in Tables 2, 3, and 4. It should be noted that the mean water content of the normal bovine, normal rabbit, and normal

cat lens is between 60 and 70 percent if the two extremes of age are excluded. As the age of the animal increases, the percentage of water decreases. This relationship is shown in Figures 1, 2, and 3. The percentage of water in the lenses of similar age groups in all of the mammals studied is approximately equal, within limits of experimental error.

Figures 4, 5, and 6 show the growth curves of the lenses. A similar type of curve is obtained for each of the three species. The growth rates of bovine lens, rabbit lens, and cat lens agree approximately with the data obtained by Donaldson and King[6] on the Norway rat, if similar age groups are compared. There appears to be little difference in the growth rates of bovine, rabbit, and cat lenses.

DISCUSSION

Lenticular growth occurs by the proliferation of new fibers from the lens bow, with the result that the older fibers are pushed toward the nucleus. As the nucleus is approached these fibers become more inspissated than those peripherally located. Lebensohn[7] found that the cortex of normal ox lens contained 69.9-percent water, while the

nucleus contained only 51.0 percent.

The data presented above show a striking similarity in the water content of the lenses of the three species represented. These percentages are approximately 5 to 8 percent above those found by Donaldson and King[6] for comparable groups of Norway rats. However, the percentage of water of the lens continues to decrease with age in all of the animals studied. Thus the lens is similar to other body tissues in showing an inverse ratio between age and percentage of water.

CONCLUSIONS

1. The mean water content of bovine, rabbit, and cat lenses is between 60 and 70 percent, if the two age extremes are excluded.

2. Growth curves of bovine, rabbit, and cat lenses are similar.

3. The percentage water content of the crystalline lenses of cattle, rabbits, and cats varies inversely with the age and weight of the lens.

4. The percentage water content of the crystalline lenses of comparable age groups of the animals studied is approximately equal, within limits of experimental error.

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METABOLISM OF THE CRYSTALLINE LENS*

II. Respiration of the Intact Lens and Its Separated Parts

Lawrence O. Ely, M.D.

Iowa City, Iowa

Few studies on the respiration of the intact crystalline lens have been made because: (1) The oxygen uptake of the lens is so small that a reliable result is difficult to obtain, necessitating the measuring of the oxygen uptake for 3 to 6 hours; (2) any prolonged shaking of the lens in the common Barcroft-Warburg flask having a center well causes the lens to disintegrate.

In the few studies that are available the results have not been calculated on a dry-

the substrates were not all alike; little attention was given to the age of the animal; and no record was made as to whether the capsule was intact at the conclusion of the experiment. Later in this paper it will be shown that a significant difference in QO_2[†] is found if the capsule is ruptured.

To aid in the understanding of the metabolism of the lens it is important to know the respiration of the separated parts of the lens. Experimentally the lens may be divided

TABLE 1

Calculated QO_2* of Rabbit Lens from Data Taken from the Literature

Author	Temp. °C.	QO_2 (wet)	QO_2 (dry)
Mashimo[1]	30	0.260	0.867
Schmerl[2]	37.5	0.0174	0.058
Schmerl[3]	37.5	0.039 –0.113	0.13 –0.377
Kronfeld & Bothman[4]	37.0	0.0174–0.13	0.058 –0.433
Field,† et al.[5]	30	0.0203–0.0528	0.066–0.172
	37.0	0.047	0.154
Pignalosa[6]	37.5	0.152 –0.196	0.507–0.65

* The microliters of O_2 consumed per mg. of tissue per hour, assuming an average lenticular weight of 230 mg. and a dry weight of 30 percent.
† Wet weight of 216 mg. and a dry weight of 30.7 percent.

weight basis, but have been given as the oxygen uptake of an entire lens, or as the oxygen uptake per gram of wet weight. From data taken from the literature in Table 1 is shown the calculated QO_2 of the rabbit lens, both on a wet-weight and a dry-weight basis, assuming the average lenticular weight to be 230 mg. and the dry weight to be 30 percent of the wet weight.

Of special interest is the wide range of results, for the dry weight QO_2 ranges from 0.058 to 0.867, a difference of 14 fold. An analysis of these results shows that this wide spread may be due to several factors. The temperatures were not standardized;

conveniently into the capsule, the cortical fibers and epithelium, and the nucleus.

Schmerl[2] first made the observation that the nucleus of a rabbit's lens showed no oxygen consumption over a 2-hour period. The same negative result was found by Pignalosa,[6] Field and others,[5] and Campos.[7] No information was found concerning the respiration of the capsule of the lens of any other animal.

Methods

Rabbit lenses (age 3 to 8 weeks) were used in the measurement of the QO_2 of the intact lenses, while both bovine and rabbit

† Unless otherwise specified QO_2 is defined as the microliters of oxygen consumed per mg. of dry-weight tissue per hour.

lenses were used for the study of the separated parts. The lenses were removed carefully, extreme care being taken to obtain a lens with an intact capsule.

A special Warburg flask was used in this work, by means of which it was possible to shake the lens for 6 to 8 hours without rupturing the capsule. The flasks used were approximately 10 ml. in capacity and had a vessel constant of 0.8 to 0.9. They differed

TABLE 2

The QO_2 of whole rabbit lens

Lens Number	Calculated Dry Weight	QO_2
1	82.3 mg.	0.06
2	88.6	0.11
3	86.9	0.10
4	81.4	0.17
5	69.9	0.08
6	86.4	0.07
7	98.7	0.09
8	95.5	0.06
9	82.1	0.21
10	101.0	0.08
11	78.5	0.05
12	83.2	0.09
13	105.0	0.10
14	129.0	0.10
15	130.0	0.07
16	98.0	0.07
17	98.5	0.08
18	118.9	0.06
19	122.9	0.09
20	86.1	0.08
21	84.7	0.07
22	76.6	0.12
23	72.9	0.06
24	79.0	0.08
25	82.3	0.09

Mean	0.09
Range	0.05–0.21
S.D.	0.035

from standard flasks in that they had no center wells. The 10-percent potassium hydroxide used to absorb the CO_2 was placed in the side arm along with the usual filter paper. The substrate was a modified phosphate Ringer's solution, pH 7.35, with 200 mg. percent glucose. The temperature of the water bath was 37.5°C. Air was used in the gas space. Measurements were made with both intact lenses and those in which the lenticular capsule had been ruptured with a pithing needle.

Three rabbits of the same age and size were used in each day's determinations. The wet weight of each lens was taken immediately after removal, and only one of the lenses was used for a dry-weight determination. It was assumed that this lens was representative of the percentage of water in all of the lenses of the three rabbits (see "Metabolism of the crystalline lens: I. Water content and growth rate," pages 215-219).

In the study of the separated parts of the lens the capsules were removed by grasping them with a toothed forceps and forcibly
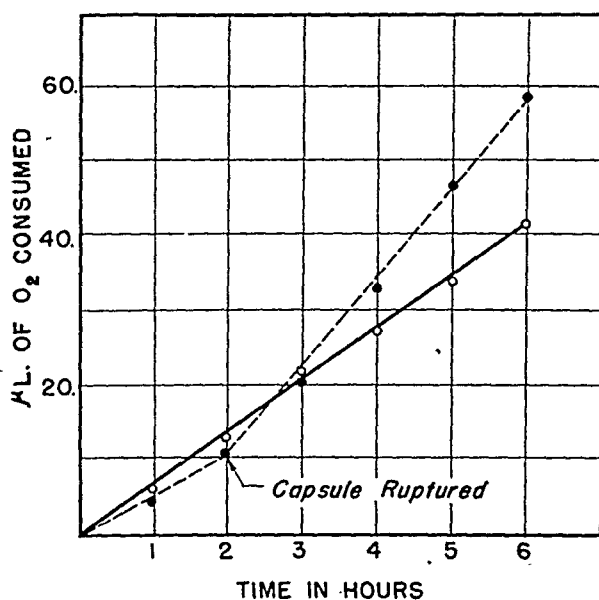
Fig. 1 (Ely). Respiration of whole rabbit lens and effect of rupturing the capsule.

stripping them from the lens. The inner surface of the capsule was scraped with a scalpel so that no epithelium or cortex would remain adherent. One or two capsules were placed in each Warburg flask.

The lenticular fibers were removed by teasing with a dissecting needle. These teased fibers with the epithelium adherent were weighed on a cover slip, and the fibers from each lens were placed in a separate Warburg flask. The fibers of one of the lenses were dried at 104°C. for 48 hours in order to determine the percentage of water. This percentage was assumed to be representative of the water content of the other lens fibers inasmuch as they came from normal animals

of approximately the same age. This assumption was checked by drying the entire contents of a flask at the conclusion of an experiment and subtracting the dried weight of the quantity of glucose buffer used from the dried weight of the entire flask's contents. Less than 2 percent difference was found in the two methods.

After the cortical fibers had been stripped from the lenses, each nucleus was placed in a separate Warburg flask.

Several precautions in the procedures

deviation of 0.034. The range of the QO_2 was 0.05 to 0.21, and accounts for the high standard deviation. Figure 1 depicts a typical effect on the QO_2 due to rupturing the capsule of the lens. This procedure was performed on a total of 15 lenses, and the increase in oxygen uptake which resulted from rupturing the capsule was always between two and four fold.

Table 3 shows a compilation and statistical analysis of the respiration of the separated parts of the lens. It is obvious that neither

TABLE 3

QO_2* OF VARIOUS SEGMENTS OF THE CRYSTALLINE LENS OF BEEF AND RABBITS

Kind of Lens	Temp. °C.	Nucleus		Capsule		Teased Cortex			
		Number	QO_2	Number	QO_2	No. of Lenses	QO_2		Standard† Deviation
							Range	Mean	
Rabbit	37.5	11	0	11	0	20	0.09 0.21	0.145	0.028
Beef	37.5	8	0	8	0	20	0.08 0.26	0.168	0.042

* QO_2 is defined as the microliters of O_2 consumed per mg. of dry tissue per hour.

† Standard deviation, $\sigma = \sqrt{\dfrac{\Sigma x^2}{N}}$

x = deviation of individual items from the mean.
N = total number of cases.

should be noted if reliable results are to be obtained:

1. For valid results in the measurement of the oxygen uptake of the intact lens, no rupture of the capsule should be noticeable at the end of the experiment.

2. In the study of the respiration of the capsules, an oxygen uptake will result occasionally because bits of cortical fibers and epithelium remain adherent if the capsules are not scraped.

3. Care must be taken to remove all cortex from the nucleus or a small amount of respiration will occur.

RESULTS

Table 2 is a compilation of the results obtained in the study of the respiration of the intact lens. The QO_2 of a young rabbit's lens was found to be 0.09, with a standard

the capsule nor the nucleus of the bovine and rabbit lenses respire, or that the oxygen uptake is so low that it cannot be measured by these methods. Teased cortical fibers have a mean QO_2 of 0.145 with a standard deviation of 0.028 for the rabbit lens and 0.169 with a standard deviation of 0.042 for the bovine lens.

DISCUSSION

Because the oxygen uptake of the intact lens increases when the capsule is ruptured, it is possible that the permeability of the capsule is an extremely important factor in regulating the rate of oxygen uptake. Several explanations are possible: (1) The rate of diffusion of oxygen through the capsule may be too slow for the maximal respiration. (2) The substrate may not diffuse through the capsule with sufficient rapidity. (3) The waste products such as CO_2 and lactic acid

may not diffuse out as rapidly as formed and thus retard the oxygen consumption. Further studies on the physical structure and physiologic function of the capsule should be made to clarify this phenomenon.

These studies indicate that the cortical fibers and adherent epithelium are the only part of the lens that respires. The respiration that results may be due to either the cortical fibers or the epithelium, or both. No method has been devised as yet to separate them in order to determine the role each plays in the total respiration. One is led to speculate that the epithelium plays the dominant role in the oxygen uptake, because if any epithelium remains adherent to the capsules that structure exhibits a measurable amount of oxygen consumption.

CONCLUSIONS

1. The mean QO_2 of an intact, young rabbit's lens is 0.09, with a standard deviation of 0.035.

2. Rupturing the capsule of the rabbit's lens increases the oxygen uptake 2 to 4 fold.

3. The capsules and nuclei of both bovine and rabbit lenses have a negligible respiration.

4. The QO_2 of teased cortical fibers of rabbit lenses is 0.145, with a standard deviation of 0.028.

5. The QO_2 of teased cortical fibers of bovine lenses is 0.168, with a standard deviation of 0.042.

University Hospitals.

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DISCUSSION

Dr. V. Everett Kinsey (Boston, Massachusetts): Mr. Chairman, Warburg has calculated that diffusion of oxygen becomes limiting in slices of tissue greater than 0.2 mm. in thickness. This shows that the diffusion of oxygen into the lens and carbon dioxide out of this structure are probably limiting factors in the oxygen uptake of the lens. One way of testing this would be for the speaker to plot as a scattergram the weights of the lenses against the oxygen uptake. I made such a plot mentally, as accurately as possible, in the time during which the slide was shown, and was rather surprised to find that the small lenses did not appear to have a greater oxygen uptake per gm. of tissue than did the larger ones. This lack of correlation between higher oxygen uptake and small lenses might be suggestive

evidence of the speaker's hypothesis that most of the oxygen uptake of the lens comes from the epithelium.

Dr. Ely: Field and his co-workers made such a scattergram. They were able to show that there is a decrease in oxygen consumption per gm. of wet weight with an increase in weight of the lens.

I have sufficient data now to show graphically the same thing, and am in preparation of laying out such a comparison. It is going to show with statistical significance, I am sure, if there is a decrease in oxygen consumption with an increase in age.

Such a result would be expected as the nucleus comprises an increasingly greater percent of lens weight as age increases, and the nucleus does not respire.

Dr. David G. Cogan (Boston, Massachu-

setts) : I judge it would be desirable to determine the respiration of the lens epithelium alone but it has been impractical to isolate it. Nevertheless, its volume and number of cells can be readily determined. It would be interesting, then, to calculate the QO_2 on the basis of the volume of the epithelium alone and, assuming that the entire respiration is carried on by the epithelium, to compare this with respiration of epithelial tissue elsewhere in the body.

DR. ELY: Such a procedure has occurred to me several times. In a similar approach, at the University of Wisconsin, Potter has been working on such a problem with Snyder. They actually studied the different parts of cells which had been separated by ultracentrifugation.

By such methods they were able to show that certain enzyme systems were connected with specific structures of the cell. It is quite possible that such a method of separation could be applied to the lens in order to separate the epithelial portion, that is, the nuclear portion, of the cells from the other tissue.

It is also quite possible, as suggested, to calculate the fraction that is represented by epithelium and on such a basis to calculate the QO_2 for the epithelial portion of the lens.

DR. ERNST SCHMERL (Toledo, Ohio): When I studied the respiration of the lens many years ago, I determined the weight of the lens capsule and considered the possibility that the whole oxygen consumption of the lens might be ascribable to the respiration of the epithelium of the capsule. In this case the respiration of the lens epithelium would be of the same magnitude as that of other epithelial tissues. Rupture of the capsule was found to increase the respiration of the lens.

DR. ELY: Yes, I read your papers and noted the same thing you have mentioned. The way that I circumvented having the epithelium on the capsule, as I pointed out, was by scraping the capsule. I did this because most of the nuclei clung to the cortical fibers. Thus, it became convenient, at least experimentally, to include the epithelium with the cortical fibers, inasmuch as there was no way of getting the epithelium and capsule intact.

FLICKER FUSION FREQUENCY IN AMBLYOPIA EX ANOPSIA*

PAUL W. MILES, M.D.

Saint Louis, Missouri

Amblyopia ex anopsia is characterized by a defect in visual acuity of one eye, beginning in infancy, often with strabismus. The amblyopia disappears upon occlusion of the dominant eye in children, but not readily in adults. Peripheral acuity and sensation remain normal in field and threshold studies. It is believed that the origin of the amblyopia is in the macular projection of the visual cortex, and that the lesion is of the nature of a suppression or a conditioned reflex.

Although visual acuity is defective, other visual sensations in the central retina appear to be normal.[1] This may limit the lesion more definitely to the cortical layers involved in form vision, preserving the more primitive levels, namely, those for light or brightness contrast, dark-adaptation thresholds, color thresholds, and the capacity of the eye to fixate and localize accurately small points of light on the fovea. Wald and Burian[1] suggested that these layers might be outside the cortex, since in monkeys only pattern vision is lost after cortex ablation.

Visual acuity tests, as performed in the office, test pattern vision. Visual field tests with small targets and good illumination are chiefly tests of pattern vision. When targets are made larger and less contrasting to the background, or if the illumination is reduced, a different sensation, brightness contrast, is being stimulated.

Experiments on the "central" retina in amblyopia may not be exactly central. Wald and Burian found that the amblyopic eye was slightly less capable of centering on a 1-degree target than the dominant eye, and that the threshold curves showed the effect of rod stimulation, although supposedly only

the rod-free area was being stimulated. Eccentric fixation is to be expected in an amblyopic eye. Anomalous correspondence is common. It is possible that a small target may stimulate rods because of ametropia or diffusion or reflection within the eye.[4] This is particularly likely in the dark-adapted eye, where cones are inhibited and rods sensitized.

It has been postulated that fixation is determined not by an anatomic fixed area in amblyopia, but by the visual acuity gradient present. According to Simon (quoted by Weymouth[2]), a normal eye will fixate as much as 2 degrees eccentrically when completely dark adapted. In dark adaptation, the central cones undergo suppression similar to that in amblyopia ex anopsia.

Against this evidence is the fact that introduction of disparity between the central and peripheral retina in experiments with aniseikonia have shown that a distortion of binocular space perception is produced. Retinal correspondence is a fixed and constant phenomenon. Studies of stereopsis and space distortion should be made in dark-adapted eyes.

Ludvigh[3] pointed out that patients with amblyopia ex anopsia first lose acuity, then light differential sensitivity. He proposed that when light differential sensitivity deteriorates, the condition becomes irreversible. However, reversibility is a relative phenomenon, practical under the age of 8 years, possible under the age of 20 years, but improbable over the age of 20 years. Apparently, the primitive visual sensations persist indefinitely.

Flicker fusion frequency is one of the latter. It is the frequency per second below which a flickering light appears to flash intermittently and above which it appears steady. It is a stable and repeatable phe-

nomenon, which can be more easily elicited in unskilled, unapt patients than can visual acuity or field studies.

Figure 1 illustrates flicker fusion. It is an electroretinogram copied from Granit,[5] with flickering stimulation shown below, which gradually decreases in frequency until subjectively (A) flicker begins, and until (B) the recording apparatus can follow. It is evident that if a second flash of light

tients with normal acuity and fields who had brain lesions.

Countless studies have been made of flicker fusion frequency since the time of Plateau.[9] Two accounts of flicker fusion frequency in amblyopia ex anopsia occur in the literature. Lohmann,[10] in 1908, reported that in a young woman, aged 23 years, with amblyopia ex anopsia, the central flicker fusion frequency in the amblyopic eye was
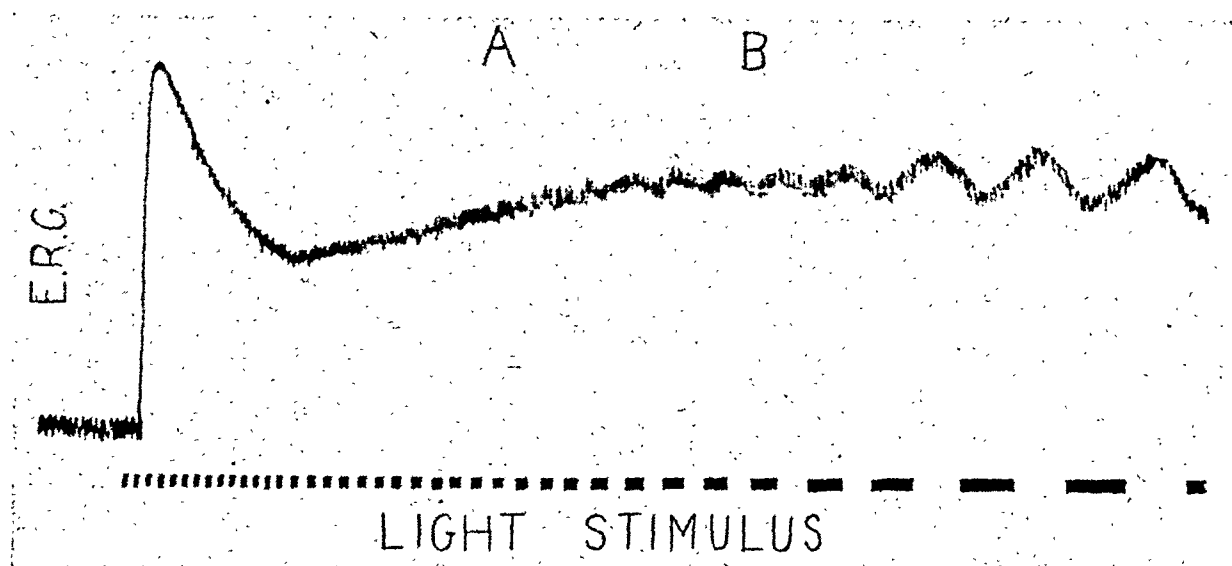
Fig. 1 (Miles). Electroretinogram (Granit) with stimulus of flickering light of decreasing frequency. Subjective flicker at (A) electrical response detected at (B).

occurs before the persisting visual sensation from the first is over, the second is not detected as separate.

It is the phenomenon of the movie screen. If the illumination gets a little too bright, or if the screen is viewed on the peripheral retina, or if the projector shutter is changed to decrease the duration of the flash, or if the flashes decrease in frequency, the movie screen flickers.

Flicker fusion frequency involves not only local rod and cone function, but is influenced by the interaction of various parts of the retina and optic pathway. From the rod-free area, it is low, due to greater visual image persistence. It is much higher from peripheral retina. Phillips,[6] Werner,[7] and Enzer[8] found decrease in flicker fusion frequency in pa-

46 per second, compared to 34 in the normal eye. Visual acuity was: O.D., 5/4; O.S., 5/25. Specifically his results were:

	Central	15°	30°	45° (peripheral retina)
O.D.	34	43	54	57
O.S.	46	43	43	42

Teraskeli[11] reported in 1934 that, in 21 out of 50 cases of amblyopia ex anopsia, the central flicker fusion frequency of the amblyopic eye was equal to that of the periphery 10 degrees out. She concluded that the fovea is lacking in the affected eye, leading to strabismus.

APPARATUS AND METHOD

The present study confirms these flicker fusion frequency findings, and introduces the use of an electronic flickering light

source for clinical studies. There are basic differences in this light source from those used previously. In the past, a rotating disc was used, sectors of which were cut out to permit a flash of light. The disc was motor driven, and the speed was determined by a galvanic speedometer. The moving shutter did not produce an instantaneous shut off and on, as does the electronic device. With the sector disc, the light phase was always directly proportional to the dark phase. With slow speeds, the light interval was longer,

SIZE OF TARGET
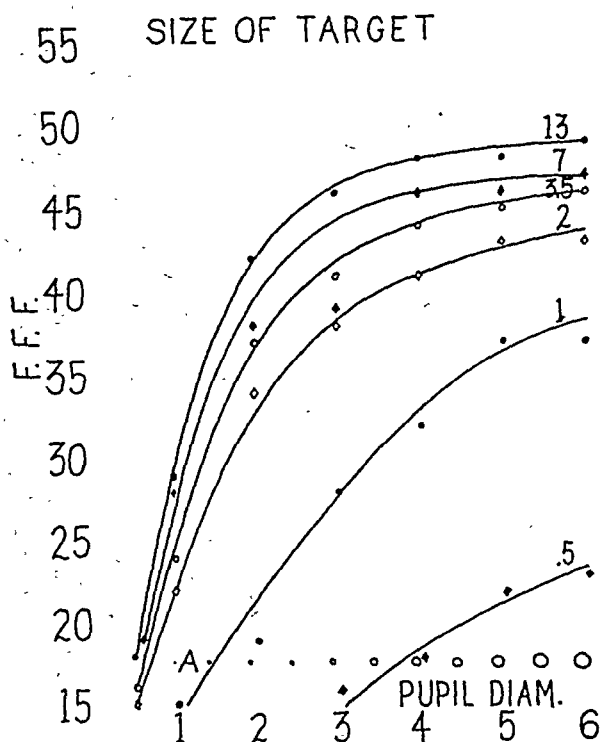
Fig. 2 (Miles). Flicker fusion frequency produced by targets 13, 7, 3.5, 2, 1, and 0.5 cm. in diameter. (A) represents the artificial pupil size.

and the stimulus was, therefore, stronger. The light interval in the electronic instrument used in the present work was 0.010 seconds regardless of the frequency.

This lamp was mounted like a headlight in a reflector. For experimental purposes, the 13-cm. protruding glass crystal was covered by typing paper, 4 cm. from the lamp. The target color was orange-white. The flicker frequency could be read directly from an illuminated dial at the top of the instrument.

This target subtended 8 arc degrees at the distance of one meter used, forming a retinal image of 2.25 mm. Figure 2 shows the results of experiments to determine the ideal size of target for experiments with flicker
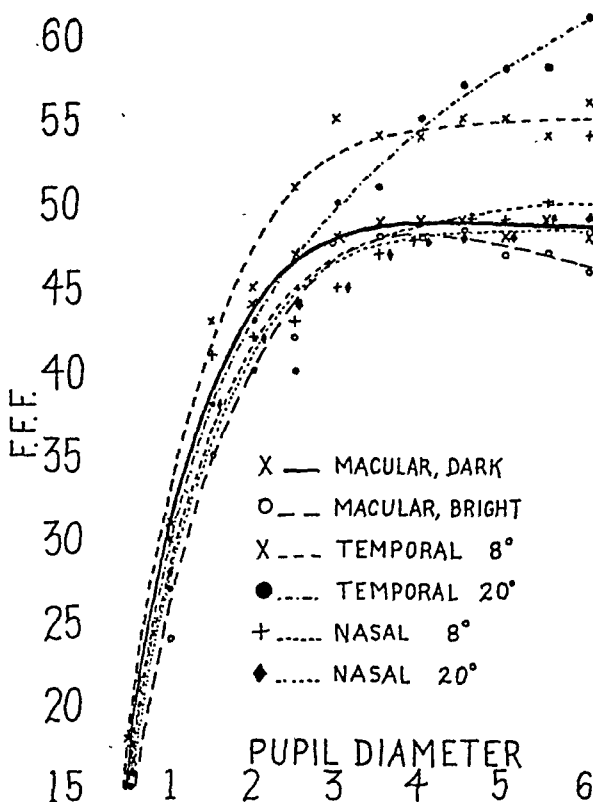
Fig. 3 (Miles). The "macular, dark" line represents the flicker fusion frequency taken with the artificial pupil stick with the room dark and the background dark. The "macular, bright" line is not greatly different, but was taken with the room bright and the background in contrast. The other lines represent the stimulus applied to the peripheral retina.

fusion frequency with this light source. The flicker fusion frequency of subject P. W. M. was taken with central fixation on various sized targets at one meter. Artificial pupils, illustrated at (A), varying in diameter from 0.5 to 6.0 mm., in a strip of brass countersunk to a keen precise edge and painted black, were held 3 mm. in front of the cornea, centered on the target. The marked effect on flicker fusion frequency of decrease in pupil size can easily be seen. Since the retinal image size was constant, this decrease was due to decrease in light intensity.

The flicker fusion frequency was highest, and the curve with pupil size was most precise with the largest diameter target.

The flicker fusion frequency of cones in-
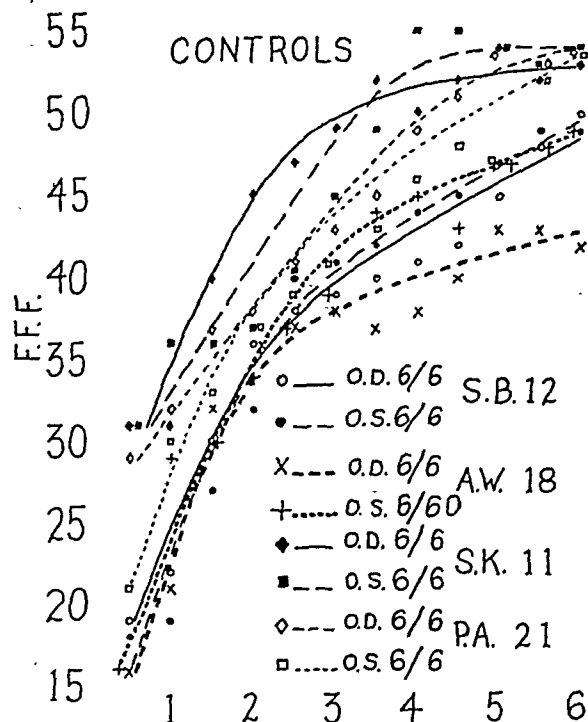
Fig. 4 (Miles). Flicker fusion frequency variation with artificial pupils in three normal individuals and one patient with amblyopia ex anopsia. Note that the flicker fusion frequency curves match in the paired eyes except in A.W., where the normal eye has a low central flicker fusion frequency and the amblyopic eye has a high central flicker fusion frequency.

creases slightly in light adaptation.[13] A more intense small light would be an advantage, but would vary with ametropia, if uncorrected, and would necessitate perfect fixation.

Figure 3 shows the results of experiments made to determine how important contrast and background is in tests of flicker fusion frequency and which areas of the peripheral retina should be selected for routine testing. The subject was P. W. M., and the full 13 cm. target was used. The heavy solid line was taken with the artificial pupil stick as described above, with the room darkened so that the gray walls reflected about 0.5 foot-candles. A black tangent screen was placed behind the instrument.

The curve "o" with wide dashes represents the same experiment except that the room was illuminated to reflect about 25 foot-candles, and contrasting objects were placed behind the instrument. There is slight difference in the curve toward a lower flicker fusion frequency. There was little difference on stimulation of the nasal retina out to 20
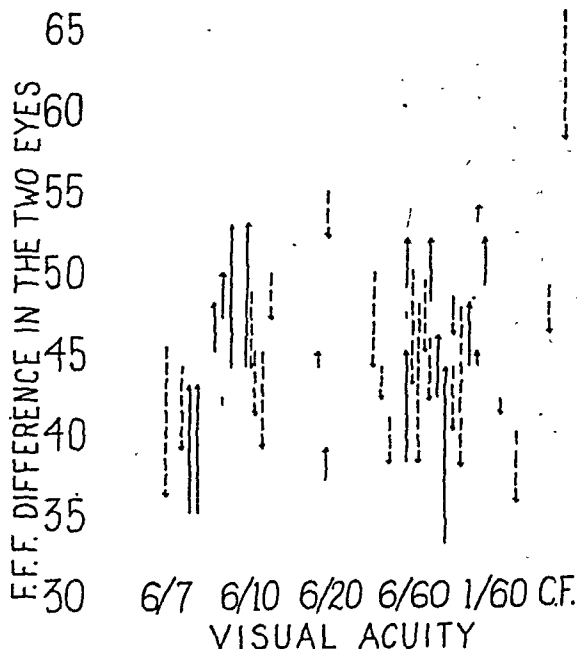
Fig. 5 (Miles). Flicker fusion frequency variation in 43 patients with amblyopia ex anopsia, plotted against the visual acuity. The tail of each arrow represents central flicker fusion frequency of the amblyopic eye, and the head that of the normal. Where that of the amblyopic eye exceeds that of the normal, the arrow is a broken line, and the point is down.

degrees, but a difference of from 6 to 12 flashes per second occurred on the temporal retina. Therefore, the temporal retina was chosen for routine testing.

The tests were carried out on patients as follows: The eye not under test was covered with gauze and black celluloid, and the patient asked to look at the center of the target. The flickering light was speeded up until the patient reported "now," as the light appeared steady. Then the speed of the steady light was decreased until the patient reported flicker. This always proved easier for patients. The average of the difference in the

two readings was recorded as the "precision" of that patient. Usually several determinations were taken. This "precision" was from 1 to 2 flashes per second in most individuals.

The values of flicker fusion frequency for various sized artificial pupils resembles Sloan's[12] curve for light thresholds measured with various sized pupils, especially curve .—.— in Figure 3.

Figure 4 shows the variation of flicker fusion frequency with artificial pupils in three normal individuals and one patient with amblyopia ex anopsia. Note that the flicker fusion frequency curves match in the paired eyes except in A. W., where the normal eye has a low central flicker fusion frequency, and the amblyopic eye has a higher central flicker fusion frequency. The high precision obtained in untrained subjects can be seen on the chart.

Opacities of the media of the eye do not necessarily decrease the flicker fusion frequency. In fact, diffusion may scatter the light to peripheral retina, increasing the flicker fusion frequency. A colorless Maddox rod before an eye reduces acuity to zero, but does not decrease the flicker fusion frequency. On the contrary, one patient, P. G., aged 16 years, had a visual acuity of 6/4 in one eye, a 6-mm. pupil, and glaucoma. Although normal flicker fusion frequency is central 45 and temporal 50, this boy had central 36 and temporal 44.

RESULTS

Forty-four patients with amblyopia ex anopsia were tested. Pupils in each pair of eyes were equal in size. Only 5 patients had pupils under 3 mm. Individual variation proved greater than apparent differences in this series due to pupil size. In each case, the flicker fusion frequency of the amblyopic eye was compared to a perfect control, its normal fellow.

Figure 5 represents the flicker fusion frequency of 43 patients with amblyopia ex anopsia plotted against acuity of the amblyopic eye. The tail of each arrow represents the central flicker fusion frequency of the amblyopic, and the head that of the normal eye. If the flicker fusion frequency of the amblyopic eye exceeded that of the normal, the arrow is a broken line, and the point is down. If the flicker fusion frequency of the amblyopic eye was less, the arrow is solid and points up. The amblyopic flicker fusion
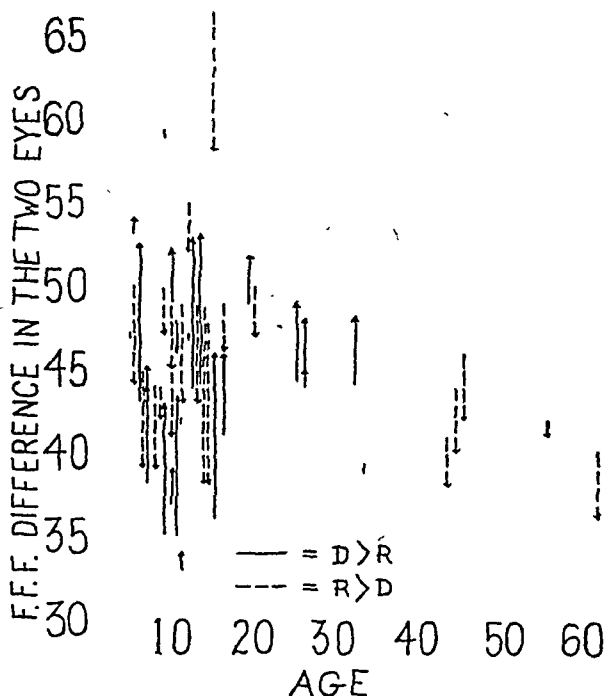
Fig. 6 (Miles). The same data as in Figure 5 plotted against the patient's age.

frequency exceeds the normal slightly, 21 to 18, 5 equal. Most patients had poor acuity, but there is no evident variation in flicker fusion frequency with visual acuity.

Figure 6 shows the same data plotted against the patient's age. There is a tendency for the central flicker fusion frequency to decrease with age, possibly due to smaller pupils. Four of the patients had tropia, one had definite abnormal retinal correspondence, but no significant change from the average is evident.

The average flicker fusion frequency of the normal eye with central fixation was 45.1, of 8-degree temporal retina, 50.4; of the amblyopic eye with central fixation it was 46.4, of 8-degree temporal retina, 50.2. The average increase on shifting stimulation

from central to temporal retina was 5.3 in the normal eye, 3.8 in the amblyopic.

SUMMARY AND CONCLUSIONS

Flicker fusion frequency was determined in 44 patients with amblyopia ex anopsia. The central area of the amblyopic eye performed like the peripheral retina—that is, had a higher flicker fusion frequency than normal. This suggests suppression of central cones.

Normal flicker fusion frequency, with the equipment described in this paper, is 45 flashes per second centrally, and 50 on 8-degree temporal retina.

Defects in central flicker fusion frequency may occur in eyes with 6/4 central acuity, but it may be normal in eyes with 1/60 or less acuity. Like light and color threshold and contrast, it is considered a primitive sensation, and is received in different centers of the cortex from those involved in visual acuity or pattern vision.

The flicker fusion frequency is easily determined in patients who are unapt in other subjective tests. This test may prove an aid in determining whether certain apparently normal eyes with normal acuity are defective. It may prove useful in studying the function of the retina in patients with opacities of the media. Flicker fusion frequency varies over various parts of the retina, but, unlike field studies, higher sensitivity is elicited in the periphery.

640 South Kingshighway (10).

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DISCUSSION

DR. DAVID MAHER (Winnetka, Illinois): Mr. Chairman, there is a great deal of work done in Dr. Miles' review of the flicker fusion frequency. There are a great many questions I would like to ask because I have had some experience with flicker fusion frequency. First as to the type of light or bulb that was used. We have found that by using a neon bulb, a bulb with neon gas in it, we had a complete on-and-off effect so that we did away entirely with the question of two discs rotating toward each other while there was a gradual loss of illumination as the discs passed each other.

Secondly, he makes the statement that some of the more fundamental conditions of

which the eye has attributes, such as light sense and color sense, are perhaps regarded as better methods of testing lesions in the eye than the visual acuity.

We have been taught and we have found that in amblyopia ex anopsia where there is a loss in visual acuity, there is also a loss of light stimuli and certainly a very definite loss in color stimuli. I would like a little more information on those things.

DR. MILES (closing): The type of bulb that is used in this machine made by General Radio is a gas discharge tube. The light and dark phases are instantaneous cut-offs. I have not had experience with the circular disc method and that is why I stated that these data were definitely not to be correlated with data taken previously.

The light sense and color threshold data were taken by Burian and Wald, published in the AMERICAN JOURNAL OF OPHTHALMOLOGY as noted in my bibliography. They and Lohmann represent the authorities that I have quoted. I have not done work on that subject myself. The biggest question is, in these experiments, whether the amblyopic eye was capable of holding exactly central fixation. A man named Simon in Germany claims that the dark-adapted eye is capable of fixing only on the retinal element which has the highest visual acuity under dark-adapted conditions.

In dark adaptation, the cones and the fovea are inhibited and the rods and the periphery are sensitized so that if fixation depends on the visual acuity gradient, eccentric fixation is to be expected in the amblyopic eye. In any dark-adapted eye, fixation will be eccentric and not centrifoveal. That may have been a source of error in the past on this particular type of patient because we all know that these patients are inclined to anomalous correspondence and are inclined to use extrafoveal fixation. As Burian and Wald pointed out, their experiments on light and color discrimination in amblyopia ex anopsia showed the effect of some rod vision and not just an absence of cone vision, so it is perfectly possible that eccentric fixation could explain the findings in those experiments.

I haven't tried to repeat those experiments myself, so actually all I can report is what I have given you here.

THE ANATOMIC BASIS FOR CERTAIN REFLEX
AND AUTOMATIC EYE MOVEMENTS*

JOHN WOODWORTH HENDERSON,† M.D.

Ann Arbor, Michigan

With progressive phylogenetic development, the dominant level of control of eye movement ascends from lower to higher brain centers and finally to the cerebral cortex. One of the more primitive mechanisms governing ocular movement is that of the vestibular system. The interaction between the vestibular nuclei and the nuclear masses serving the extraocular muscles by way of the median longitudinal fasciculi is present in all vertebrates which have eyes and ears, and extends back in the scale to certain of the Cyclostomes.

As cerebral cortex develops, it assumes a controlling position over the more primitive vestibulo-ocular reflexes. Cortical inhibition has been shown to occur in the rabbit utilizing rotational and postrotational nystagmus as an indicator (Henderson, 1947). In this series of experiments definite inhibition of postrotational nystagmus was produced by allowing ocular function during rotation, probably acting by means of cortical participation in the ocular movement. Such inhibition can conceivably be either voluntary or automatic depending upon the needs of the organism at the moment.

Midbrain dominance over extraocular movement reaches its highest expression in birds, where "consciousness" is said to lie at the mesencephalic level. Here all the sensory stimuli from the body, as well as visual, vestibular, and auditory impulses, are channelled into the tectum of the midbrain, and resultant responses are carried out by way of the tectospinal and tectotegmentospinal pathways. Since the "brain" of the bird above the level of the midbrain consists chiefly of highly developed basal ganglia, control from these higher centers is rela-

tively nonspecific. In mammals, this pattern is reflected by the presence of direct fibers from the retinas which reach the tectum by way of the optic nerves without the interposition of a cortical arc. This makes possible subcortical ocular reflex movements.

The midbrain pattern for ocular movement has been established anatomically in mammals by various workers. This is related to the arrangement of the incoming direct optic-nerve fibers on the one hand, and the nuclear arrangement of the oculomotor and trochlear nerves on the other.

The nuclear arrangement is such that the impulse for elevating the eyes and raising the upper lids arises in the rostral portions of the oculomotor nuclei. The stimulus for turning the eyes downward takes origin in the more caudal portions (the neighboring trochlear nuclei also taking part).

More recent studies (Bender and Weinstein, 1943, Szentagothai, 1942) show a partial reversal of the previously accepted anatomic pattern. These latter investigations have been based upon direct electrical stimulation using a Horsley-Clark type of apparatus where presumably the results could be produced by effects gained through the median longitudinal fasciculi, in which the nuclear masses are embedded. The position of the eyes after destruction of the individual nuclei was not mentioned by these workers.

Experimental studies of the projection of the retinal quadrants on the optic tectum in the rabbit (Brouwer and Zeeman, 1926, Brouwer, 1927), and to a lesser extent in the monkey, have indicated that the inferior quadrants, which are stimulated from the superior visual field, are projected by the optic tracts on the medial and rostral portions of the superior colliculi, and that the superior quadrants, which are stimulated from the inferior visual field, are projected

on the lateral and caudal portions of the optic tectum.

A comparable pattern of projection on this midbrain region was obtained in the rat by Lashley (1934). This pattern would confirm the nuclear localization of the earlier anatomic workers. It acts by direct oculomesencephalic reflex connections in lower mammals without the interposition of a cortical arc. Such direct fiber connections are fewer in number in primates, but it is probable that the pattern is much the same in the monkey. These connections seem to be inoperative or very greatly reduced in man. Nevertheless, their presence and arrangement in lower mammalian forms would serve to confirm the midbrain nuclear arrangement of the earlier workers.

In primates, where the direct oculomidbrain reflex connections are much less important, a cortical arc assumes the major responsibility for reflex ocular movement. This is in disagreement with the older view that many reflex ocular movements in primates have a subcortical origin. Thus automatic eye movements at a cortical level appear to supersede and control the function of both the vestibular and midbrain arcs. Such movements are based upon visual stimuli which reach Area 17 (the striate cortex) by way of the visual pathways.

Experimental work on the monkey (Crosby and Henderson, 1948) shows that a distinct pattern of cortical localization exists in both Area 17 and in Area 19 (the parastriate cortex) which can be related anatomically and functionally to the more primitive midbrain arrangement. The experiments were performed using a very light ether anesthesia and stimulating the brain areas concerned with a faradic current. The directions of ocular movement were recorded in each instance.

Stimulation of the portion of the striate cortex above the calcarine fissure (F, fig. 1) produced a combined conjugate movement down and to the opposite side; of that below the fissure (E, fig. 1), a conjugate

movement up and to the opposite side. This result was that expected from the known cortical pattern of termination of the visual pathway, and confirmed the work of Walker and Weaver (1940).

Area 19 (the parastriate cortex) was shown to have a definite pattern of ocular movement in response to stimulation. Upper Area 19 (A, fig. 1) produced upward conjugate movement, upper-intermediate Area 19 (A', fig. 1) gave movements obliquely upward and toward the opposite side, and middle Area 19 (B, fig. 1) elicited conjugate deviation horizontally toward the opposite side. Stimulation of lower-intermediate Area 19 (C', fig. 1) produced a conjugate deviation obliquely downward and toward the opposite side, and lower Area 19 (C, fig. 1) gave conjugate downward movement.

It must be emphasized that such results required a level of ether anesthesia just below the point where voluntary ocular movement would occur and where the blink reflex to stimulation of the cilia was still present. Deeper anesthesia abolished the upward movements first, then the downward, leaving finally only the horizontal conjugate deviation. Sodium pentobarbital anesthesia was found to carry the monkeys to too deep a level to elicit satisfactory responses. This difference in level of anesthesia may explain the classical view that Area 19 produces only conjugate deviation of the eyes to the opposite side such as was described by Foerster (1931 and elsewhere) in man.

The fiber pathways which link Areas 17 and 19 to the tectum of the midbrain have been termed the internal corticotectal tracts (Crosby and Henderson, 1948). Those from the striate area are designated the occipital division of the internal corticotectal tract, and are further subdivided into dorsal and ventral divisions on the basis of their origin from either above or below the calcarine fissure.

These tracts sweep forward in a layer just outside the visual radiations and parallel them as far forward as the pulvinar of the
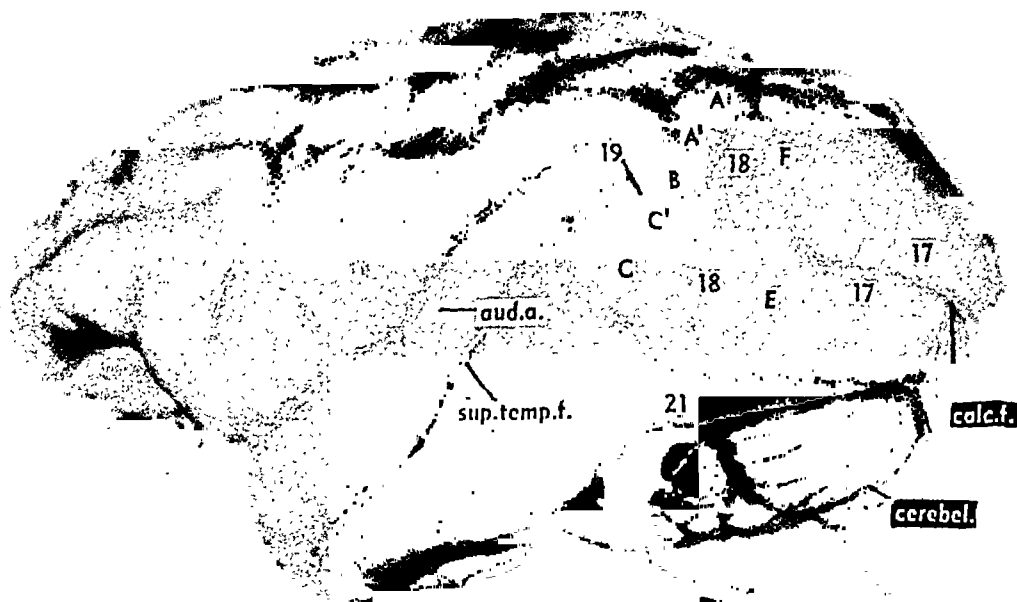
Fig. 1 (Henderson). The left side of the brain of a Macaca mulatta as shown in a photograph (×1.8). Areas 17, 18, 19, and 21 are designated. On Areas 17 and 19 the various points from which eye movements were elicited are indicated by letters (see text). (Reproduced by permission of E. C. Crosby and J. W. Henderson: J. Comp. Neurol., 88:53-92, 1948.)

ABBREVIATIONS FOR FIGURES

aud. a., auditory area.
calc. f., calcarine fissure.
caud. n., caudate nucleus.
cer. ped., cerebral peduncle.
cerebel., cerebellum.
corp. cal., corpus callosum.
cort. teg. tr., corticotegmental tract.
cort. tect. tr., aud. div., corticotectal tract, auditory division.
ext. cort. tect. tr., external corticotectal tract.
F, fornix.
fim., fimbria.
hip., hippocampus.
hip. g., hippocampal gyrus.
int. cort. tect. tr., oc. div. dors. p., internal corticotectal tract, occipital division, dorsal part.
int. cort. tect. tr., oc. div. vent. p., internal corticotectal tract, occipital division, ventral part.
int. cort. tect. tr., preoc. div. dors. p., internal corticotectal tract, preoccipital division, dorsal part.
int. cort. tect. tr., preoc. div., vent. p., internal

corticotectal tract, preoccipital division, ventral part.
m. l. f., medial longitudinal fasciculus.
med. lem., medial lemniscus.
med. tect. sp. tr., medial tectospinal tract.
n. III, oculomotor nucleus.
op. tr., optic tract.
ped. inf. col., peduncle of inferior colliculus.
pul., pulvinar.
str. med. prof., deep medullary stratum.
str. term., stria terminalis.
sub. nig., substantia nigra.
sup. cerebel. dec., decussation of superior cerebellar peduncle.
sup. temp. f., superior temporal fissure.
tect. oc. tr., tecto-oculomotor tract.
tect. pont. tr., tectopontine tract.
tect. teg. tr., tectotegmental tract.
vis. rad., visual radiations.
x, termination of occipital division of internal corticotectal tract in superior colliculus.
y, termination of preoccipital division of internal corticotectal tract in superior colliculus.

thalamus. Here they turn medially across the internal capsule, through the pulvinar, and

terminate in the tectum of the midbrain (fig. 2). Those from the upper calcarine
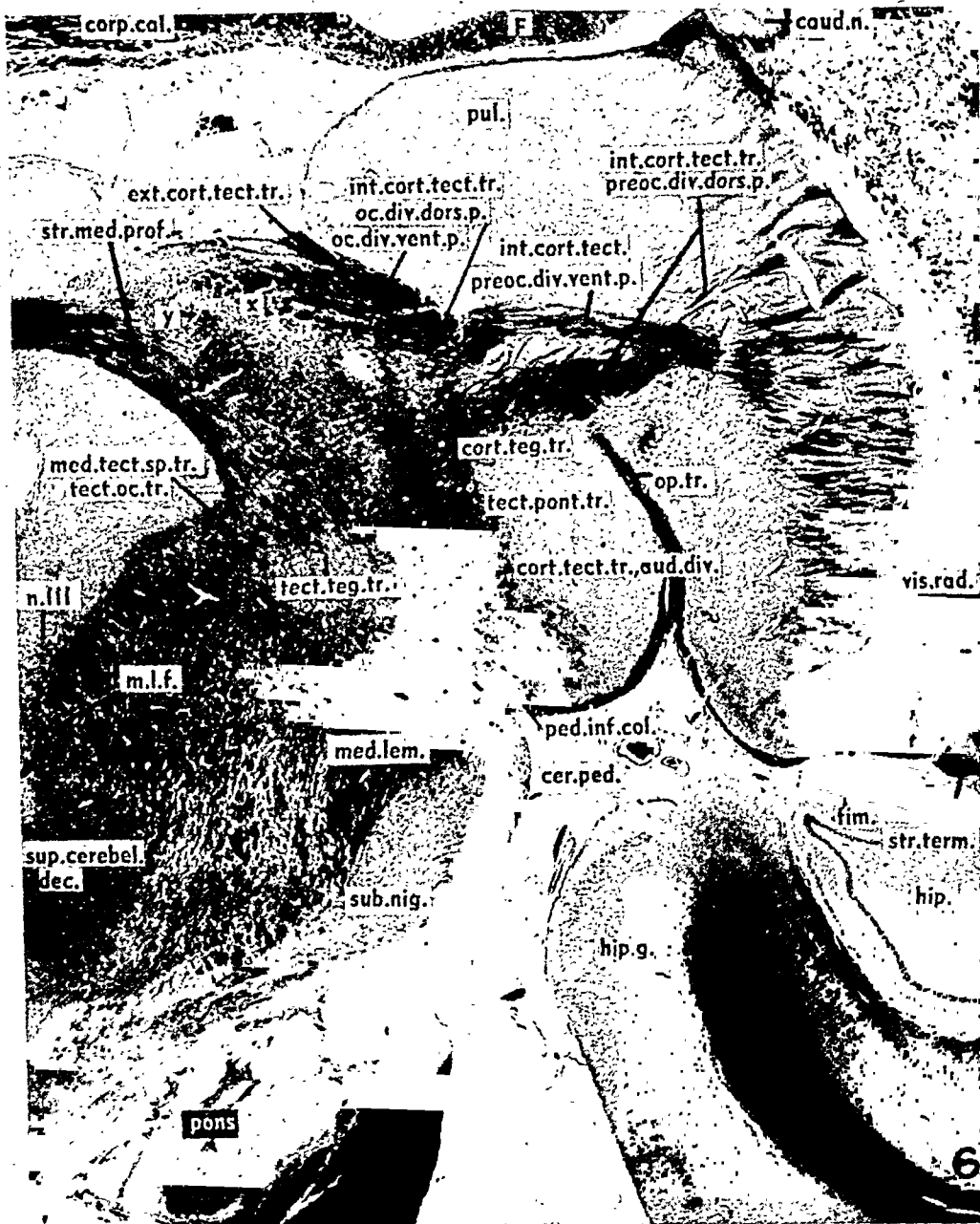
Fig. 2 (Henderson). A photomicrograph of a section near the rostral end of the superior colliculus from a transverse series of a Macaca mulatta brain stained by the Weil technique (×4). For a more comprehensive series see Crosby and Henderson, 1948. (Reproduced by permission of E. C. Crosby and J. W. Henderson: J. Comp. Neurol., 88:53-92, 1948.)

See Fig. 1 for explanation of abbreviations.

area (dorsal division) reach the caudal portions of the tectum, and those from the lower calcarine area terminate in the more rostral tectum of the midbrain. Thus the dorsal division relates inferior visual field, superior calcarine area, and caudal tectum to the more caudal portion of the oculomotor complex. Conversely, the ventral division relates superior visual field, inferior calcarine area,

and rostral tectum to the more rostral portion of the oculomotor nucleus. The expected responses in reflex ocular deviation to stimuli lying in the visual field can therefore be related anatomically.

The internal corticotectal tracts from Area 19 have been designated the preoccipital division, which likewise is divided into dorsal and ventral parts based on origin either from

upper or lower parastriate cortex (fig. 2). These fibers course forward to pulvinar levels along with the occipital division in the same layer just outside the visual radiations. The dorsal portion can be traced to the rostral tectum, while the ventral part reaches the more caudal tectum. Thus an interrelationship between upper Area 19 and rostral oculomotor nucleus can be seen, and, conversely, between lower Area 19 and caudal oculomotor nucleus.

The pathways described were traced both in normal anatomic preparations and by experimental degeneration. It has previously been noted (Kronfeld, 1929) that they follow the visual radiations forward, but the fact that cortical localization can be related to the anatomic pattern of arrangement of the extraocular muscle nuclei has, to the best of our knowledge, not been heretofore noted.

It is interesting that the termination of such fiber tracts fails to confirm the more recent work on the arrangement of the oculomotor nuclear complex. The parallel course of the tecto-oculomotor fibers which carry the impulses into the various portions of the oculomotor nucleus speaks against any reversal of pattern within the midbrain itself.

The fact that the pattern described for Area 19 is inverted from that of Area 17 can be explained by the presence of short association bundles which can be seen to connect lower Area 17 with upper Area 19, and vice versa.

Both the occipital and preoccipital divisions of the internal corticotectal system were seen to give off fibers which turned into the tegmentum of the midbrain without reaching the tectal areas (cort. teg. tr., fig. 2). These lay midway between the dorsal and ventral portions of both divisions in their course forward from the occipital lobe and presumably relate the areas for horizontal movement with the abducens complex by means of tegmental pathways. They could be traced with certainty only as far as the inferior collicular level.

Judged by the relatively great number of corticotectal and corticotegmental pathways, a large percentage of normal eye movements can be explained as visual automatisms—cortical, yet subconscious in a voluntary sense. This would include the movements subserving fixation, since it is well known that injury to Area 19 interferes with the holding of fixed gaze.

McCulloch (1944) has shown that cortical conduction occurs from Area 8 of the frontal cortex to the parastriate area, but not in the opposite direction. This places the cortical centers for automatic eye movements under the control of the voluntary motor centers, with Area 8 able either to utilize the direct corticobulbar pathway to the brain stem, or to exert a modifying effect upon the cortical ocular automatisms by way of the parastriate area. It should be stressed that higher centers utilize previously laid-down mechanisms for the control of ocular movement. In each instance, the more primitive pattern can be recognized, but is made use of by more recent phylogenetic brain centers.

It should be noted that there is a difference in level between the internal corticotectal fibers entering the tectum of the midbrain and the corticobulbar fibers which lie just above the cerebral peduncles. Since the fibers from the occipital lobe are more superficial in the colliculus, pressure downward from above should affect the reflex ocular movements much earlier than those which have a voluntary origin from Area 8 of the frontal lobe. Thus there should be a difference noted between command movements of the eyes and following movements in such an instance.

University Hospital.

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DISCUSSION

DR. DAVID G. COGAN (Boston, Massachusetts): I would like to ask two specific questions and I hope they weren't covered in the paper. I was so interested in some of the parts I may have lapsed in the others.

Did you mention what the threshold was in Areas 17 and 19? It seems to me there has been some conflict between what Walker and Weaver and what others have found in the relative thresholds in 17 versus 18 and 19.

Also, it seems to be anomalous that there should be such a reversal of vertical representation in 19 and 17. You say that that is executed by means of intracortical association pathways but it seems to me curious in the economy of the nervous system that such a reversal should take place.

DR. P. J. LEINFELDER (Iowa City, Iowa): I want to congratulate Dr. Henderson on a very difficult piece of work. I am sure he has labored much more extensively than you might realize from seeing the few slides that he has shown.

The importance of his contribution, I think, should not be estimated in terms of its applicability to any one lesion of the nervous system, but rather in his confirmation of the intimate reflex association between vision, binocular vision, and the ocular motor system.

He has demonstrated the pathways that carry the impulses for adequate coördination of ocular movements and fixation.

DR. PIERRE DANIS (Brussels, Belgium): I think the localization of the muscles he referred to is still open to question because I think you base your general opinion on the work of Brouwer but you have other workers who gave a reverse pattern. Bach and von Biervliet gave a reverse pattern, too.

DR. HENDERSON (closing): I would like to answer Dr. Cogan's questions first while I have them in my mind more specifically. The difference in threshold actually does exist. It is not something to be measured in any specific terms. If we had the current and stimulation high enough, we would get movement which we attributed to Area 17 by a spread from Area 19, which was of that type. Also the work of Walker and Weaver was performed under a light anesthesia, as I recall, which again brings the question of anesthesia into it.

The problem of the difference between Areas 17 and 19 bothered me, too. The pathways I think are there all right. There is no question about the association pathways being there but why two different areas so closely related should have inverse correlation with the midbrain arrangement I do not know.

However, the fact that the stimulus which comes back and influences automatic movements comes from Areas 8 to 18 and then into 19 would indicate that perhaps 19 is more related to the voluntary centers while 17 is related to the visual receptive pattern. We know that there are the two different sets of pathways that run forward into the midbrain; this may have some bearing on the reversal of pattern.

As Dr. Danis has said, there has been an argument about the nuclear localization all along. This includes the work of Brouwer, of Bernheimer, of Starr, and several others, all of whom to a greater or lesser extent destroyed individual muscles and looked for individual nuclear degeneration. That, to the anatomist, is incontrovertible. To the physiologist, perhaps, it is not. It has also raised the question in my mind, which may be just "woolgathering," as to whether the inverse difference between these physiologic and anatomic patterns is going to make us change our conception of what is going on.

Is the primary thing that is happening the contraction or is the primary thing the inhibition? Perhaps that might have some bearing on the ocular movements. I know there isn't a good way of reconciling the two views but we are hoping that further work will help in bringing the two views closer together.

COMPRESSION TESTS ON AQUEOUS VEINS OF GLAUCOMATOUS EYES*

APPLICATION OF HYDRODYNAMIC PRINCIPLES TO THE PROBLEM OF INTRAOCULAR-FLUID ELIMINATION

K. W. ASCHER,[†] M.D., AND W. M. SPURGEON,[‡] PH.D.

Cincinnati, Ohio

Although nothing similar to the diagnostic clues obtained in glaucoma by the use of the ophthalmoscope, perimeter, and tonometer can be pointed to in the field of gonioscopy and biomicroscopy, sufficient evidence has accumulated to permit the hope that eventually the aqueous veins and their roots deep inside the scleral tissue will become significant for the understanding, if not also for the early diagnosis, of glaucoma.

Since intraocular fluid can be seen streaming in the biomicroscopically visible aqueous veins,[1] we are allowed to approach the glaucoma problem from a new viewpoint.[3-5] The work of recent years[2, 6-12] has added confirmation to our assumption that the intraocular-fluid elimination can be studied biomicroscopically, and increasing attention is being given to the aqueous veins.[13-20]

While different new roads may lead to a more lucid interpretation of the inexhaustible glaucoma problem, up to this time pertinent information has been made available in three directions: Gartner[6] initiated photographic recording of the influence on aqueous veins of miotics, a method which, in the future, may reveal conclusive evidence of pharmacologic effects on glaucomatous eyes.

Secondly, the fundamental compression test of the recipient vessel of aqueous veins (reference 1, p. 36; references 3, 4, and 5; reference 11, p. 78f.) revealed differences in the results obtained on glaucomatous eyes as compared to those obtained on eyes with normal intraocular pressure.

Thirdly, the increment-pressure test, performed on the cornea and observed on aqueous veins or better on recipient vessels, promised further differentiation in the response of glaucomatous eyes and eyes of normal pressure.

In this paper, the effect of miotics and of other drugs on the aqueous veins will not be discussed; this does not mean that previous investigations[3, 21] have answered sufficiently all pertinent questions. We shall restrict our discussion to the second and third topics, the compression test on the recipient vessel, and the increment-pressure test on the cornea.

COMPRESSION TEST ON THE RECIPIENT VESSEL

After compression of the recipient vessel of an aqueous vein either one of the following phenomena will be observed: clear fluid may expel the blood from the blocked area or, in other aqueous veins, all clear fluid may become expelled by blood. The first phenomenon was formerly called—for purely descriptive purposes—the glass-rod phenomenon (reference 1, p. 36); this name was chosen because of the similarity of the vessel filled by clear fluid to a glass rod. The opposite effect, entrance of blood into the blocked vessel section, was called the negative glass-rod phenomenon.

These terms, although accepted,[2, 11, 16, 20] and in most instances well understood, are not clear enough to exclude occasional misunderstandings. Therefore, a more unequivocal expression will be substituted. Instead of "positive glass-rod phenomenon" we shall use the expression "aqueous-influx phenomenon," and the term "negative glass-rod

phenomenon" will be replaced by "blood-influx phenomenon."

Both the aqueous-influx and the blood-influx phenomena were shown[3-5, 11] to be due to pressure differences which prevail between the two fluids running in the same vessel parallel to each other and to the vessel wall, namely aqueous humor and blood.

To De Vries's thorough and scholarly monograph we owe the first photographic recording of the blood-influx phenomenon. The response to the compression test is characteristic for each individual aqueous vein; that is, the result is the same when the test is repeated after months and years. Only under pathologic conditions, the result of the compression test, and even the appearance of the undisturbed aqueous vein, may change. Hyperemia may temporarily conceal the clear stream in an aqueous vein; the latter will reappear again when the eye assumes its previous appearance.

It has been found[3-5, 11] that the aqueous-influx phenomenon does not appear in glaucomatous eyes as long as the intraocular pressure remains elevated. This, however, is not a quality restricted to glaucomatous eyes; the blood-influx phenomenon occurs as well in eyes with normal intraocular pressure but, in glaucomatous eyes, it is the regular response of an aqueous vein subjected to the compression test on its recipient vessel.

In only one eye out of the series studied by De Vries[11] an aqueous-influx phenomenon was found in spite of the presence of glaucoma; this eye, however, was observed during a period of decrease of intraocular pressure. This is a confirmation of previous observations which revealed that in eyes suffering from primary compensated glaucoma, aqueous veins fail to show the aqueous-influx phenomenon; after successful surgery, or after response to miotics, the same aqueous vein which showed a blood-influx phenomenon, may show an aqueous-influx phenomenon. In patients suffering from unilateral glaucoma, the fellow eye with normal in-traocular pressure may show an aqueous-influx phenomenon while a symmetrically located aqueous vein in the glaucomatous eye will show the blood-influx phenomenon.[3, 4]

With an increase of the intraocular pressure, a longer or wider stream of clear fluid might be expected in the aqueous veins of glaucomatous eyes, provided the chamber angle is open.[22] It has been found, however, that the clear fluid in aqueous veins of glaucomatous eyes and in their recipient vessels does not extend farther nor expand wider than in eyes with normal intraocular pressure. This fact and the absence of the aqueous-influx phenomenon on glaucomatous eyes prove that the aqueous flow in the aqueous veins of glaucomatous eyes is less vigorous than in eyes with normal intraocular pressure. Together, these facts suggest the presence of an obstacle to the intraocular-fluid elimination, located somewhere between the anterior chamber and the biomicroscopically visible aqueous veins.

INCREMENT-PRESSURE TEST ON GLAUCOMATOUS EYES

Both Goldmann[9] and De Vries[11] extended, independently from each other, an observation published by one of us, namely that pressure applied externally to the eyeball but not to an aqueous vein may increase the flow of clear fluid in aqueous veins and in recipient vessels (reference 23, p. 1197).

Applying a dynamometer to the lower lid, De Vries observed regularly an increase of flow in the aqueous veins. Far from the site of an aqueous vein, he pressed a dynamometer onto the temporal extremity of the lower lid while a nasally located aqueous vein was watched biomicroscopically. When a dynamometer pressure of 30 gm. was exerted upon the lower lid, the clear stream in the aqueous vein, far from the compressed area, became faster and, inside the aqueous vein, the clear fluid content increased and the blood content decreased. Discontinuation of the dynamometer pressure was immediately followed by mingling of the aqueous

and sanguineous vessel content so that an undivided stream of diluted blood became visible. After a few seconds, however, the original distribution of blood and aqueous humor reappeared as it was seen prior to the compression.

This approach has been carried further by Goldmann.[9] He exerted graduated pressures against the center of the cornea by means of a spring balance, watching until an aqueous vein under biomicroscopical observation showed visible dilatation of its clear content. The anesthetic used for this examination was not mentioned, but it is known[21] that all drugs instilled into the conjunctival sac alter the appearance of the aqueous veins. Goldmann observed a widening of the clear stream in aqueous veins when a 5- to 12-gm. increment of pressure was exerted upon the cornea. The average of 8 gm. additional pressure corresponds, according to Goldmann's calculation, to an intraocular pressure increase of 10.4 mm. Hg.

Goldmann believes that the actual pressure difference between anterior chamber and anterior ciliary veins in the normal human eye is one half to one fourth of the value obtained with his increment-pressure method. For the pressure difference between chamber and ciliary veins, he uses the expression "outflow pressure"; for the increment-pressure values obtained by observation of aqueous veins, he proposes the term "scheinbarer Abflussdruck" which means "apparent outflow pressure."

Goldmann found increased values of "apparent outflow pressure" in eyes suffering from compensated glaucoma even when the intraocular pressure was normalized by drugs. In eyes suffering from acute glaucoma, however, the "apparent outflow pressure" was normal after successful use of miotics. The pressure values in glaucomatous eyes were above 20 gm., most of them between 26 and 30 gm.

However interesting these results appear, they are much less convincing when the whole series of facts is closely sifted. Then it will become manifest that the high values of "apparent outflow pressure" are not at all restricted to glaucomatous eyes. In the second paragraph of page 84,[9] there is a phrase printed in italics and saying that very narrow aqueous veins showed markedly higher values and, therefore, "they should not be used for these experiments." In a footnote on the same page, Goldmann mentioned that recipient vessels of eyes with normal intraocular pressure, located in the inferior parts of the eyeball and conspicuous by slow current, may show "anomalously high" readings.

From these exemptions it becomes evident that Goldmann arbitrarily decided to consider as normal values exclusively those in the lower ranges of his spring-balance readings despite the fact that markedly higher values were also obtained on eyes with normal intraocular pressure. Therefore, the figures listed in Goldmann's tables are not conclusive for the pressure gradient prevailing between anterior chamber and anterior ciliary veins; they may be characteristic of the individual aqueous vein which was observed in each single experiment.

More confusion is created by the repeated omission of the adjective "apparent" before the noun "outflow pressure" whereby the impression arises that the real outflow pressure has been measured. Therefore, we should prefer to term the values reported by Goldmann "increment pressure" rather than "apparent outflow pressure." This increment pressure will depend upon different factors, the most important of which seems to be the vessel diameter (see under "Hydrodynamics").

It is very probable that all aqueous veins with high increment-pressure readings are either narrow throughout their course—as those mentioned by Goldmann[9] in the second paragraph of page 84—or that they have a localized constriction or narrowing somewhere in their roots. A sclerosis of the trabeculum could also be held responsible

for high increment pressure readings if found in all aqueous veins of the same individual eye; this, however, is in contradiction to facts known about the backflow phenomena into the canal of Schlemm.

GONIOSCOPY AND AQUEOUS VEINS

For more than three decades ophthalmologists have been fascinated by gonioscopy, a method to which many interesting facts are owed. It seems, however, that as far as glaucoma problems are concerned too far-reaching conclusions were drawn from gonioscopic findings. Magitot,[17, 25] Busacca,[26] and also one of the pioneers in gonioscopy,

angle glaucoma, however, cannot even be attempted on the basis of gonioscopy. Here, it seems that observations on aqueous veins may fill a gap in our understanding. While Schlemm's canal is accessible to intravital examination by means of gonioscopy, the outlets of the canal themselves are not visible intravitally; only ascending branches, connecting them with the episcleral meshwork, become accessible to biomicroscopic examination. Thus, biomicroscopy and gonioscopy complement each other to further our knowledge of the admirable exhaust system which consists of the canal of Schlemm and its outlets.

TABLE 1

EFFECT OF WIDTH OF CANAL OUTLETS AND OF AQUEOUS VEINS

	A. With Wide Outlets	B. With Narrow Outlets
1. Gonioscopic findings Backflow of blood into the canal of Schlemm	Frequent	Rare
2. Biomicroscopic findings a. Rate of flow of aqueous humor, observed on recipient vessel	High	Low
b. Compression test, performed on recipient vessel, observed on aqueous vein: Influx phenomenon	Aqueous influx	Blood influx
c. Increment-pressure test, performed on cornea, observed on recipient vessel: Dynamometer readings	Low	High
3. Intraocular pressure Tonometer readings:	If no other pathologic condition: normal	If many outlets narrow: high

Troncoso,[16] (page 231) have sounded impressive warnings. Busacca has not been able to detect signs characteristic of glaucoma in the chamber angle. He concluded that the part played by the iridocorneal angle in the pathogenesis of glaucoma is insignificant. Troncoso stressed the fact that shallowness of the chamber angle is only a predisposing factor and cannot be the primary cause of acute glaucoma, as recent writers have been inclined to believe. Kronfeld[27] conceded that the gonioscopic findings do not always enable one to tell with certainty whether the anatomy of the chamber angle has been altered to such an extent that the function of the normal channels of outflow is permanently or irreparably impaired.

The explanation of the so-called wide-

It may well be that a different trend of gonioscopic examination will yield more useful results than the observations of the anatomic relationship between corneoscleral tissue, on one side, and uveal tissue, on the other, have furnished during the last decades.

Gonioscopy proved[28, 29] that blood rarely entered the canal of Schlemm of glaucomatous eyes; whereas, in eyes with normal pressure, the canal often showed the presence of blood in varying amounts. If an obstacle were situated between the anterior chamber and the canal of Schlemm (that is, in the trabecular meshwork), blood could still enter the canal. The case of blood backflow into the canal of normal eyes, and the rarity of the same phenomenon in glau-

comatous eyes,[28,29] could be explained tentatively by obstruction of visibility of the canal in shallow-angle eyes; such an explanation, however, cannot be valid for Kronfeld's[29] (page 1167) experiments performed on eyes which suffered from wide-angle glaucoma.

An impediment to flow, located somewhere between the canal of Schlemm and the deep scleral venous meshwork, is to be postulated. If this impediment were situated in the trabecular area, a relatively low pressure should be expected inside the canal of Schlemm, and there would be no reason why blood should not easily gush into the canal. Only a narrowing of the outlets or a marked decrease in their number can explain the missing backflow of blood into the canal together with the high increment-pressure readings, the absence of a longer or wider aqueous stream in the biomicroscopically visible elimination pathways, the absence of the aqueous-influx phenomenon in glaucomatous eyes and, possibly, even the intraocular-pressure increase due to insufficient fluid elimination (Table 1).

APPLICATION OF HYDRODYNAMIC PRINCIPLES TO THE PROBLEM OF INTRAOCULAR-FLUID ELIMINATION

If one considers from the point of view of hydrodynamics the system comprising Schlemm's canal, its outlet tubes, and the conjunctival and anterior ciliary veins into which they finally empty, it is possible to list a number of factors that may influence the rate of discharge of aqueous humor from the canal and hence may also affect the intraocular pressure. Such a list, not necessarily complete, is given in Table 2.

The question now arises as to the relative magnitudes of the effects of these factors. For making the comparisons, we use Poiseuille's equation for the rate of streamline flow of a viscous liquid through a sufficiently long straight tube of circular cross section:

$$(1) \qquad \frac{Q}{t} = \frac{\pi r^4 \Delta p}{8 \eta l},$$

where Q is the quantity of liquid of viscosity η flowing in time t through a tube of radius r and length l under the influence of a pressure difference Δp $(= p_0 - p_1)$ between the ends of the tube, where p_0 is the pressure at the origin and p_1 the pressure at the emptying point of the tube. We use the values

TABLE 2

SOME FACTORS AFFECTING THE RATE OF DISCHARGE OF AQUEOUS HUMOR FROM THE CANAL OF SCHLEMM

A. Number of outlet tubes, part of them becoming visible aqueous veins
B. Rate of flow per tube, dependent on:
  1. Radius of tube, including effect of enlargements, contractions, or obstructions
  2. Distensibility of tube
  3. Shape of cross section of tube
  4. Length of tube
  5. Straightness of tube
  6. Nature of tube inlet and outlet
  7. Branching of tube
  8. Pressure in Schlemm's canal
  9. Pressure in the conjunctival and episcleral veins at point of junction with aqueous veins
  10. Temperature gradients across the veins
  11. Diffusion and osmotic effects
C. Viscosity of aqueous humor, dependent on its
  1. Composition, in turn dependent on
    a. Salt content
    b. Protein content (dissolved in the fluid or present as blood corpuscles)
  2. Temperature, dependent on exposure of the veins to
    a. The temperature of the interior of the eye
    b. The temperature at the surface of the eye
    c. Rate of flow of the liquid
    d. Thermal conductivity of the covering tissues

shown in Table 3 as typical for the normal human eye. A simple calculation shows that these data are reasonably self-consistent.

We consider first the effect of the number (n) of the outlets, assuming the other variables to remain constant. An adaptation of the Poiseuille equation gives:

$$(2) \qquad \left(\frac{Q}{t}\right)_{total} = \sum_{i=1}^{n} \frac{\pi r_i^4 \Delta p_i}{8 \eta l_i}$$

If n is taken to be the only variable this becomes:

$$(3) \qquad \left(\frac{Q}{t}\right)_{total} = \frac{n \pi r^4 \Delta p}{8 \eta l} \approx 18.8 \, mm.^3/min.$$

This value is of the same order of magnitude, although somewhat higher than the

TABLE 3

TYPICAL VALUES FOR THE NORMAL HUMAN EYE OF QUANTITIES USED IN THE POISEUILLE EQUATION

p_o: pressure at origin of outlets of Schlemm's canal ≈ 20 mm. Hg
p_l: pressure at junction of outlet or aqueous vein with recipient vein ≈ 10 mm. Hg
l: length of outlet plus aqueous vein ≈ 2 mm. (range 1–10 mm.)
η: viscosity of aqueous humor—0.00715 poise (the approximate value for one percent sodium-chloride solution at 37°C. or 98.6°F.)
r: radius of circular outlet (most of them are elliptic, see later) assumed ≈ 0.013 mm.
a: major semiaxis of elliptical outlet ≈ 0.0169 mm. (many of them are larger)
b: minor semiaxis of elliptical outlet ≈ 0.010 mm. (many of them are wider, some are smaller)
Q/t: rate of flow of aqueous humor from Schlemm's canal ≈ 18.8 mm.³ per min. for 30 tubes or about 0.626 mm.³ per min. for one tube
n: number of separate outlets ≈ 30.

values found by previous investigators.[24] We take n to be equal to 30 for the typical normal human eye, and use this equation to calculate Δp, the pressure drop along the tube, as a function of n for a constant outflow rate. The results are given in Table 4 and in Figure 1.

Fig. 1 (Ascher and Spurgeon). Dependence of pressure drop on number of outlets.

It can be seen that, for other factors remaining the same, a decrease of about 50 percent in the number of outlets leads to the upper limit of normal values of Δp, the pressure drop, and hence of p_o, the pressure at the origin of the outlet in Schlemm's canal. Further decrease of the number of outlets may cause a definitely dangerous increase in Δp. In the extreme case of no outlets Δp, p_o, the pressure in Schlemm's canal and, therefore, the intraocular pressure be-

comes very great or the outflow rate decreases markedly, or both.

The next factor to be considered is the most important one from the hydrodynamic point of view: the radius (r) of the outlet and of the aqueous vein. Its outstanding importance lies in the fact that it occurs to the fourth power in the Poiseuille equation; whereas, the other factors occur to the first power only, or else as relatively small cor-

TABLE 4

DEPENDENCE OF Δp ON NUMBER OF OUTLETS

Number of Outlets, n.	Pressure Drop along Outlet (Δp in mm. Hg)	Pressure at Origin of Outlet (p_o in mm. Hg)
30	10	20
25	12	22
20	15	25
15	20	30
10	30	40
5	60	70
4	75	85
2	150	160

rections of the equation. For constant values of η, l and Q/t, the effect of radius change on pressure is shown in Table 5 and Figure 2.

It is seen that as r decreases from the assumed norm, Δp, the pressure drop, increases enormously, if the other factors remain unchanged. Assuming p_l, the pressure in the recipient vein, to remain unchanged, p_o, the pressure in Schlemm's canal must, therefore, also increase very rapidly as r decreases if the same rate of outflow is to be maintained. The value of p_o could become seriously high for a decrease of r of only three microns, that is, from 13μ to 10μ.

These calculations were based on the assumption that all outlets have the same radius. Actually, of course, this is not true, and it becomes of interest to calculate the relative outflow from tubes of various sizes. As a simple case, consider a set of 30 tubes arranged "in parallel," 27 of them having a radius of 0.006 mm., corresponding to the smallest minor-axis values measured by Theobald,[32] and three of them having radius 0.026 mm., the other variables remaining unchanged. For a value of Δp of 10 mm. Hg, the 27 small tubes could carry 0.768 cubic millimeters per minute of aqueous humor, whereas, the three large tubes could carry 30.1 cubic millimeters per minute. In other words, the three large tubes could carry about 40 times as much liquid as the 27 small tubes. If the three large tubes were destroyed, Δp would have to increase to 402 mm. Hg to maintain the same total outflow rate through the small tubes. It is not meant to imply that the same total outflow rate must be maintained or that the pressure increase would actually amount to 402 mm. Hg. The point is that destruction of the three large tubes would very greatly increase the resistance to flow of the aqueous humor.

So far the discussion has concerned only tubes of uniform cross section. We now inquire as to the effect if there is a constriction or an obstruction in a relatively large tube. Such a tube can be considered as a large and a small resistance to flow, joined in series (fig. 3). The Poiseuille equation can be applied to each part separately. As an example we may calculate the pressure drop along each section of the tube shown
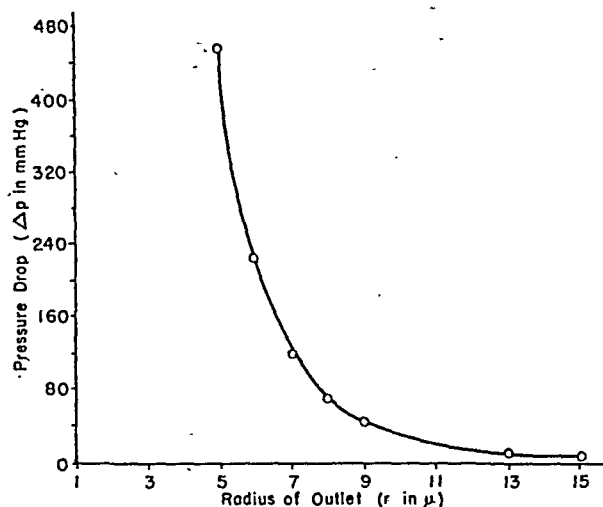
Fig. 2 (Ascher and Spurgeon). Effect of radius change on the pressure drop, Δp.
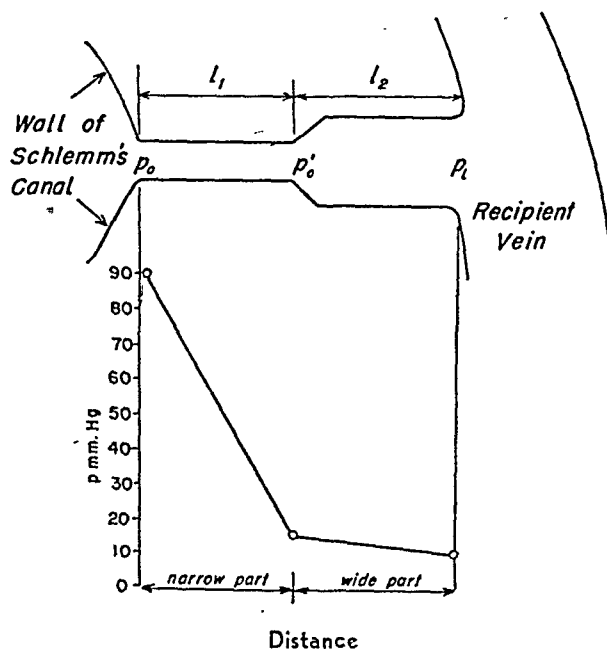
Fig. 3 (Ascher and Spurgeon). Effect of a constriction in an outlet.

in Figure 3, taking $r_1 = 0.0065$ mm., $r_2 = 0.013$ mm., and $l_1 = l_2 = 0.1$ mm. The results are as follows:

$$\Delta p_1 = (p_o - p_o') = 80 \text{ mm. Hg,}$$
$$\Delta p_2 = (p_o' - p_l) = 5 \text{ mm. Hg.}$$

TABLE 5
EFFECT OF RADIUS CHANGE ON THE PRESSURE DROP, Δp

Radius of Outlet (r in μ)	Pressure Drop Along Outlet (Δp in mm. Hg)	Pressure in Schlemm's Canal (p_o in mm. Hg)
15	6	16
13	10	20
10	28	38
9	44	54
8	70	80
7	119	129
6	226	236
5	456	466

The pressure drop along the constriction amounts to 94 percent of the total pressure drop along the tube. The gradients are shown also in Figure 3. It is seen that such a constriction greatly reduces the effectiveness of the tube as a carrier for the aqueous humor. This calculation again illustrates the profound influence of radius changes.

It might be inquired whether the distensibility or elasticity of the primary outlets and the visible aqueous veins would play a part
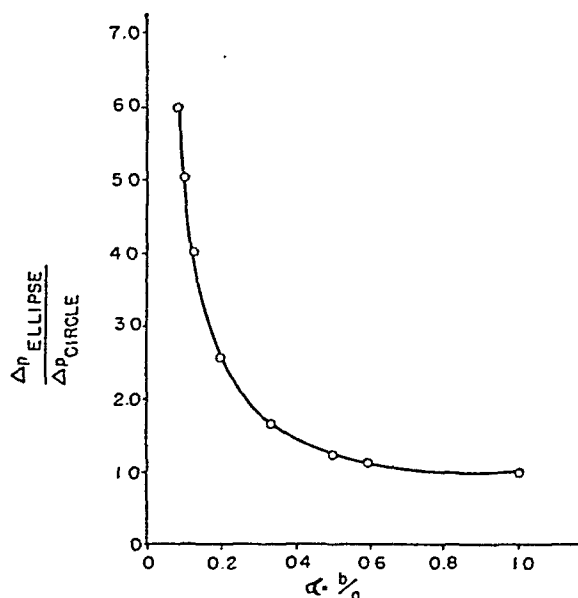
Fig. 4 (Ascher and Spurgeon). Effect of eccentricity of ellipse on Δp, the pressure drop.

here. Undoubtedly it would, to a limited extent. If the outlet is obstructed, however, or embedded in tissue that strongly resists expansion of the vein (for example, if such tissue is the original cause of the constriction), the elasticity of the tube walls would not help matters very much. Now it is known that the primary outlets are embedded in stiff scleral tissue. The aqueous veins, if superficially located, can be seen to be easily distensible.

So far we have considered only tubes with circular cross section. It is known, however, that the cross sections of many outlets and possibly of aqueous veins is roughly elliptical.[11, 32] For this case Poiseuille's equation

must be modified to the following form:[31]

$$(4) \qquad \frac{Q}{l} = \frac{\pi a^3 b^3 (p_0 - p_l)}{4\eta(a^2 + b^2)l}$$

It is known also that the ratio

$$\frac{Q}{t}\Big]_{\text{(ellipse)}} \div \frac{Q}{t}\Big]_{\text{(circle)}}$$

is given by the expression

$$(5) \qquad \frac{2\alpha}{1 + \alpha^2}$$

where

$$(6) \qquad \alpha = \frac{b}{a} = \frac{\text{minor semiaxis}}{\text{major semiaxis}}$$

This shows that if other factors are the same, the discharge rate from an elliptical tube is less than the rate from a circular tube of the same cross-sectional area.

Equation 4 can be used to calculate the pressure drop for constant values of Q/t, η and l, and for various values of a and b. The results of sample calculations are given in Table 6 and Figure 4. It can be seen, for example, that for a tube of elliptical cross section that is 10 times as wide as it is deep, the pressure drop must be 5 times as great as for a tube of circular cross section and the same cross-sectional area.

The Poiseuille equation shows that a greater pressure must be exerted to force a given amount of liquid of specified viscosity through a long tube than is required for a short tube of the same radius. For example, the pressure drop, Δp, would have to be 5 times as great for a tube 10-mm. long as for one 2-mm. long, other things being equal. In this connection it must be remarked that for very short tubes the Poiseuille equation does not hold rigorously.[30]

The nature of the junction of the outlet tube with Schlemm's canal and with the recipient veins will influence the flow of aqueous liquid. The sharpness or roundness of the corners at the junctions, and the angle of contact between the outlet tube or visible

aqueous vein and the vein into which it empties will be factors of some importance. Their effects, however, will probably amount to a small correction to the Poiseuille equation, and they will not be considered further at this time.

Some of the outlet tubes are highly branched, particularly near the canal. The Poiseuille equation can be applied to each branch, and the entire network can be treated as an arrangement of series and

2 percent per degree, then, using the values given in Table 3, it is found that an increase in pressure of 2.0 mm. Hg is necessary in order to maintain the same rate of flow. Consideration of this temperature influence may help to explain the higher incidence of glaucoma in the cold season of the year.

Finally, we must mention the effect of individual differences and the consequent possibility that, in some individuals, a combination of several of the factors discussed

TABLE 6

EFFECT OF ECCENTRICITY OF ELLIPSE ON ΔP, THE PRESSURE DROP

Major Semiaxis (a in mm.)	Minor Semiaxis (b in mm.)	$\alpha = \dfrac{b}{a}$	Pressure Drop in Elliptic Tube Compared to Pressure Drop in Circular Tube $\dfrac{\Delta p_{el.}}{\Delta p_{cir.}} = \dfrac{1+\alpha^2}{2\alpha}$
0.120	0.01	0.0835	5.99
0.100	0.01	0.100	5.05
0.080	0.01	0.125	4.03
0.050	0.01	0.200	2.60
0.030	0.01	0.333	1.67
0.020	0.01	0.500	1.25
0.017	0.01	0.592	1.14
0.010	0.01	1.00 (circle)	1.00

parallel conductors. Giving illustrative calculations for such a system, however, would merely complicate the presentation of the essential features that we wish to emphasize. Similarly, we will not now discuss the possible effects of bending of the tubes, temperature gradients across an aqueous vein, diffusion or osmotic effects.

The viscosity of the aqueous humor can be of some importance as a factor influencing the rate of discharge. The principal factors that influence the viscosity are the composition (salt, protein, and cell content) and the temperature of the aqueous humor. Increased protein content would result in increased viscosity, that is, in increased resistance to flow. If a considerable length of an aqueous vein is near the surface of the eye so that its contents can be cooled to, say, 10°C. lower than the anterior-chamber temperature, and if we take the increase in viscosity of the liquid (on cooling) to be

above, all working in the same direction, could result in greatly decreased drainage from Schlemm's canal and higher intraocular pressure. Thus, an individual with abnormally few outlet tubes, and with those elliptical and unusually narrow, would be expected to be subject to the development of a dangerous increase of intraocular pressure.

Several times in the preceding discussion of factors that increase the resistance to flow of aqueous humor we have used such expressions as "the pressure in Schlemm's canal must be increased in order to maintain the same rate of flow." We do not mean thereby that a certain outflow rate must necessarily be maintained, as was suggested by Bárány,[19] or that the intraocular pressure must go up by the amounts calculated. The calculations must be considered as illustrative, rather than as giving absolute values, and are given for the purpose of pointing

the way for further research. They show that as the resistance to flow increases, either the intraocular pressure goes up, or the outflow rate goes down, or both. Above all, they show the predominant role played by the number and—especially—by the width of the outlets from Schlemm's canal and of the visible aqueous veins.

No claim is made that the hypothesis of a narrowing of the canal outlets could explain all cases of primary compensated glaucoma; this hypothesis is proposed to stimulate further research, clinical as well as histologic and experimental.

From the surgical viewpoint, sparing of visible aqueous veins during an eye operation seems to be advisable. Gartner[6] is of the same opinion, but De Vries[11] (page 85f.) objected that the aqueous humor, having many collateral pathways available, will find its return into the blood stream anyway. Only where there is a choice for the site of an operation, De Vries would agree to locate it at a place lacking aqueous veins.

Considering the location of the largest outlets from Schlemm's canal in Theobald's plate reconstruction models,[12, 32] we find, in her specimen 705, among 29 outlets only 1 on the nasal and only 3 on the temporal side to have a diameter wider than 100 micra; in specimen 791 there are on either side only two outlets with a cross section of more than 5 cuts, that is, only 4 among 24 outlets. In her specimen 947, there are, among 31 channels, 3 temporal and 2 nasal outlets with a cross section surpassing 5 microscopic cuts.

In other words, all three eyes had only a few large outlets and many smaller ones. If one or more of the large outlets were severed during an operation, they might or might not become replaced by the function of those spared. From the foregoing calculations it is evident that at least a tendency to intraocular-pressure increase will result from the loss of even a few of the larger outlets.

If, for instance, after a cataract incision a very exact readaptation of the wound lips

is secured, a complete recovery of the individual severed outlet is possible but not necessarily to be hoped for. If the original path is not restored, it is doubtful whether the neighboring smaller channels could suffice to substitute for the lost outlet without increase of resistance to the aqueous flow.

CONCLUSIONS

The evidence afforded by gonioscopy, on one side, and by biomicroscopy, on the other, is far from complete, and much still remains to be done in all aspects of this subject in connection with the explanation of glaucoma. Histologic verification should be supplied for the working hypothesis that a transient or permanent narrowing of the outlets of Schlemm's canal seems to be connected with, or even may be responsible for, the intraocular pressure increase in eyes suffering from compensated primary glaucoma.

This working hypothesis was arrived at by the following considerations. With increase of intraocular pressure and with a patent fluid-elimination system, a more vigorous fluid elimination should be expected in the aqueous veins of glaucomatous eyes. The bulk of evidence, however, points in an opposite direction, with the clear stream in aqueous veins of glaucomatous eyes neither longer nor wider than in those of eyes with normal intraocular pressure, and with the failure of glaucomatous eyes to show the aqueous-influx phenomenon upon compression of the recipient vessel.

There must be an obstacle somewhere between anterior chamber and biomicroscopically visible veins to explain this discordance. If this impediment were in the trabecular area, a relatively low pressure would prevail inside the canal as compared to the anterior chamber and blood could easily enter the canal of Schlemm. Gonioscopic evidence, however, indicates that, during the stage of high intraocular pressure, no backflow of blood takes place into the

canal despite the fact that, upon compression of the recipient vessel, backflow of blood toward the canal does take place.

The summary of recorded evidence of increment-pressure values, if not invalidated by arbitary omission of high values in eyes with normal pressure, indicates that narrow aqueous veins and those with a narrow root-deep in the scleral meshwork need a higher increment pressure, exerted upon the cornea, to become filled with more aqueous humor as compared to wider aqueous veins.

In wide aqueous veins, a slight increment pressure suffices to produce a perceptible increase of aqueous flow. A satisfactory understanding of the recorded increment-pressure values cannot be provided by the simplification attempted by discarding values which do not conform to a preconceived opinion. By this criticism of Goldmann's interpretation, our appreciation for his findings is in no way lessened. However, our attention must be focused on all available data concerning the whole space which is limited by the lining of the anterior chamber on one side, and by the corneal and conjunctival surface on the other. We must consider the normal and the pathologic microscopic anatomy of this region, as well as the physiologic facts about the pressure potentials governing the sanguineous and aqueous contents of the vascular and vessel-like structures in this significant region.

The varying, sometimes oscillating, pressure balance between the two fluids which pass that elimination unit—the canal of Schlemm, its invisible outlets, and the visible aqueous veins—as well as the pathologic changes, anatomic or functional, which may occur in this space and may lead to intraocular-pressure increase, must be taken into account.

In eyes with normal intraocular pressure, narrow and wide outlets from Schlemm's canal are found; so are the aqueous-influx phenomenon and the blood-influx phenomenon, and so are backflow of blood into the

canal and missing backflow. High and low increment-pressure readings are also encountered together in the same normal eye yet not in the same individual aqueous vein.

On the other hand, in eyes affected by primary compensated glaucoma, no aqueous-influx phenomenon is observed, no backflow of blood into the canal takes place other than in rare exceptions, and only high increment-pressure values are encountered, even when the eye pressure has been normalized by treatment. The expected narrowing of the canal outlets is still to be proved by histologic examination.

Summary

1. The intraocular-fluid elimination of the human eye can be studied biomicroscopically.

2. A working hypothesis is proposed that, in at least some eyes affected by primary compensated glaucoma, many or all outlets from the canal of Schlemm are narrower than in normal eyes. This hypothesis would explain:

  a. The increase of intraocular pressure, due to impaired elimination of aqueous humor.

  b. That, in glaucomatous eyes, the clear-fluid stream in aqueous veins and in recipient vessels is neither longer nor wider than in eyes with normal intraocular pressure.

  c. That, in glaucomatous eyes, compression of a recipient vessel of an aqueous vein fails to produce the aqueous-influx phenomenon.

  d. That, in glaucomatous eyes, compression of the recipient vessel results in backflow of blood toward the limbus while blood rarely becomes visible inside the canal of such eyes.

  e. That in glaucomatous eyes controlled by either miotics or surgery, compression of the recipient vessel may result in the expulsion of blood from the blocked vessel section.

  f. That more pressure needs to be ap-

plied to the globe in order to increase the visible flow of aqueous humor in narrow aqueous veins and in those of glaucomatous eyes.

3. Previous to ocular surgery, aqueous veins should be carefully located and, if possible, they should not be severed during eye operations.

5 West Fourth Street (2).
2034 Dallas Avenue.

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DISCUSSION

DR. P. C. KRONFELD (Chicago, Illinois): This is a very interesting hydrodynamic study, and I can see that several pieces of valid evidence speak in favor of a relative block situated at the level of the outlets of the canal of Schlemm. Dr. Ascher's hypothesis rests more heavily on our findings than we would like to see it at this time. We don't feel that we have settled the matter gonioscopically. It is true that the methods that bring blood into the canal of Schlemm in normal human tissue fail when applied to

eyes with wide-angle glaucoma. One of the reasons is that those methods do not create the same state of relative hypotony in the normal and in the glaucomatous eye.

The simplest method to bring blood into the canal in the normal eye is to lower the intraocular pressure by compression of the globe. That method in the glaucomatous eye brings about a slighter drop in intraocular pressure than in the normal eye and that may be the main reason why the canal doesn't fill with blood in the glaucomatous eye. Therefore, we have continued our work on what might be called angiography on the canal of Schlemm in the wide-angle glaucoma.

All that I wish to say at this time is that there are wide-angle glaucomas in which, by the routine method of compression of the globe, the canal can be made to fill with blood. In the majority of chronic simple glaucomas, however, blood cannot be made to appear in the canal and it is quite possible that Dr. Ascher's explanation applies to the latter group.

DR. ASCHER (closing) : I am very happy to hear from Dr. Kronfeld that he agrees to a certain extent with my explanation and I do confess that his experiments, which consisted in withdrawing of aqueous humor, offered some of the leading ideas in my considerations. I think Dr. Kronfeld's experiments are wonderful and deserve further study in comparison with the paralleling changes in the aqueous veins of these particular eyes.

AMERICAN JOURNAL OF OPHTHALMOLOGY

Published Monthly by the Ophthalmic Publishing Company

SEVENTEENTH MEETING

of the

Association for Research in Ophthalmology, Inc.

Proceedings

Business Session

Auditor's Report

Constitution

New Members

Officers of the Association

Directory of Members

Geographical List

Editor

JAMES H. ALLEN, *Iowa City, Iowa*

Publications Committee

PHILLIPS THYGESON, *San Jose, California*

KENNETH C. SWAN, *Portland, Oregon*

V. EVERETT KINSEY, *Boston, Massachusetts*

Committee on Arrangements

WILLIAM A. MANN, *Chairman*

FRANK W. NEWELL

WILLIAM F. HUGHES

Chicago, Illinois

June 21 and 22, 1948

The business session of the Association for Research in Ophthalmology, Inc., convened at 1:45 o'clock in Thorne Hall, Northwestern University, Chicago, Illinois, with Dr. Phillips Thygeson presiding.

DR. PHILLIPS THYGESON (Chairman): Will the meeting please come to order?

For lack of time, we are omitting the minutes of the last meeting. They are available here with the secretary-treasurer and in the *Proceedings.*

I will ask first for the report of the secretary-treasurer.

DR. JAMES H. ALLEN: Mr. Chairman, as of the first of June, 1948, the treasurer listed the following assets:

Cash in bank, First National
  Bank, Iowa City $4,246.04
U. S. Treasury Bonds carrying
  an interest rate of 2½ percent
  at a cost of 4,099.84

    Total assets $8,345.88

The Treasury bonds and the interest from them, as you know, are the research medal fund or the Proctor Medal, so that cash in the bank as of the first of June was $4,246.04.

The membership as of the first of June, 1948, carries 21 sustaining members; 320 active members, 8 honorary members, 1 life member, and 42 active members who had not paid their dues as of the first of June. I may say that since the first of June we have received dues from a number of those 42 members. We have at the present time 61 new members to add to this list.

CHAIRMAN THYGESON: I will ask for the report of the auditing committee.

DR. BRITTAIN F. PAYNE: Mr. Chairman, Gentlemen: The committee has examined the financial statement for the year ending May 31, 1948, and finds it in order and recommends its approval. It is recommended that the fiscal year ending May 31 of each year be changed to December 31 each year to conform with income-tax regulations and membership requirements.

Attention is called to the years 1943 and 1945 when statements were not available due to the wartime inactivity of the association. It is requested that the secretary insert an explanatory footnote at the end of this statement to this effect. (Respectfully submitted, B. F. Payne and R. J. Masters.)

CHAIRMAN THYGESON: You have heard the report of the auditing committee. What is your pleasure? (Motion was made and seconded that the report be accepted; the motion was duly put to a vote, and it was carried.)

CHAIRMAN THYGESON: Next I ask for the report of the committee on the revision of the constitution. As you know, at the meeting last year, certain changes were recommended by the session and these have been studied by the committee who now has a report for your consideration.

DR. KENNETH SWAN: Mr. Chairman, members of the association: it has been the purpose of this revision to strengthen the society by two major changes, namely a change to facilitate the admittance into the society of workers in the basic-science field by establishing a new class of membership entitled the "educational membership." The educational membership, as you will note, provides a special class with reduced annual dues for fulltime workers in research, and for men completing their training.

The second major change is the establishment of sections. It is not the purpose of these sections to provide organizations which will duplicate the functions of the national society but rather to supplement and aid it.

In bringing about these changes, there were some practical problems which necessarily had to be met by compromise. Another major change has already been approved by the society, namely the deletion of the commission. Copies of the revision are in the hands of members. (Respectfully submitted

by Drs. Payne, Berens, Allen, and Swan.)

CHAIRMAN THYGESON: These changes submitted by the committee have been studied by the board of trustees and have been approved by them for submission to the membership. What is your pleasure on these projected changes in the constitution?

DR. POST: I move its acceptance. (The motion was duly seconded, put to a vote, and it was carried.)*

CHAIRMAN THYGESON: There are certain announcements that should be made.

The next meeting has been set for June 6 and 7, 1949, at Philadelphia. The reason for setting Philadelphia has been the difficulty that we had last year in Atlantic City. It was almost impossible to obtain suitable meeting halls.

A Western Section has already been projected in line with the constitutional changes, and an organizational meeting was held last March in San Francisco at which plans were made for a yearly meeting. Dr. Orwyn Ellis of Los Angeles was named chairman and Dr. Michael J. Hogan, secretary.

The Eastern Section organizational meeting has been announced and set for November 13, 1948, at New York at the Lenox Hill Hospital, and the Midwestern Section organization meeting is to be announced in the fall.

The committee on arrangements under the chairmanship of Dr. Mann has done an exceedingly good piece of work for this meeting and I think the association should give him and his committee a vote of thanks.

MEMBER: I so move. (Applause.)

DR. THOMAS D. ALLEN (Chicago): There are certain things that are coming up constantly before the Committee on Optics and Visual Physiology that are highly technical. We would like to have on our committee some of the members of this organization to help us decide some of these problems. I think we ought to empower the trustees to appoint members to the committee as representatives of this association.

DR. CONRAD BERENS (New York City): Mr. Chairman, I think that Dr. Allen has explained things very well indeed. We do need help. The American Committee on Optics and Visual Physiology has asked that this association appoint three members, one for one, one for two, and one for three years on the American Committee on Optics and Visual Physiology.

It seems to me that all we will have to do is to empower you to do that. I would like to move that the trustees be empowered to appoint three members to the American Committee on Optics and Visual Physiology.

DR. THOMAS ALLEN: I second the motion. (The motion was duly put to a vote and carried.)

CHAIRMAN THYGESON: I might announce that at the trustees' meeting, action was taken approving of the report of a committee from the New York Academy of Medicine —I believe that Dr. Berens is chairman— concerning the use of silver-nitrate prophylaxis, and the trustees have requested Dr. James H. Allen, who is making a study of prophylaxis of ophthalmia neonatorium, to report to this society next year.

Dr. Vail, are you ready to make the report of the nominating committee?

DR. DERRICK VAIL (Chicago): Yes. The committee on nominations recommends Dr. Robb McDonald of Philadelphia to be appointed a member of the board of trustees to succeed you, since you are retiring. It also recommends that Dr. James Allen be reelected secretary-treasurer of the organization.

CHAIRMAN THYGESON: You have heard the report of the nominating committee.

DR. CONRAD BERENS: I move the nominations be closed and the secretary will cast a ballot. (The motion was duly seconded and carried.)

CHAIRMAN THYGESON: The secretary will be asked to cast a ballot. There is no further business before the society, and we will proceed to the first paper of the afternoon. (The business session adjourned at 2:15 o'clock.)

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* See revised version of Constitution, page 259.

We have examined the accounting records of the secretary-treasurer of the Association for Research in Ophthalmology, Inc., Iowa City, Iowa, for the fiscal year ended May 31, 1948. We submit as our report the following statements together with comments thereon:

Exhibit A. Statement of Cash and Securities as of May 31, 1948.

Exhibit B. Statement of Cash Receipts and Disbursements for the fiscal year ended May 31, 1948.

Exhibit C. Statement of Membership as of May 31, 1948.

SCOPE OF EXAMINATION

Cash receipts as recorded in the cash book were traced to the bank deposits for the entire period and were reconciled with the number of members.

Disbursements were verified by examination of paid checks and available supporting invoices and other data. All disbursements appeared to be proper.

Cash in bank was reconciled to the amount reported to us by the depository. We inspected the U. S. Treasury bonds.

On *Exhibit C* is presented a statement of membership as of May 31, 1948. The unpaid dues for 1948 were not confirmed directly with the members.

We have not attempted to determine the number of members who have failed to pay dues prior to 1948, because of the difficulties involved in securing this information, and also because it is our understanding that no attempt will be made to collect these delinquent dues. We were informed that an effort will be made to collect delinquent dues for the fiscal year 1948 and subsequent years.

ACCOUNTANTS' OPINION

In our opinion, the accompanying balance sheet and statement of cash receipts and disbursements fairly present the fund balances of the Association for Research in Ophthalmology, Inc., Iowa City, Iowa, as of May 31, 1948, and the total receipts and disbursements of the association for the fiscal year then ended.

<div align="center">

Respectfully submitted,

McGladrey, Hansen, Dunn & Company.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

EXHIBIT A

STATEMENT OF CASH AND SECURITIES

May 31, 1948

</div>

ASSETS

Cash in bank—First National Bank, Iowa City, Iowa	$4,246.04
U. S. Treasury bonds—s ½%, 1967/72 (at cost)	4,099.84
TOTAL ASSETS	$8,345.88

NET WORTH

General Fund	$4,234.51
Proctor Medal Fund	4,111.37
TOTAL NET WORTH	$8,345.88

EXHIBIT B

STATEMENT OF CASH RECEIPTS AND DISBURSEMENTS

For the Fiscal Year Ended
May 31, 1948

CASH RECEIPTS

1948 Dues:

21 Sustaining Members at $25.00	$ 525.00	
278 Active Members at $5.00	1,390.00	$1,915.00

1947 Dues:

1 Sustaining Member at $25.00	$ 25.00	
37 Active Members at $5.00	185.00	210.00

Total Dues		$2,125.00
Bond Interest		100.00
Sundry Refund		8.50
Total Cash Receipts		$2,233.50

CASH DISBURSEMENTS

Secretary's Salary		$ 283.80
Convention Expense		
Printing Programs	$ 232.56	
Party	601.96	
Projector	54.00	
Public Address System	35.00	
Reporting Meeting	65.00	
Expenses of Secretary-Treasurer	100.00	
Other Convention Expense	12.00	1,100.52
Stationery, Supplies, Printing and Postage		232.59
Founder's Award		131.00
File Cabinet		96.49
Auditing		60.00
Premium — $5,000.00 Position Bond — Secretary-Treasurer		25.00
Express Charges		10.51
Safety Deposit Box Rental		3.60
Social Security Taxes		.75
Total Cash Disbursements		1,944.26

EXCESS OF CASH RECEIPTS OVER DISBURSEMENTS		$ 289.24
CASH BALANCE (May 31, 1947)	$3,946.95	
Add: Adjustment to Cash Balance as of May 31, 1947	9.85	
ADJUSTED CASH BALANCE (May 31, 1947)		3,956.80
CASH BALANCE (May 31, 1948) EXHIBIT A		$4,246.04

EXHIBIT C

STATEMENT OF MEMBERSHIP
May 31, 1948

SUMMARY OF MEMBERS

Sustaining	21
Active	320
Honorary	8
Life	1
Total Members	350

MEMBERS BY YEARS

1948	350
1947	306
1946	324
1945	Not Available*
1944	283
1943	Not Available*
1942	281
1941	279
1940	270
1939	268
1938	272
1937	249
1936	240
1935	245
1934	230
1933	219
1932	203
1931	193
1930	134

UNPAID DUES FOR 1948 42

* Due to wartime inactivity of the association.

CONSTITUTION

ARTICLE I

NAME

The association shall be known as the Association for Research in Ophthalmology, Inc.

ARTICLE II

OBJECTS

The objects of the association are set forth in its application for a charter as follows: To encourage, promote, foster, and assist investigations and research in ophthalmology; in furtherance of the purpose of the corporation to purchase, lease, or otherwise acquire, hold, sell, lease, convey or otherwise dispose of real and personal property or any interest therein; to receive, hold, and invest funds and endowments and to receive and expend the income thereof, and to hold and dispose of such sums of money as may be deemed expedient; and generally to do any and all things which may be necessary or proper in connection with the objects and purposes of the corporation and which may not be contrary to law.

ARTICLE III

MEMBERS

Members of recognized ophthalmologic societies in the United States and Canada and other individuals especially qualified shall be eligible to membership when proposed in writing by a member of the association and shall become members upon election by the Board of Trustees after the recommendation of the committee on admissions, upon payment of the dues hereinafter provided for.

1. Educational Membership. Individuals may be elected to this class of membership during a period of graduate education in ophthalmology or related scientific fields and/or during a period of full-time research. In no instance may an educational membership be held longer than three years without reapplication.

2. Active Membership. Individuals not eligible for educational membership shall be elected to active membership but may choose either this class or sustaining membership.

3. Sustaining Membership. Individuals elected to membership in any class may voluntarily choose to become sustaining members.

4. Life Membership. Upon recommendation of the Board of Trustees and by a majority vote of the members of the association present at its annual meeting, a member may be elected to life membership.

5. Honorary Membership. Upon recommendation of the Board of Trustees and by unanimous vote of the members of the association present at its annual meeting, an individual may be elected to honorary membership.

ARTICLE IV

BOARD OF TRUSTEES

There shall be a Board of Trustees consisting of six members, who shall be elected for a term of six years, and the secretary-treasurer of the association. The secretary-treasurer of the association shall be a member of the Board of Trustees, ex officio. The senior member of the Board of Trustees shall be chairman and in the absence of the chairman the member next in seniority shall act as chairman. At the first meeting of the board, the members shall draw lots for the purpose of determining which of them shall serve for one year, which for two, which for three, which for four, which for five, and which for six years; and the term

of each member shall come to an end according to the lot which he shall have drawn. At the first annual meeting thereafter, a member of the association shall be nominated for the Board of Trustees by the nominating committee of the association for a term of six years in the place of the member whose term then expires, and thereafter at each meeting a member of the Board of Trustees shall be elected for a term of six years.

ARTICLE V

OFFICERS

The officers of the association shall be a secretary-treasurer and a section secretary and a chairman for each section.

ARTICLE VI

SECTIONS

Regional, national, or international sections of the association may be established by petition of twenty members in various geographical units either within or outside of the United States.

The officers of the sections shall be a section secretary nominated by the secretary-treasurer and approved by the Board of Trustees and a chairman elected by the section.

ARTICLE VII

NOMINATING COMMITTEE

The Board of Trustees shall appoint at each annual meeting a nominating committee of three to serve for the following year. It shall be the duty of the nominating committee to nominate members for the office of secretary-treasurer and one member of the Board of Trustees.

ARTICLE VIII

DUTIES AND POWER OF OFFICERS AND TRUSTEES

The Board of Trustees shall have general charge of the affairs, funds, and property of the association. It shall prepare the programs for the meetings of the association. It shall also appoint a committee on publications and a committee on admissions. It shall elect desirable applicants for membership approved by the committee on admissions. It shall have full power and it shall be its duty to carry out the purpose of the association according to the Charter, Constitution, and By-laws. A majority of its members shall constitute a quorum. Between meetings of the Board of Trustees, the executive power of the association shall be vested in the chairman of the Board of Trustees and the secretary-treasurer.

Chairman of the Board of Trustees. The chairman of the Board of Trustees is the chief executive of the association. He shall preside at all meetings, call all meetings, and perform all duties customary to the office.

Secretary-Treasurer. The secretary-treasurer shall keep a record of the proceedings of all meetings; shall notify officers, trustees, and members of committees of their election; certify official records; keep a list of members; issue notices of all meetings; and perform all duties which may be required of him. He shall have charge of all funds of the association; he shall keep the same and make disbursements therefrom as directed by the Board of Trustees. He shall also obtain two copies of all scientific communications at the time the papers are read. The secretary-treasurer shall furnish bond and have his accounts audited yearly by a certified accountant.

Section Secretary. Section secretaries shall act as assistants to the secretary-treasurer and will serve as secretaries of sectional organizations.

The Section Chairman shall act as assistant to the chairman of the Board of Trustees in the execution of sectional meetings of the association. He shall preside at all meetings of the sections, call all such meetings and perform all executive duties customary to the office.

ARTICLE IX

ELECTION OF OFFICERS

The secretary-treasurer of the association shall be elected by ballot at the annual meeting to serve for one year. A member of the association shall be elected to the Board of Trustees by ballot at each annual meeting to serve for six years. Vacancies occurring in any office shall be filled by the Board of Trustees for the unexpired term until the next annual election.

With the approval of the Board of Trustees, the secretary-treasurer shall appoint a member of each section to act as sectional secretary for one year.

ARTICLE X

MEETINGS

The annual meeting of the association shall be held at a time and place selected by the Board of Trustees.

Sectional meetings shall be held at a time and place selected by the section secretary and chairman and approved by the secretary-treasurer and a member of the Board of Trustees.

ARTICLE XI

AMENDMENTS

Amendments to the Constitution may be made in the following manner: The amendment shall be written and shall be signed by three members of the association and submitted to the Board of Trustees at least thirty days before the annual meeting of the association. At the next annual meeting thereafter the Board of Trustees shall report at the meeting upon said proposed amendment. The amendment shall then be voted upon and two thirds of all the votes cast at the meeting shall be necessary for the adoption of the amendment.

BY-LAWS

ARTICLE I

MEETINGS

Meetings of the association shall be held at such time and place as the Board of Trustees shall determine. Twenty members shall constitute a quorum of the executive sessions of the meetings.

ARTICLE II

COMMITTEE ON ADMISSIONS

The Board of Trustees shall appoint annually a committee upon admissions consisting of three members. The names of all applicants shall be submitted to said committee which shall report its recommendations to the Board of Trustees.

ARTICLE III

DUES

The dues of the association shall be five dollars per annum for an active member and twenty-five dollars per annum for a sustaining member, the fiscal year starting January first. The dues for an educational member shall be two dollars per annum. Dues shall be remitted for life members and honorary members. To defray the expense of sectional meetings, the section secretary may levy dues not to exceed one dollar per annum. The secretary-treasurer, with the approval of the Board of Trustees, may distribute funds to meet unusual expenses of sections. This distribution of funds generally shall be in proportion to the size of the sectional membership.

ARTICLE IV

AMENDMENTS

The By-Laws may be amended in the same manner and with the same procedure as outlined for an amendment to the Constitution.

ARTICLE V

MEETINGS

All executive meetings shall be conducted according to Robert's Rules of Order unless specified otherwise in the Constitution and By-Laws.

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1948

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1949

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1948

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Thygeson, Phillips, Los Altos, California
Vanzant, Thomas J., Houston, Texas

DECEASED

Horner, Warren D.

RESIGNED

Meyer, Karl

MEMBERS

A

Adler, Francis H.,[1] 313 S. 17th St., Philadelphia, Pa.
Aiken, Samuel D., 384 Post St., San Francicso 8, Calif.
Albaugh, Clarence H., 727 W. 7th St., Los Angeles 14, Calif.
Allen, James H.,[1-4] University Hospitals, Iowa City, Iowa.
Allen, Lee,[5] University Hospitals, Iowa City, Iowa.
Allen, Thomas D.,[1] 122 S. Michigan Ave., Chicago, Ill.
Alvaro, Moacyr Eyck, 1151 Rua Consolacoa, São Paulo, Brazil.
de Andrade, Cesario,[2] Bahia, Brazil.
Ames, Adelbert, Jr., Dartmouth College, Hanover, N.H.
Armstrong, Richard C., 595 E. Colorado St., Pasadena 1, Calif.
Ascher, Charles K. W.,[1] 2508 Auburn Ave., Cincinnati, 19, Ohio.
Atkinson, Walter S., 129 Clinton St., Watertown, N.Y.
Auten, Hanford Louis,[1] Dartmouth Eye Institute, Hanover, N.H.

[1] Attended 1948 Meeting
[2] Honorary Member
[3] Life Member
[4] Sustaining Member
[5] Educational Member

B

Bahn, Charles A., 1026 Maison Blanche Bldg., New Orleans, La.
Baird, J. Mason, 511 Medical Arts Bldg., Atlanta, Ga.
Balding, Laurence G., 101 S. Madison, Pasadena 1, Calif.
Barkan, Hans, 2351 Clay St., San Francisco, Calif.
Barkan, Otto, 490 Post St., San Francisco, Calif.
Barnett, Irving F., 30 North Michigan Ave., Chicago, Ill.
Bassen, Edward J., 70 E. 66th St., New York, N.Y.
Beach, S. Judd, 704 Congress St., Portland, Me.
Bedell, Arthur J.,[1] 344 State St., Albany, N.Y.
Beetham, William P., 108 Bay State Rd., Boston, Mass.
Bellows, John, 30 N. Michigan Ave., Chicago 2, Ill.
Benedict, William L., Mayo Clinic, Rochester, Minn.
Benson, Clifton E., 515 Sixth St., Bremerton, Wash.
Berens, Conrad,[1-2] 35 E. 70th St., New York, N.Y.
Bettman, Jerome W., 2400 Clay St., San Francisco, Calif.
Black, Nelson M., 703 Huntington Bldg., Miami, Fla.
Blake, Eugene M., 305 Whitney Ave., New Haven, Conn.
Blum, John, 1 Rue Marignac, Geneva, Switzerland.
Bonner, William R., 3 W. White St., Summit Hill, Pa.
Borley, W. E., 450 Sutter St., San Francisco, Calif.
Bothman, Louis,[1] 30 N. Michigan Ave., Chicago, Ill.
Boyd, James L., 10 Edge Hill Rd., Glen Cove, L.I., N.Y.
Boyes, Truman L., 654 Madison Ave., New York, N.Y.
Braley, Alson E.,[1] 635 W. 165th St., New York, N.Y.

Brandenburg, K. C., 110 Pine Ave., Long Beach, Calif.
Brault, Jules, 418 E. Sherbrooke St., Montreal, Canada.
Bribach, E. J., 603 Commercial St., Atchison, Kan.
Bronk, Henry N., 321 E. Tremont Ave., New York 57, N.Y.
Brown, Albert L., 1137-38 Carew Tower, Cincinnati, Ohio.
Brown, E. V. L.,[1] 122 S. Michigan Ave., Chicago, Ill.
Bruner, Abram B., 1214 Guardian Bldg., Cleveland, Ohio.
Bruner, William E., 1214 Guardian Bldg., Cleveland, Ohio.
Budd, Francis X., 4240 W. 58th St., Cleveland, Ohio.
Buffington, W. R., 1206 Hibernia Bank Bldg., New Orleans, La.
Bulson, Eugene L., 347 W. Berry St., Fort Wayne, Ind.
Burch, Edward P., 424 Hamm Bldg., St. Paul, Minn.
Burch, Frank E., 424 Hamm Bldg., St. Paul, Minn.
Burian, Hermann M., 520 Commonwealth Ave., Boston 15, Mass.
Burke, John W., 1740 M St., N.W., Washington, D.C.
Burr, Sherwood P., Jr.,[5] 1629 Truxtun Ave., Bakersfield, Calif.
Buschke, William H., 138-52 Jewel Ave., Flushing, N.Y.
Byrnes, Victor Allen, 278 W. Wildwood Dr., San Antonio, Tex.

C

Calhoun, F. Phinizy, 478 Peachtree St., Atlanta, Ga.
Callahan, Alston,[1] Dept. of Ophthalmology, University of Alabama Medical College, Birmingham, Ala.
Campion, George Stuart, 490 Post St., San Francisco, Calif.
Carrasquillo, Honorio F.,[1] Medical Arts Bldg., San Juan, Puerto Rico.
Carroll, Frank D., 635 W. 165th St., New York, N.Y.
Cary Edward H., 631 Medical Arts Bldg., Dallas, Tex.
Casten, Virgil C., 412 Beacon St., Boston, Mass.
Castroviejo, Ramon,[4] 9 E. 91st St., New York, N.Y.
Chace, Robert R., 635 W. 165th St., New York 32, N.Y.
Chalfant, W. Paxson, Jr., 1915 Sixteenth St., N.W., Washington, D.C.
Chamberlain, Webb Parks, Jr.,[4] 7405 Detroit Ave., Cleveland, Ohio.
Chandler, Paul A., 5 Bay State Rd., Boston, Mass.
Chan-Pong, Norman Ronald,[4] 88 Frederick St., Port-of-Spain, Trinidad, B.W.I.
Chapman, Vernon A., Palm Springs, Calif.
Clapp, Clyde A.,[1] 513 N. Charles St., Baltimore, Md.
Clark, Cecil P., 23 E. Ohio St., Indianapolis, Ind.
Clark, William B., 200 Carondelet St., New Orleans, La.
Clothier, William L., 407-411 Kane Bldg., Pocatello, Idaho.
Cloutier, Roland, 50 Haven Ave., New York 32, N.Y.
Cogan, David G.,[1] 243 Charles St., Boston, Mass.
Cohen, Martin, 29 E. 64th St., New York, N.Y.
Colson, Z. William, 501 Essex St., Lawrence, Mass.
Constantine, F. H., 17 E. 72nd St., New York, N.Y.
Constantine, K. W., 229 Barton Ave., Palm Beach, Fla.
Cordes, Frederick C., 384 Post St., San Francisco, Calif.
Courtney, R. H., 501 E. Franklin St., Richmond, Va.
Courvoisier, Earl A., 55 E. Washington St., Chicago, Ill.
Covey, John Knox, 140 W. High St., Bellefonte, Pa.
Craig, Paul C., 232 N. 5th St., Reading, Pa.
Crawford, H. C. Orr Doctors Bldg., Atlanta, Ga.
Crawford, Joseph William, 490 Post St., San Francisco, Calif.
Cregar, John S., 440 Harrison St., East Orange, N.J.
Crisp, William H., 1276 Emerson St., Denver, Colo.
Cross, George H., 525 Welsh St., Chester, Pa.
Culler, Arthur M.,[1] 150 E. Broad St., Columbus, Ohio.
Cummings, Mrs. Edith L. W., 429 New Budge Rd., Bergenfield, N.J.
Cushman, Beulah,[1] 25 E. Washington St., Chicago, Ill.
Cutler, Morton, Medical Arts Bldg., Twin Falls, Idaho.

D

Dasilva, Antonio Isidore, Rua Santa Catarina 1011, Belo Horizonte, Minas Gerais, Brazil, South America.
Dean, Alfred, 26 Sheldon Ave., Grand Rapids, Mich.
De Ocampo, Geminiana, Philippine General Hospital, Manila, P.I.
DeVoe, Arthur Gerard, 635 W. 165th St., New York, N.Y.
Dewey, C. H., 760 S. Oak Knoll, Pasadena, Calif.

DeWitt, Edward N., 1600 N.E. 4th Pl., Fort Lauderdale, Fla.
Dickson, Owen C., 2628 Telegraph Ave., Berkeley, Calif.
Dillahunt, Jack A.,[5] University Hospitals, Iowa City, Ia.
Doherty, William B., 150 W. 55th St., New York, N.Y.
Drell, Maurice Joseph, 630 Medical Arts Bldg., Seattle 1, Wash.
Duane, T. D.,[1] 215 S. Dodge St., Iowa City, Iowa.
Duke-Elder, Lady Phyllis,[2] London, England.
Duke-Elder, Sir Stewart,[2] London, England.
Dunnavan, Floyd L., Suite 514 Medical Arts Bldg., Vancouver, Wash.
Dunnington, John H., 635 W. 165th St., New York, N.Y.

E

Ehrenfeld, Edward, 185 Lexington Ave., Passaic, N.J.
Elles, Norma B., 800 Travis St., Houston 2, Tex.
Elliott, Alfred J., 170 St. George St., Toronto 5, Canada.
Ellis, Orwyn H.,[1] 727 W. 7th St., Los Angeles 14, Calif.
Elvin, Norman L., 309 Medical Arts Bldg., Winnipeg, Manitoba, Canada.
Engel, Samuel, 350 Post St., San Francisco, Calif.
Evans, John N., 23 Schermerhorn St., Brooklyn, N.Y.
Evans, Samuel Davidson, 1502 Park Bldg., Pittsburgh, Pa.
Evans, William Hiram, 510 Dollar Bank Bldg., Youngstown, Ohio.

F

Ferrer, Horatio,[2] Havana, Cuba.
Fine, Max, 655 Sutter St., San Francisco 2, Calif.
Fink, Austin I., Valley Forge General Hospital, Phoenixville, Pa.
Fink, Walter H.,[1-4] 1029 Medical Arts Bldg., Minneapolis 2, Minn.
Fonda, Gerald Emmett, Milburn Theater Bldg., 350 Milburn Ave., Milburn, N.J.
Foote, Franklin M.,[1] 1790 Broadway, New York, N.Y.
Fralick, F. Bruce, 408 First National Bank Bldg., Ann Arbor, Mich.
Freeman, Sheldon B., 196 Linwood Ave., Buffalo, N.Y.
Friedenwald, Harry, 1212 Eutaw Pl., Baltimore, Md.
Friedenwald, Jonas S.,[1] 1212 Eutaw Pl., Baltimore, Md.
Friedman, Benjamin, 6 W. 77th St., New York, N.Y.
Fritschi, Ulrich A., 523 Medico-Dental Bldg., Sacramento, Calif.

G

Gallardo, Edward, 2800 Kitchener Ct., Oakland 2, Calif.
Gifford, Harold, 1620 Medical Arts Bldg., Omaha, Neb.
Gill, Earl King, 323 Medical Arts Bldg., San Antonio, Tex.
Gill, William D., 323 Medical Arts Bldg., San Antonio, Tex.
Gillette, David F., 109 S. Warren St., Syracuse, N.Y.
Givner, Isadore, 108 E. 66th St., New York 16, N.Y.
Goar, Everett L.,[1] 1304 Walker Ave., Houston, Tex.
Goldberg, Sol, 8082 Jenkins Arcade, Pittsburgh, Pa.
Goodfellow, Thomas John, 20 Arcade Bldg., Saratoga Springs, N. Y.
Gradle, Harry S., 14060 Valley Vista Blvd., Sherman Oaks, Calif.
Grant, Hendrie W.,[4] 330 Lowry Medical Arts Bldg., St. Paul Minn.
Gray, John Edward, 430 36th St., Sacramento, Calif.
Green, John, 3720 Washington Blvd., St. Louis, Mo.
Gresser, Edward B., 39 E. 75th St., New York, N.Y.
Griffey, Edward W.,[4] 1022 Medical Arts Bldg., Houston, Tex.
Guerry, du Pont, III, 7102 Glen. Pwky., Richmond, Va.
Guibor, George, 30 N. Michigan Ave., Chicago, Ill.
Gundersen, Trygve,[1] 5 Bay State Rd., Boston, Mass.
Guy, Loren P., 40 E. 62nd St., New York, N.Y.
Guyton, Jack S., Johns Hopkins Hospital, Baltimore 5, Md.

H

Haessler, F. Herbert, 561 N. 15th St., Milwaukee, Wis.
Hanson, A. George, 1528 Medical Dental Bldg., Seattle 1, Wash.
Harbridge, Delamere, 12 N. Central Ave., Phoenix, Ariz.
Hardesty, John F., 634 N. Grand Blvd., St. Louis, Mo.
Hardy, LeGrand H., 23 E. 79th St., New York, N.Y.
Hare, Robert, 416 N. Bedford Dr., Beverly Hills, Calif.

Harley, Halvor L., 101 S. Indiana Ave., Atlantic City, N.J.
Harley, Robison D., 101 S. Indiana Ave., Atlantic City, N.J.
Harrington, David O., 384 Post St., San Francisco 8, Calif.
Hartenbower, G. E.,[1-4] 410 Unity Bldg., Bloomington, Ill.
Hartman, Deane C., 727 W. 7th St., Los Angeles 14, Calif.
Hartshorne, Isaac, 30 W. 59th St., New York, N.Y.
Heare, Louis C.,[1] Box 312, Room 221, Bluestein Bldg., Port Arthur, Tex.
Heath, Parker,[1] 243 Charles St., Boston, Mass.
Heitger, Joseph D., 701 Heyburn Bldg., Louisville, Ky.
Henderson, John W.,[1] University Hospital, Ann Arbor, Mich.
Henderson, Lawrence E., 139 Clinton St., Watertown, N.Y.
Hendy, Margaret, 384 Post St., San Francisco 8, Calif.
Hildreth, H. Rommel, Metropolitan Bldg., St. Louis, Mo.
Hilgartner, H. L., 202 W. 13th St., Austin, Tex.
Hill, Howard F., Professional Bldg., Waterville, Me.
Hogan, Michael J., 450 Sutter St., San Francisco, Calif.
Holmes, Dorothy B.,[1] 1816 R St., N.W., Washington 9, D.C.
Holmes, William John, 45 Young Bldg., Honolulu, Hawaii.
Holstein, Theodore, 411 Medico-Dental Bldg., Sacramento 14, Calif.
Holzer, William F., 36 Pleasant St., Worcester, Mass.
Hosford, George N., 450 Sutter St., San Francisco, Calif.
Howard, Harvey J., Park Plaza Hotel, St. Louis, Mo.
Howell, Homer P., 3022 E. 14th St., Oakland, Calif.
Hughes, William F., Jr.,[1] 536 Sheridan Rd., Evanston, Ill.

I

Imus, Henry A., Lt. Comdr.,[1] 907 Crescent Dr., Alexandria, Va.
Ingalls, Raymond George, 635 W. 165th St., New York, N.Y.
Irvine, Rodman,[4] 9730 Wilshire Blvd., Beverly Hills, Calif.
Irvine, Wendell C., 13485 Contour Dr., Sherman Oaks, Calif.

J

Jacobs, Clyde H., George F. Geisinger Memorial Hospital, Danville, Pa.
Jakobovits, Rafael, 655 Sutter St., San Francisco, Calif.
James, William M., 508 N. Grand Ave., St. Louis, Mo.
Jensen, Carl D. F., Medical-Dental Bldg., Seattle 1, Wash.
Johns, Juanita P., 313 Commonwealth Ave., Boston, Mass.
Johnson, Lorand V.,[1-4] Carnegie Medical Bldg., Cleveland, Ohio.
Judd, John Hewitt,[1] 1020 Medical Arts Bldg., Omaha, Neb.

K

Kahler, Arthur R., 1422 40th St., Sacramento, Calif.
Katz, Dewey, 99 Pratt St., Hartford, Conn.
Key, S. N. Jr., 120 W. 7th St., Austin, Tex.
Kilgore, George L., 411 Thorn St., San Diego 3, Calif.
Kinsey, V. Everett,[1] 243 Charles St., Boston, Mass.
Kirby Daniel B.,[1-4] 780 Park Ave., New York, N.Y.
Knapp, Arnold, 10 E. 54th St., New York N.Y.
Knapp, Arthur A., 112 E. 73rd St., New York, N.Y.
Knighton, Willis S., 121 E. 61st St., New York, N.Y.
Koch, F. L. Philip, 60 E. 75th St., New York, N.Y.
Kornzweig, Abraham L., 1200 Fifth Ave., New York, N.Y.
Krause, Arlington C.,[1] 950 E. 59th St., Chicago, Ill.
Kronfeld, Peter C.[1] 904 W. Adams St., Chicago 7, Ill.
Krug, Joseph H., 988 Fifth Ave., New York 21, N.Y.
Kuhn, Hedwig Steiglits, 60 Glendale Park, Hammond, Ind.

L

Lancaster, Walter B., 520 Commonwealth Ave., Boston, Mass.
Lang, Louis R., 555 Park Ave., New York, N.Y.
Larkin, Bernard J.,[1] 23 E. Ohio St., Indianapolis, Ind.
Last, Murray A., 1095 Park Ave., New York, N.Y.
Lee, Otis S., Jr., University Hospitals Iowa City, Iowa.
Leinfelder, P. J.,[1] University Hospitals, Iowa City, Iowa.
Lemoine, Albert N., 1100 Realton Bldg., Kansas City, Mo.
Leopold, Irving Henry,[1] 1930 Chestnut St., Philadelphia, Pa.

Lepard, C. W., 1025 Whitney Bldg., Detroit, Mich.
Lerner, Macy L., 332 Park Ave., Rochester, N.Y.
Levey Mark R., Wells Pavilion, University Hospital, Edmonton, Alberta, Canada.
Levy, Abram, 1401 Plainfield Ave., S., Plainfield, N.J.
LeWin, Thurber, 112 Linwood Ave., Buffalo, N.Y.
Lewis, Philip M., Exchange Bldg., Memphis, Tenn.
Liebman, Sumner D., 115 Bay State Rd., Boston, Mass.
Linn, Jay G., Jr.,[1] 7075 Jenkins Arcade, Pittsburgh 22, Pa.
Linn, Jay G., Sr.,[1] 7075 Jenkins Arcade, Pittsburgh 22, Pa.
Lipp, Frank E., 516 Medical Arts Bldg., Omaha 2, Neb.
Little, Milton F., 49 Pearl St., Hartford, Conn.
Lloyd, Ralph I., 14 Eighth Ave., Brooklyn, N.Y.
Loutfallah, Michel, 1826 State St., Santa Barbara, Calif.
Luedde, Philip S., 310 Metropolitan Bldg., St. Louis, Mo.
Luedde, William H., 508 N. Grand Blvd., St. Louis, Mo.
Lutman, Frank C., Germantown Professional Bldg., Greene and Coulter Sts., Philadelphia 44, Pa.
Lyle, Donald J., 601 Union Trust Bldg., Cincinnati, Ohio.

M

McAlester, A. W., III,[1] 2003 Bryant Bldg., Kansas City, Mo.
McAlpine, Paul T., 129 Summit Ave., Summit, N.J.
McBain, Earle H., 490 Post St., San Francisco, Calif.
McCulloch, Clement,[1] 830 Medical Arts Bldg., Toronto, Canada.
McDonald, Philip Robb,[1] 1930 Chestnut St., Philadelphia 3, Pa.
McGarvey, William E.,[1] 802 Jackson City Bank Bldg., Jackson, Mich.
McGavic, John S., 132 Morris Ave., Bryn Mawr, Pa.
McGuire, H. H., 105 N. Braddock St., Winchester, Va.
McGuire, William P., 105 N. Braddock St., Winchester, Va.
McKay, Edward Danson, Scott and White's Clinic, Temple, Tex.
McKee, Joseph W., 1105 Grand Ave., Kansas City, Mo.
McMurray, John B., 6 S. Main St., Washington, Pa.
McRae, John H., Medical Arts Bldg., Grand Rapids, Mich.
MacDonald, Alexander, 10 Edgar Ave., Toronto, Canada.
MacLean, Angus L., 1201 N. Calvert St., Baltimore, Md.
Macnie, John P., 635 W. 165th St., New York 32, N.Y.
Madeley, H. Randall,[4] 727 Sonoma St., Vallejo, Calif.
Magee, George R., 1311 Hillside Dr., Reno, Nev.
Mann, William Alfred,[2] 30 N. Michigan Ave., Chicago 2, Ill.
Masters, Robert J.,[1] 805 Hume-Mansur Bldg., Indianapolis 4, Ind.
Matthews, John S., 929 Nix Professional Bldg., San Antonio, Tex.
Mesirow, M. E.,[4] 117 E. Cook St., Santa Maria, Calif.
Meyer, Samuel J., 58 E. Washington St., Chicago, Ill.
Miller, Miriam,[1] 350 Post St., San Francisco 8, Calif.
Miles, Paul W.,[1] 640 Kingshighway, St. Louis 10, Mo.
Mills, Lloyd, 609 S. Grand Ave., Los Angeles, Calif.
Minnes, James F., 825 Granville St., Vancouver, B.C.
Minsky, Henry, 2 E. 95th St., New York, N.Y.
Moncreiff, William F.,[1] 58 E. Washington St., Chicago, Ill.
Moore, Paul G., 1701 Republic Bldg., Cleveland, Ohio.
Morrison, W. Howard,[1] 1500 Medical Arts Bldg., Omaha, Neb.
Motto, Paul, 650 Rose Bldg., Cleveland, Ohio.
Mullen, Carroll R., 0225 Locust St., Philadelphia 3, Pa.
Myers, Roscoe W., 36 Pleasant St., Worcester, Mass.

N

Nethercut, Glenway, 25 E. Washington St., Chicago, Ill.
Newell, Frank W.,[1] 30 N. Michigan Ave., Chicago 2, Ill.
Norene, Robert A., 727 W. 7th St., Los Angeles 14, Calif.
Nugent, Maurice W., 2007 Wilshire Blvd., Los Angeles 5, Calif.

O

Oaks, Lewis W., 677 N. University Ave., Provo, Utah.
O'Brien, Cecil S., University Hospitals, Iowa City, Iowa.
Odom, Robert E., 510 Dollar Bank Bldg., Youngstown, Ohio.

Ogle, Kenneth N., (Ph.D.), Mayo Clinic, Division of Physics and Biophysical Research, Rochester, Minn.
Ohly, John H., 22 Schermerhorn St., Brooklyn, N.Y.
O'Rourke, Donald H., 920 Republic Bldg., Denver 2, Colo.
Osler, Jay Kershner, 150 State. St., Bangor, Me.
Owens, William C., Johns Hopkins Hospital, Baltimore 5, Md.

P

Parker, Walter R.,[2] 1551 Woodward Ave., Detroit, Mich.
Paton, Leslie,[2] London, England.
Paton, R. Townley, 927 Park Ave., New York, N.Y.
Paul, Thomas O., 2205 Highland Ave., Birmingham 5, Ala.
Payne, Brittain F.,[1-4] 17 E. 72nd St., New York, N.Y.
Perera, Charles A., 70 E. 66th St., New York, N.Y.
Pfingst, Harry Adolph, 1014 E. 102nd St., Cleveland, Ohio.
Phillips, Josephine Dirion, 2010 E. 102nd St., Cleveland, Ohio.
Pichette, Henri, 425 St. John St., Quebec City, Quebec, Canada.
Pischel, Dohrmann K.,[4] 490 Post St., San Francisco, Calif.
Plumer, John S., 121 University Pl., Pittsburgh, Pa.
Post, Lawrence T.,[1] 508 N. Grand Blvd., St. Louis, Mo.
Post, Martin Hayward, Jr.,[1] 520 Metropolitan Bldg., St. Louis, Mo.
Potter, William Bentley,[1] 816 Strand, Galveston, Tex.
Prangen, Avery D.,[1] Mayo Clinic, Rochester, Minn.

R

Raffo, Julio C., Gremios No. 465, Lima, Peru, South America.
Rasgorshek, Robert H.,[1] 425 Aguila Court, Omaha, Neb.
Reeder, James E., Jr., 523 Davidson Bldg., Sioux City 13, Iowa.
Redding, Willis A., Towanda, Pa.
Reeh, Merrill John, 4212 N.E. Broadway, Portland 10, Ore.
Reese, Algernon B.,[1-4] 73 E. 71st St., New York, N.Y.
Regan, James J., 520 Commonwealth Ave., Boston, Mass.
Reid, Frederick K., 500 N. George St., Rome, N.Y.
Reid, Horace W., 2205 Union Central Bldg., Cincinnati, Ohio.
Reid, John J., Jr., 105 E. 63rd St., New York 21, N.Y.
Rigg, James P., 521 Rood Ave., Grand Junction, Colo.
Robbins, Alfred R., 1930 Wilshire Blvd., Los Angeles, Calif.
Roberts, Walter L.,[1] 8225 Ramsgate, Los Angeles, Calif.
Rodin, Frank H., 490 Post St., San Francisco, Calif.
de Roetth, Andrew F. M.,[1-4] 1006 Overbluff, Spokane, Wash.
Romaine, Hunter, 111 E. 65th St., New York, N.Y.
Romejko, Walter J., 1810 K St., N.W., Washington 6, D.C.
Rones, Benjamin, 1601 Eye St., N.W., Washington, D.C.
Roper, Kenneth Lawrence,[1] 58 E. Washington St., Chicago, Ill.
Rosenthal, Benjamin C., 140 New York Ave., Brooklyn, N.Y.
Rosner, Robert Samuel,[1] 10300 Carnegie, Cleveland 6, Ohio.
Ross, Cecelia, 1318 Second St., Santa Monica, Calif.
Row, Hamilton D., 906 Hume-Mansur Bldg., Indianapolis, Ind.
Rowland, Louise Sloan, Wilmer Institute, Johns Hopkins Hospital, Baltimore, Md.
Rowland, William M., 1118 St. Paul St., Baltimore, Md.
Ruedemann, A. D., Wayne University, Detroit, Mich.
Rutherford, Cyrus W.,[3] 4601 N. Pennsylvania St., Indianapolis, Ind.
Ryan, William F., 520 Commonwealth Ave., Boston, Mass.
Rychener, Ralph Orlando,[1-4] 130 Madison Ave., Memphis, Tenn.

S

Sachs, Erich,[1] 913 W. Agatite St., Chicago, Ill.
Samuels, Bernard, 57 W. 57th St., New York, N.Y.
Sanders, T. E.,[1] 508 N. Grand Blvd., St. Louis, Mo.
Scala, Norman Philip, 1201 Nineteenth St., N.W., Washington, D.C.
Schachat, Walter S., 30 E. 60th St., New York, N.Y.
Scheie, Harold G.,[1] 313 S. 17th St., Philadelphia 3, Pa.

Schlaegel, Theodore F., Jr.,[1] Indiana University Medical Center, Indianapolis, Ind.
Schmerl, Ernest,[1] Toledo Hospital, Institute of Medical Research, 2805 Oatis Ave., Toledo, Ohio.
Scholz, Roy O., 11 E. Chase St., Baltimore, Md.
Schultz, Jacob F., 1304 Walker Ave., Houston, Tex.
Schuster, Stephen A., First National Bank Bldg., El Paso, Tex.
Scobee, Richard G., 640 S. Kingshighway, St. Louis, Mo.
Schaffer, Robert N., 490 Post St., San Francisco 2, Calif.
Shahan, Philip T., 508 N. Grand Blvd., St. Louis 3, Mo.
Shahan, William E., 508 N. Grand Blvd., St. Louis 3, Mo.
Shannon, C. E. G., 1930 Chestnut St., Philadelphia, Pa.
Shapira, Theodore,[1-4] 109 N. Wabash Ave., Room 1920, Chicago, Ill.
Sharbaugh, George B., 212 W. State St., Trenton, N.J.
Sheard, Charles, Mayo Clinic, Rochester, Minn.
Sheppard, L. Benjamin,[4] Medical Arts Bldg., Richmond, Va.
Sherman, A. Russell, 671 Broad St., Newark, N.J.
Sherman, Elbert S., 671 Broad St., Newark, N.J.
Siegel, Edward, 45 Oak St., Plattsburgh, N.Y.
Simonton, John T., 108-41 63rd Dr., Forest Hills, L.I., N.Y.
Sitchevska, Olga, 30 Fifth Ave., New York, N.Y.
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Sloan, Henry L., 6 W. 7th St., Charlotte, N.C.
Smith, Byron, 927 Park Ave., New York, N.Y.
Smith, E. Gerard, 339 N. Duke St., Lancaster, Pa.
Smith, E. Terry,[4] P.O. Box 42, West Hartford, Conn.
Smith, Hiram J., 30 N. Michigan Ave., Chicago, Ill.
Smith, Homer E., 54 E. S. Temple St., Salt Lake City 1, Utah.
Smith, James W., 1016 Fifth Ave., New York 28, N.Y.
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Snell, Albert C., 53 S. Fitzhugh St., Rochester, N.Y.
Sommers, Ignatius G., 981 S. Westmoreland Ave., Los Angeles 6, Calif.
Spaeth, Edmund B., 1930 Chestnut St., Philadelphia, Pa.
Spiegelglass, A. B., 417 Main St., Hackensack, N.J.
Steinberg, Bernhard, Toledo Hospital Institute of Research, 2805 Oatis Ave., Toledo, Ohio.
Steinberg, Theodore, 603 Patterson Bldg., Fresno, Calif.
Stevens, Ralph W., Baker Bldg., Walla Walla, Wash.
Stine, George H., 304 Burns Bldg., Colorado Springs, Colo.
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Swab, Charles M., 1316 Medical Arts Bldg., Omaha, Neb.
Swan, Kenneth C.,[1] University of Oregon Medical School, Marquam Hill Rd., Portland, Ore.

T

Tait, Edwin Forbes,[1] 1324 W. Main St., Morristown, Pa.
Tanner, Owen R., 300 Homer Ave., Palo Alto, Calif.
Tassman, Isaac S.,[1] 712 Medical Arts Bldg., Sixteenth and Walnut Sts., Philadelphia, Pa.
Taylor, E. Merle,[4] 1020 S.W. Taylor, Portland, Ore.
Theobald, G. D., 715 Lake St., Oak Park, Ill.
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V

Vail, Derrick,[1] 700 N. Michigan Ave., Chicago, Ill.
Van Poole, G. M., 45 Young Bldg., Honolulu, Hawaii.
Vanzant Thomas J.,[4] 2233 N. MacGregor Dr., Houston, Tex.
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W

Waldman, Joseph, 1930 Chestnut St., Philadelphia 3, Pa.
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Weih, Elmer P.,[1] 605 Wilson Bldg., Clinton, Iowa.
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Z

Zekman, Theodore N.,[1] 58 E. Washington St., Chicago, Ill.
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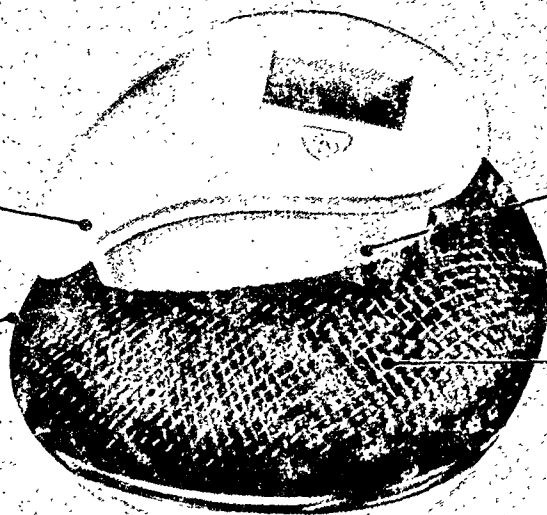
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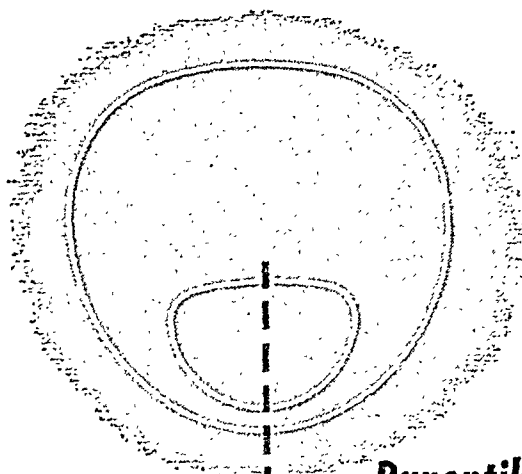
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Lenses that have been heat treated to increase their resistance to impact have been widely used by industry. In many plants, the use of case hardened lenses is compulsory and has resulted in a sharp drop in the number of eye injury cases.

We feel that case hardened lenses should be used more widely for general wear especially for children and for grown-ups who go in for sports, handball for example, where a splintered lens could result in serious injury.

It may be interesting to see what goes into the making of hardened lenses. To start with the lens to be treated must be at least 2.8 mm. at its thinnest point. 3.0 mm. or 3.4 mm. minimum thickness is better because a more resistant lens results.

The lens is placed in a furnace and heated almost to the softening point. This point is critical and must be controlled exactly because if heated above the softening point, it would sag and distort; if heated below its strain point, no marked increase in impact resistance would result.

When the lens is at exact temperature a cold air blast is turned on both sides of the lens simultaneously. The cold air blast contracts the glass on the surface and sets up stresses on the surface which are relieved in the core. The result is a high state of compression on the surface of the glass.

A lens so treated will easily withstand the standard test for hardened lenses which consists of dropping a steel ball, weight 1.56 ounces, from a height of 1 meter.

As pointed out earlier, it is necessary for a lens to be at least 2.8 mm. thick at its thinnest point. This minimum thickness gives the necessary volume to incorporate the stresses. So it becomes evident that case hardened lenses will be much too heavy for high minus or plus corrections. If these high plus or minus cases must have a safety lens it is better to prescribe a laminated glass. For most corrections, however, the case hardened lens works very well and in the case of the active child is almost a necessity.

"IF IT'S A LENS PROBLEM, LET'S LOOK AT IT TOGETHER"

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Frontispiece illustrating article by Jonas S. Friedenwald

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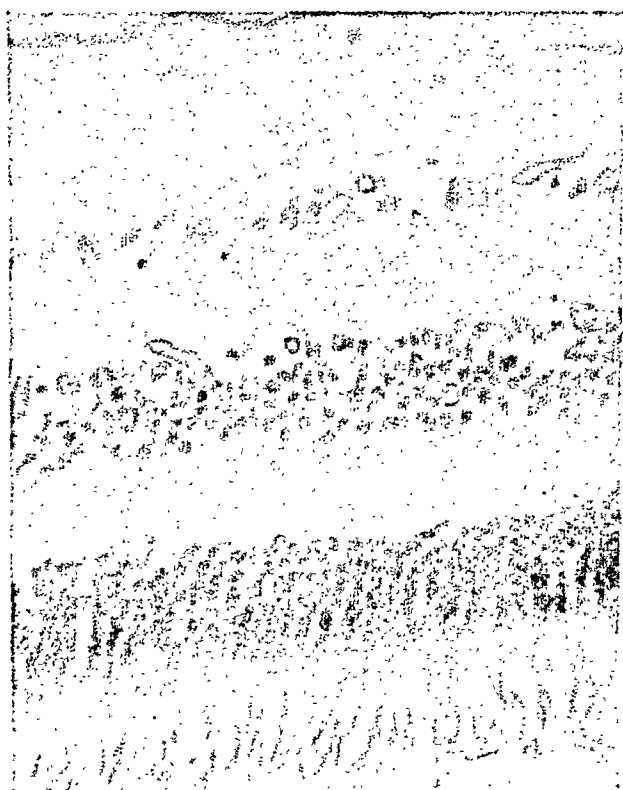
FIG. 1 (FRIEDENWALD), SECTION OF RETINA STAINED WITH HOTCHKISS STAIN AND HEMATOXYLIN,

A NEW APPROACH TO SOME PROBLEMS OF RETINAL VASCULAR DISEASE*

THE JACKSON MEMORIAL LECTURE

JONAS S. FRIEDENWALD, M.D.
Baltimore, Maryland

I am deeply grateful for the honor and privilege of delivering the Jackson Memorial Lecture. The memory of Dr. Jackson's commanding personality is an inspiration to all of us. His teachings and the JOURNAL which he founded and edited are still a most potent force in American ophthalmology. Within the domain of our science the problems of refraction engaged his deepest interest. Next to these, in his heart, came those of medical ophthalmology. The subject that I have chosen to present is, therefore, one in which I believe he would have been interested.

The problems of retinal vascular disease can be approached from one or the other of two very different viewpoints. One can ask oneself what are the systemic lesions and symptoms that are correlated with a given ophthalmoscopic picture, or one can ask oneself what precisely are the changes in the retinal blood vessels that are responsible for this or that ophthalmoscopic finding.

It is to the second of these questions that I wish to invite your consideration. In the past our studies in this field have been handicapped by considerable technical difficulties. We see a particular type of exudate or hemorrhage in the retina, either ophthal-moscopically or histologically, but the precise point in the vascular tree from which the exudation or hemorrhage arose usually escapes us. Even when we reconstruct in serial sections the neighborhood of a lesion, we can only rarely be sure of the interrelations of our findings.

It has seemed to me, for a long time that, if we could visualize the blood-vessel walls in preparations of the whole unsectioned retina, some interesting patterns of relationships might emerge into view. By great good fortune a suitable technique has become available for this purpose, and I wish to devote this lecture to showing you some of the first fruits of its application.

The development of this technique was in some respects a happy accident, and I should like to tell you the story of how it came about in the hope that you may catch some of the excitement that we experienced, for we started this study as a routine systematic survey, not primarily directed toward retinal vascular disease.

During the last 20 years there has been a steady unfolding of techniques in the field of histochemistry; that is, the techniques by which specific chemical components of the cells and tissues can be recognized in histologic sections. This field has been expanding at an accelerated pace in the last few years, and has been given a more or less definitive pattern by the systematic studies of Wislocki[3] and his colleagues at Harvard.

They have applied one technique after an-

other to one tissue after another and have published comprehensive reports on their findings. Since their studies did not include the ocular tissues, it seemed desirable to follow their footsteps on the material that was readily available in the laboratory for pathology of the Wilmer Institute.

The first technique that we chose to apply was one for the demonstration of fixed carbohydrate that had recently been greatly refined by Hotchkiss[5] and by McManus.[8,9] The technique is simple and easily within the reach of any histologic laboratory. I shall not burden you with the chemical details (see Appendix). With this technique any cellular component that contains carbohydrate is stained red. One can counterstain with hematoxylin so that the general histologic architecture has an approximately familiar pattern, but instead of the usual undifferentiated red of eosin stain only those places in the tissue that contain glycogen, or mucoids, or glucoproteins stain red.

The application of this technique to ocular tissues reveals many points of interest. The mucus in the conjunctival goblet cells and in other mucous glands is brilliantly stained. The elastic membranes of Descemet and Bruch and the lens capsule stain intensely. In the ciliary processes a subepithelial basement membrane is easily demonstrable by this technique, although the presence of such a membrane has been debated by histologists for years. The superficial layer of the ciliary epithelium contains heavy deposits of stainable material, strongly suggesting this as the site of synthesis of the vitreous mucoid. As in other organs, all connective tissue stains faintly but definitely with this technique revealing the presence of mucoid in the ground substance of the connective tissue.

The retina is of particular interest (fig. 1). The internal limiting membrane stains brilliantly showing that this structure is a definite entity and not merely a condensation at the vitreous surface, as has been supposed by some authors. The peripheral portions of the rods and cones contain stainable material which may, perhaps, have an important role in the function of these organs as photoreceptors.

What is particularly striking in the retina is the fact that the endothelium of the whole vascular tree, arteries, capillaries, and veins, is surrounded by a brilliantly stained basement membrane. The presence of this vascular basement membrane can be recognized in some other tissues, but in organs with a connective-tissue stroma it merges into the diffusely staining ground substance of the connective tissue. The existence of a capillary basement membrane in the kidney glomerulus, is, however, well established. Whether such a membrane is demonstrable in all tissues remains still an open question. At any rate the retina is a most favorable tissue for the study of this structure.

The basement membrane is continuous with the internal elastic lamella of the arteries. In arterioles lacking the elastic lamella, the basement membrane is prominently visible and appears to surround individual muscle fibers. In the capillaries it is thinner than in the arterioles but still brilliantly visible. In the venules it is thicker than in the capillaries, but usually less thick than in arterioles of equal size. Since the parenchyma of the retina normally contains no other structures that stain with this technique, it seemed possible that we might with this technique obtain a view of the whole retinal vascular pattern in unsectioned flat preparations of the whole thickness of the retina.

The modifications in the histologic technique required to accomplish this purpose were worked out in our laboratory by Dr. Bernard Becker (see Appendix), and the applications of this technique to various pathologic problems has been pursued in collaboration with Dr. Robert Day. The specimens were prepared with great skill by Miss Sylvia Sigelman and Mrs. Mary Tracey. I am deeply indebted to all of them for their important contribution to this study, and

also to Mr. Delbert Parker for the beautiful photomicrographs which he has made.

The vascular pattern which this technique reveals varies in different portions of the retina. The perifoveal capillary ring (fig. 2) familiar from entoptic studies is well shown. In the region close to the optic disc there are two capillary nets, one in the nerve-fiber layer showing a more or less rectangu-

Fig. 2 (Friedenwald). Flat preparation of normal retina showing the perifoveal capillary net.

lar or bricklike pattern with the long axis parallel to the direction of the nerve-fiber bundles (fig. 3) and a deeper more irregular net lying mainly in the level of the inner nuclear layer (fig. 4). In the periphery of the retina only the deeper layer persists, and here an avascular zone surrounding the terminal arterioles and venules is often visible (fig. 5).

In infants up to two years of age the retinal vascular basement membrane is much thinner and less easily seen than in adults (fig. 6). In the fetus one month premature, the basement membrane is visible only in the larger vessels, not at all in the capillaries (fig. 7). It is not possible to say

Fig. 3 (Friedenwald). Normal retina. Capillary net in the nerve-fiber layer near the optic disc.

whether the membrane is nonexistent in the fetal capillaries, or merely so thin and delicate as to be invisible. What is of some interest is that the stainability of the mem-
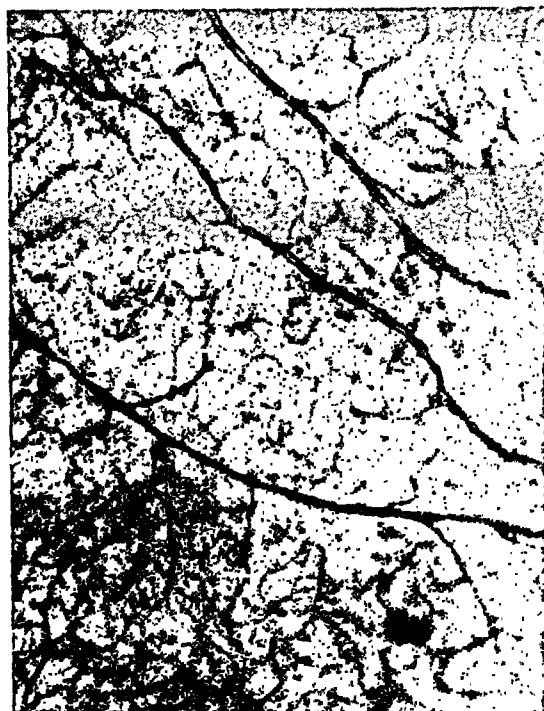
Fig. 4 (Friedenwald). Normal retina. Capillary net in the layer of bipolar cells.

Fig. 5 (Friedenwald). Normal retina. Capillary net in the periphery of the retina.

brane appears to be related to the age of the individual rather than to the age of the capillary, for newly formed capillaries, for in-
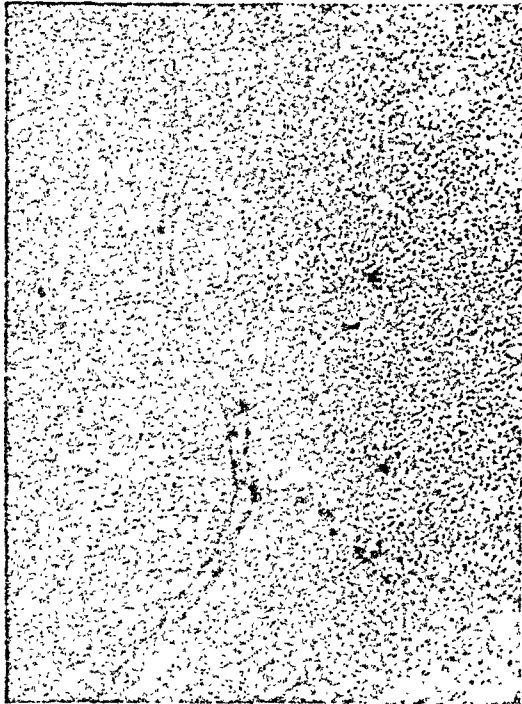
Fig. 6 (Friedenwald). Normal retina from a two-year-old infant. Note the feeble development of the vascular basement membrane.

stance in retinitis proliferans, show a well-developed basement membrane in the adult.

DIABETIC RETINOPATHY

The first pathologic problem that we have attacked with this technique is that of diabetic retinitis. Before showing you the re-

Fig. 7 (Friedenwald). Normal retina from a stillborn infant one month premature. Note that the capillary basement membrane is not visible.

sults of this study, I must ask your indulgence to allow me to correct an error which I made in this matter a number of years ago. In a paper which I presented to the scientific session of this society in 1936, I reported a study on diabetic retinitis which revealed that patients suffering from this condition quite regularly showed an increased capillary fragility. This finding has been abundantly confirmed by others.

A series of these patients whom I studied all failed to excrete in their urine any considerable quantities of vitamin C even when enormous amounts of this material were ingested. I concluded that these patients had an abnormality in their vitamin-C metabolism, and that this might be related to their

abnormal capillary fragility and to their retinal hemorrhages. This conclusion was mistaken.

As soon as methods were available for the study of the plasma vitamin-C level, it was found that these patients had, for the most part, quite normal plasma levels, and that their failure to excrete the vitamin was merely due to abnormally high renal thresholds. Fortunately the error was detected between the time of the delivery of my paper and the subsequent publication of the *Transactions,* whose editor kindly consented to allow the paper to be suppressed.

The reason why these patients commonly have a high renal threshold for vitamin C, and also for glucose, will become apparent in the further discussion, but there is no evidence that vitamin C is in any direct way concerned in the vascular lesion.

In the study of the retinal lesions which I presented at that time, it was possible to show that some of the small red spots which we observe ophthalmoscopically in these cases are not petechial hemorrhages as they appear to be, but are actually small capillary aneurysms, and can be recognized as such in serial sections. The existence of these capillary aneurysms was subsequently more elegantly demonstrated by Ballantyne and Loewenstein.[2] It has remained unclear, however, whether these aneurysms occur primarily as such without rupture of the capillary wall, or whether they begin as minute petechiae which are subsequently grown over by endothelium. Also the relation of these aneurysms to the exudates and to the frank hemorrhages has remained obscure.

Flat preparations of the retina in cases of diabetic retinitis show great numbers of capillary aneurysms (fig. 8). These aneurysms always have both an afferent and an efferent connection, and are, therefore, true aneurysmal dilatations, not endothelialized petechiae which would be connected to the vascular tree by a single channel. In some capillaries tiny knuckles can be seen in the walls, possibly representing the first stage of
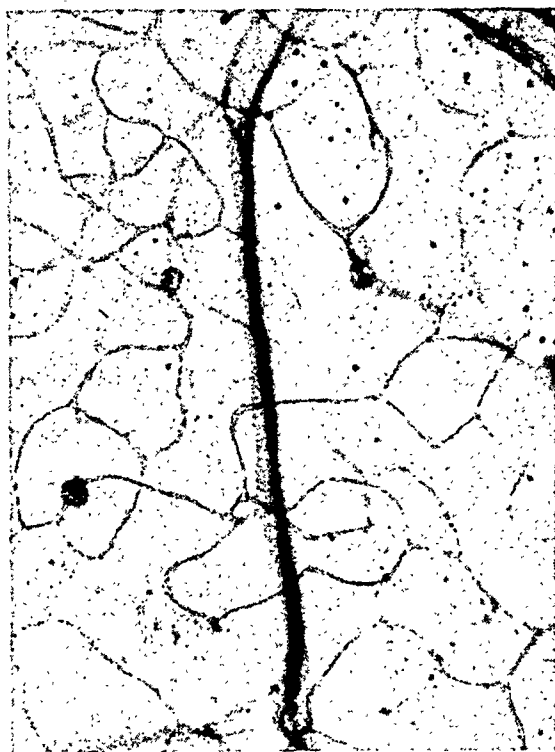
Fig. 8 (Friedenwald). Diabetic retinitis with capillary aneurysms.

aneurysm formation. The aneurysms are most frequent in the central retinal region but occasionally can be found even quite far out in the periphery.

Very commonly there is a cluster of exudates in the retina surrounding the aneurysms (figs. 9 and 10). These exudates usually lie in the outer fibrillar layer while the aneurysms are usually in the inner nuclear layer, but they surround the aneurysms so frequently as to suggest that they are formed by leakage of plasma from the aneurysmal wall. Frequently also there are frank hemorrhages in the tissue adjacent to the aneurysms (fig. 11). I do not wish to imply that hemorrhages and exudates in these cases arise only from the aneurysms, but merely that the majority do arise in this fashion.

Similar capillary aneurysms are occasionally seen in cases of retinal vascular disease in nondiabetics, but they are quite rare and when they occur we have, so far, found not more than 2 or 3 of them in a whole retina. In the diabetic retinopathy the aneurysms

Fig. 9 (Friedenwald). Diabetic retinitis. Cluster of exudates surrounding a capillary aneurysm.

are regularly present by dozens, sometimes by hundreds, and their pattern with the surrounding exudates and hemorrhages, ap-

pears, so far, to provide a characteristic picture. Up to the present we have concentrated our attention on advanced cases of retinitis in long-standing diabetics. It will be interesting to trace the early stages of this disease process.

Many of the aneurysms show thickened walls (figs. 12, 13, and 14), intensely stained by the histologic procedure that we have used, and sometimes these thickened walls show concentric lamellae as if successive layers of the material had been laid down. In some, the process seems to have reached complete occlusion of the aneurysmal cavity.
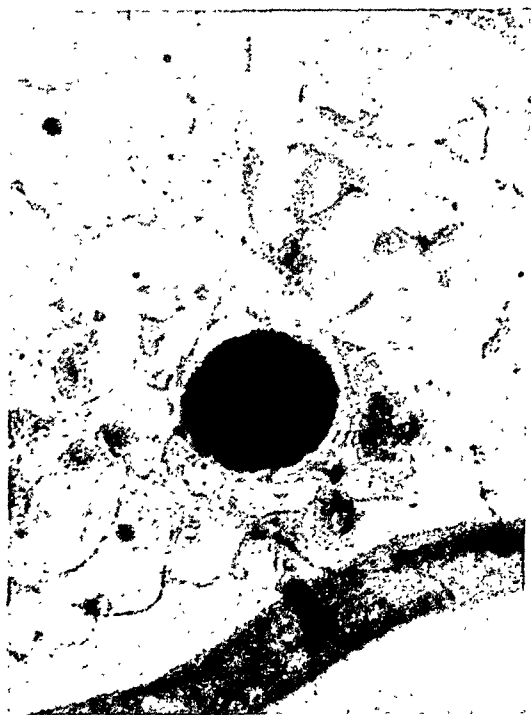
Fig. 11 (Friedenwald). Diabetic retinitis. Hemorrhages and exudates surrounding a capillary aneurysm.

Fig. 10 (Friedenwald). Diabetic retinitis. Cluster of exudates surrounding a capillary aneurysm.

Once recognized, these aneurysms with thickened walls can also be found in ordinary histologic sections in which the material composing the thickened walls has the histologic characteristics of hyalin. At first sight one would mistake these lesions for venules with hyalinized walls, but they are found in the inner nuclear layer where veins of this size are normally absent. If similar lesions should occur in other organs

they would, no doubt, be difficult to identify without serial sections, and careful reconstruction of the vascular pattern.

It is to be remembered, however, that in 1936 Kimmelstiel and Wilson[7] described a form of "intercapillary glomerular sclerosis" which they believed was characteristic of the diabetic nephropathy. In its most outspoken

Fig. 12 (Friedenwald). Diabetic retinitis. Capillary aneurysms with thickened walls.

form the lesion consists of globular masses of hyalin material lying within the glomerular tuft. Often these globular masses show concentric lamellation. In this outspoken form, the lesion occurs almost exclusively in longstanding diabetics and, as Wagener[4] and others have shown, is very commonly associated with diabetic retinitis. In our own material we have found innumerable retinal capillary aneurysms in every case of outspoken Kimmelstiel-Wilson nephropathy that we have so far studied.

When kidney sections showing the Kimmelstiel-Wilson lesion are stained for carbohydrate with the Hotchkiss technique, the characteristic hyalin nodules stain intensely red and strongly suggest the appearance of

Fig. 13 (Friedenwald). Diabetic retinitis. Capillary aneurysms with thickened walls.

the thickened walls of the retinal capillary aneurysms.

Moreover, Allen,[1] who has given the most detailed histologic analysis of the Kimmel-

Fig. 14 (Friedenwald). Diabetic retinitis with capillary aneurysms, some with thickened walls.

stiel-Wilson lesion, points out that the characteristic hyalin nodules are often associated with what he described as markedly dilated capillaries packed with red blood cells. One is tempted to suspect that these so-called dilated capillaries are, in fact, capillary aneurysms, and we have undertaken the tedious process of serial reconstruction of these lesions in order to find out whether or not this is in fact true.

Unfortunately we cannot simply stain sections of kidney with the Hotchkiss stain and thus reveal the capillary pattern. In the kidney there are tubular and glomerular basement membranes which stain very intensely and obscure the capillary pattern even in the normal glomerulus.

It would be incorrect for me to leave you with the impression that pathologists are in general agreement over the interpretation of the lesions which Kimmelstiel and Wilson were the first to describe. In the glomerules of cases showing the typical nodular masses of hyalin, one commonly finds in addition irregular hyalin thickenings of the capillary wall and hyalin sheets or bands lying between capillaries. These nonnodular lesions are, however, found also in a great many nondiabetic cases of nephrosclerosis and chronic glomerulonephritis.

Those pathologists whose attention has been focused on the nonnodular lesion have argued strongly that there is nothing about this lesion that is specific of the diabetic, and have tended to belittle the significance of the nodular lesions as presenting merely an accidental configuration of nonspecific significance. The argument, both pro and con, has recently been reviewed by Kimmelstiel and Porter.[6]

If, however, it should be found that the nodular lesions represent occluded capillary aneurysms, then the nodular configuration would bring the renal lesion into close relation with that which is so characteristically found in the retina. If it should be proved that the Kimmelstiel-Wilson lesion in the kidney and the capillary aneurysms in the retina are, in fact, manifestations of the same vascular process, then we shall have to search for similar changes in other organs.

These are, however, questions which only the future can decide. In any case, the evidence we have so far accumulated strongly supports the conclusions of Ballantyne that capillary aneurysms are a characteristic feature of diabetic retinopathy and quite characteristically distinguish this disease from the retinopathy of arteriosclerosis or of malignant hypertension.

COTTON-WOOL SPOTS

The second pathologic problem to which we have applied this technique is that of the so-called cotton-wool spots so commonly seen in the retinitis of malignant hypertension. These are white spots of fuzzy outline, generally about one fifth the diameter of the optic disc in size. They are seen only in the posterior pole of the retina and plainly lie in the retinal nerve-fiber layer. They are not pathognomonic of malignant hypertension and are found, although less frequently, in a variety of other conditions, for instance in severe anemias and in the terminal stages of carcinomatosis. Attention has recently been called to their occurrence in periarteritis nodosa, lupus erythematosus, and the related acute collagen degeneration diseases.

They are related to the Roth spots of septic retinitis in which the spots commonly have small hemorrhagic centers. The term cotton-wool spots was coined by our British colleagues, who speak of absorbent cotton as cotton-wool, and is well chosen, for these spots indeed have the appearance of tiny cotton pledgets.

On section these lesions have been shown to correspond to areas in which the retinal nerve-fiber layer is swollen and include curious cell-like bodies with a central eosinophile globule. These so-called cytoid bodies were originally thought to be swollen nerve fibers, but studies many years ago revealed that they were globular, not cylindrical, in form and, consequently, that they represent a

peculiar type of cellular degeneration. The origin of these cytoid bodies still remains obscure and I have nothing to add on that score. It seemed possible, however, with this new technique to clarify at least the relation of the total lesion to the vascular net.

The problem was considerably simplified by the fact that the cytoid bodies contain material that stains intensely in our preparations. The location of these lesions in flat

Fig. 15 (Friedenwald). Cytoid body lesion in relation to a terminal arteriole.

preparations of the retina is, consequently, clearly revealed (figs. 15, 16, and 17).

The specimens show that the lesion is regularly located between the terminal bifurcation of a terminal arteriole, and they have precisely the configuration to be expected if the arterial flow were occluded just upstream from this terminal bifurcation. It is plain, then, that these lesions represent minute ischemic infarcts.

Since, in most instances, the arteriole is not actually occluded in the section, these infarcts presumably can result from arteriolar spasm. This conclusion has indeed been

Fig. 16 (Friedenwald). Hypertensive retinitis. Cytoid body lesion in relation to a terminal arteriole.

suspected for many years. The present findings lend it much new weight.

If these lesions are ischemic infarcts, then

Fig. 17 (Friedenwald). Cytoid body lesion in relation to a terminal arteriole.

one would expect healing to be accompanied by the ingrowth of new capillaries. A careful study of a considerable number of these lesions revealed that many of them contain curiously irregular capillaries with very wide lumens and an irregular angular course differing from the normal pattern (fig. 18). They are seen usually on the venous side of the lesion and are most prominent in those

one would expect the malformed capillaries to persist. In retinas showing numerous active lesions we have sought for and found what we take to be such healed lesions showing a group of angular and dilated capillaries in a zone between the terminal fork of an arteriole with no identifiable remains of cytoid bodies (fig. 19).

The identification of the cotton-wool spots

Fig. 18 (Friedenwald). Cytoid body lesion with irregular newly formed capillaries.

Fig. 19 (Friedenwald). Newly formed capillaries in the region of a presumably healed cytoid body lesion.

lesions in which the cytoid bodies themselves are relatively feebly stained.

It would appear, then, that in the process of healing the cytoid bodies lose their carbohydrate content and disappear while new capillaries grow into the damaged area. Clinical experience indicates that these lesions usually disappear from ophthalmoscopic view in 2 to 4 weeks.

The fact that formed capillaries, presumably not more than a month old, show well-developed basement membranes supports the conclusion mentioned above that the presence of a visible basement membrane has to do with the age of the individual rather than with the age of the capillary.

After complete resorption of the lesion,

as ischemic infarcts in the nerve-fiber layer raises interesting questions as to why these lesions are limited to this portion of the retina. Are the arterioles which supply the deeper capillary net less susceptible to spasm and occlusion? Does the deeper capillary net have a more abundant system of collateral connections? Are the tissues supplied by this deeper net less susceptible to damage by ischemia, or do they manifest their injury by a different type of response,

It is, I think, usual that the introduction of a new technique into a particular field of study results in raising more new questions than answers. Consequently, I trust that you will forgive me for the many unanswered

questions which this study has brought out. The technique that we have used is an extremely simple one, and I hope that many of you will find it possible to apply it to a great variety of problems.

APPENDIX

The chemical procedure consists in exposing fixed tissue or tissue sections to the action of periodic acid, which oxidizes the alcoholic group of carbohydrates to aldehydes and ketones. These groups in the tissue are then stained with the fuchsin-sulfite reagent of Feulgen. The specificity of the staining reaction has been discussed by Hotchkiss.[5] The following directions are quoted from Hotchkiss.

STAINING PROCEDURE ACCORDING TO HOTCHKISS

Fixation may be in usual fixatives; mercury salts, if used, are removed with iodine; formaldehyde, if used, is removed by thorough washing. If glycogen, or other easily soluble polysaccharide, is to be demonstrated, fixation and washing should be in alcoholic or other fluids that do not dissolve this substance.

Approximately 70-percent alcohol has successfully been used for washing in such cases, and the standard procedure suggested here calls for this environment up to the stage at which fuchsin-sulfite is used. Whenever such precautions are unnecessary, aqueous solutions may be used.

After bringing the section or smear into alcohol:

a. Leave 5 minutes at room temperature in periodic acid solution A.

b. Flood with 70-percent alcohol, transfer to reducing rinse, leave 5 minutes.

c. Flood with 70-percent alcohol, leave 15 to 45 minutes in fuchsin-sulfite.

d. Wash 2 to 3 times with SO_2-water as for Feulgen staining, dehydrate, and mount as usual.

e. Counterstaining (if desired): If staining is mainly to show polysaccharides, counterstain with a basic dye. Malachite green in dilute aqueous solution (about 2 mg/100 cc.) has been satisfactory for some preparations. This will tend to stain the nucleic acids, which are not affected by the periodatefuchsin. If staining is intended for mucin or acid polysaccharides, it is presumably better to counterstain with an acid dye.

f. Control sections are carried through the same process, eliminating step (a).

Solutions Used

Periodic acid A. Four-hundred mg. periodic acid, dissolved in 10 cc. distilled water, add 5 cc. of $M/5$ sodium acetate (equivalent to 135 mg. of the hydrated crystalline salt) and 35 cc. ethyl alcohol. (The periodic acid, H_5IO_6, was purchased from the G. Frederick Smith Chemical Co., Columbus, Ohio.) This solution may be used for several days if protected from undue exposure to light.

Periodic acid B. Four hundred mg. periodic acid dissolved in 45 cc. distilled water, add 5 cc. of $M/5$ sodium acetate.

Reducing rinse. One g. potassium iodide, 1 g. sodium thiosulfate pentahydrate are dissolved in 20 cc. distilled water. Add, with stirring, 30 cc. ethyl alcohol, and then 0.5 cc. 2 N hydrochloric acid. A precipitate of sulfur slowly forms and is allowed to settle out, although the solution may be used immediately. (This is designed to be an iodide-thiosulfate solution containing the maximum amount of mineral acid compatible with the thiosulfate; when it ceases to be acidic, it should be reacidified or replaced.)

Fuchsin-sulfite. This may be as used for the Feulgen stain. The solution prepared as follows is satisfactory. Two g. basic fuchsin are dissolved in 400 cc. boiling water, cooled to 50°C., and filtered. To the filtrate are added 10 cc. 2 N hydrochloric acid and 4 g. of potassium metabisulfite. Stopper and leave in the dark in a cool place overnight. Add 1 g. decolorizing charcoal, mix and filter promptly. Add up to 10 cc. or more 2 N hydrochloric acid in small portions until, after the last addition, the mixture, spontaneously drying in a thin film upon a glass slide, does not become pink. Preserve in the dark, well stoppered.

Sulfite wash water. Fifty cc. distilled water containing 0.5 cc. concentrated hydrochloric acid and 0.2 g. potassium metabisulfite.

Modifications. As mentioned, aqueous solutions may be used, whenever insoluble polysaccharides only are of interest. Aqueous periodic acid (solution B) is usually somewhat more rapid and vigorous in its action than solution A.

Rinsing is needed to remove entrapped or combined periodate or iodate; either salt gives a reddish coloration with fuchsin-sulfite. While a somewhat longer rinse in 70-percent alcohol (or water) may frequently be adequate to remove these salts, the reducing rinse is more positive in its action. It would probably be dangerous to use acid iodide and thiosulfate in separate solutions, since the liberated iodine might destroy aldehyde groups if not immediately reduced by thiosulfate. Such substances as glucose or ethylene glycol reduce periodate but not iodate.

If control sections reveal that free tissue aldehydes are present before oxidation with periodic acid, treat tissues as directed by Feulgen and Voit, Arch. ges. Physiol. (Pflugers) 206:389, 1924.

Excessive egg white used in coating slides, if not well drained, contains enough carbohydrate to accept a barely perceptible stain.

Preparations stained and mounted when this work was begun are still apparently unchanged 2.5 years later.

Spot Tests With Periodate-Fuchsin

Solutions containing approximately 1 mg. of various preparations are placed in a spot plate and treated for 5 minutes with one drop of periodic acid. Toward these aqueous solutions, the fresh alcoholic solution A is fully as vigorous as solution B and the drops are of a more convenient size. Because the periodic acid (and acetate buffer) is not removed, an appropriate small excess of dilute hydrochloric acid is added immediately before the

reducing rinse. A periodic acid blank reduced in this way should give no coloration with Schiff's reagent, and also not interfere with color development when a drop of very dilute formaldehyde is added.

Satisfactory proportions are:

a. Water or polysaccharide solution, 0.05 to 0.2 cc.

b. Periodic acid solution A, 0.025 cc. (or 1 drop). Leave 5 minutes.

c. N/10 hydrochloric acid, 0.05 cc. (or 1 drop).

d. Reducing rinse (alcoholic), 0.1 cc. (or 4 drops). Mix.

e. Fuchsin-sulfite reagent, 0.05 cc. (or one drop). Leave 15 minutes.

Similar proportions of the aqueous solutions may be used, making allowance for larger drop size.

MODIFICATION OF HOTCHKISS TECHNIQUE FOR STAINING OF UNSECTIONED RETINA

The retina may be dissected out of the eye after fixation or may be recovered from paraffin embedded blocks after routine histologic sections have been cut from the block. In the former case the retina is washed in tap water for 24 hours and then in distilled water and is then ready to be treated with periodic acid. In recovering the retina from paraffin embedded material, the block is melted in a paraffin oven and the tissue transferred to xylol for 4 hours. The retina is dissected out of the eyeball and placed in fresh xylol overnight. It is then placed successively in absolute alcohol, 95-percent alcohol, 80-percent alcohol each for at least 8 hours, and then thoroughly washed in distilled water.

The tissue is placed in Hotchkiss *periodic acid solution* B for 20 minutes, washed in distilled water 30 to 60 seconds, and placed in the *reducing rinse* for 20 minutes. After washing in distilled water for 30 to 60 seconds, it is placed in the *fuchsin-sulfite* (Feulgen reagent) for 1½ hours. It is then washed in three changes of the *sulfite wash* for 10 minutes each, and then in three changes of tap water. The tissue is dehydrated in two changes of 95-percent alcohol for 10 minutes each and then in two changes of absolute alcohol for 10 minutes each, cleared in xylol and mounted in balsam (nerve-fiber layer up).

1212 Eutaw Place (17).

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USE OF TANTALUM IMPLANTS FOR INDUCING A PERMANENT HYPOTONY IN RABBITS' EYES*

MANUEL URIBE TRONCOSO, M.D.

New York

In a paper published in 1940,[†] I described some experimental and clinical work on the use of the metal magnesium as an implant after cyclodialysis operations. My purpose was to keep both sides of the wound separated from each other during the whole period of cicatrization, so that a permanent aperture could be achieved between the anterior chamber and the perichoroidal space. The magnesium was used because this metal is completely absorbed by the tissues and at the end of three weeks has entirely disappeared. Unfortunately, magnesium gives a great amount of hydrogen gas, which in some cases could not be evacuated through the incision in the sclera and produced pain in the eye.

Considering the excellent results obtained by brain surgeons who have used plates of tantalum in repairing cranial defects, I thought it would be worthwhile to find out if it could be applied also to the inner membranes of the eye without risk to the integrity of the organ.

I started a series of experiments in rabbits in an endeavor to ascertain: (1) How well the inner structures of the eye could tolerate the presence of tantalum; (2) if this metal could be used to keep the sclerocorneal hole in the limbus open permanently after trephine operations; (3) if it were possible to maintain, with tantalum, a new channel of outflow from the anterior chamber to the perichoroidal space.

Tantalum has been known and used extensively in surgery since 1940. It has a characteristic blue-gray color, is a basic element, and has a density of 16.6 gm. per cubic centimeter. It is malleable and ductile. It remains unchanged in normal tissues; is nontoxic and nonabsorbable. It can be drawn into a wire as fine as human hair or rolled into a thin foil. Its chief value in brain surgery lies in the fact that, because of its chemical properties, it allows the tissue cells to have a normal growth undisturbed by its presence. The tissue shows little or no evidence of foreign-body reaction and a minimum of leukocytic infiltration and gliosis. Some authors have demonstrated that fibroblasts may even grow attached to tantalum implants.

Ophthalmic surgeons now use this metal extensively after enucleation and evisceration of the eye to obtain permanent orbital prosthetic implants. Tantalum can be obtained from Johnson and Johnson's Ethicon Suture Laboratories in three forms: (1) Metallic wire in different thicknesses, either in spools or threaded in atraloc needles for sutures. (2) Tantalum plates or fine tantalum foil. (3) Tubes with a lumen of 1 mm. and thick walls. These can be cut to any required length with strong scissors and filed to make spurs or flanges.

EXPERIMENTAL PROCEDURES

EXPERIMENT 1

My preliminary step consisted in depositing a piece of tantalum wire in the anterior chamber of a rabbit's eye and studying the reaction of the tissues to the foreign body. The tantalum wire was about 2-mm. thick and 4-mm. long and was sterilized in the dry-heat oven. It was introduced into the eye through a scleral incision 2-mm. back from the upper limbus and deposited into the cilioscleral sinus. Its tips appeared in the anterior

chamber. The conjunctival flap over the wound was sutured as usual.

Two days later the eye showed little re-action, but the cornea was hazy in front of the implant. A small hemorrhage appeared on the iris. One week later the reaction sub-sided, but the cornea continued hazy and new vessels appeared. The intraocular pres-sure was low—5 mm. Hg (Schiøtz) (fig. 1—O.D.). One month after the operation the wire was seen, totally displaced into the anterior chamber. Finally it fell down to the bottom of the chamber and stayed in the angle without producing a marked reaction. The eye was quiet and the cornea cleared.

22 mm. Hg (Schiøtz), probably due mostly to mechanical occlusion of the angle, and stayed there during the 5th and 6th months. Later the eye appeared entirely normal. The tension remained low and continued so until the animal was killed 32 months after the operation.

Fellow eye. The left eye never showed any

RABBIT NO. I.
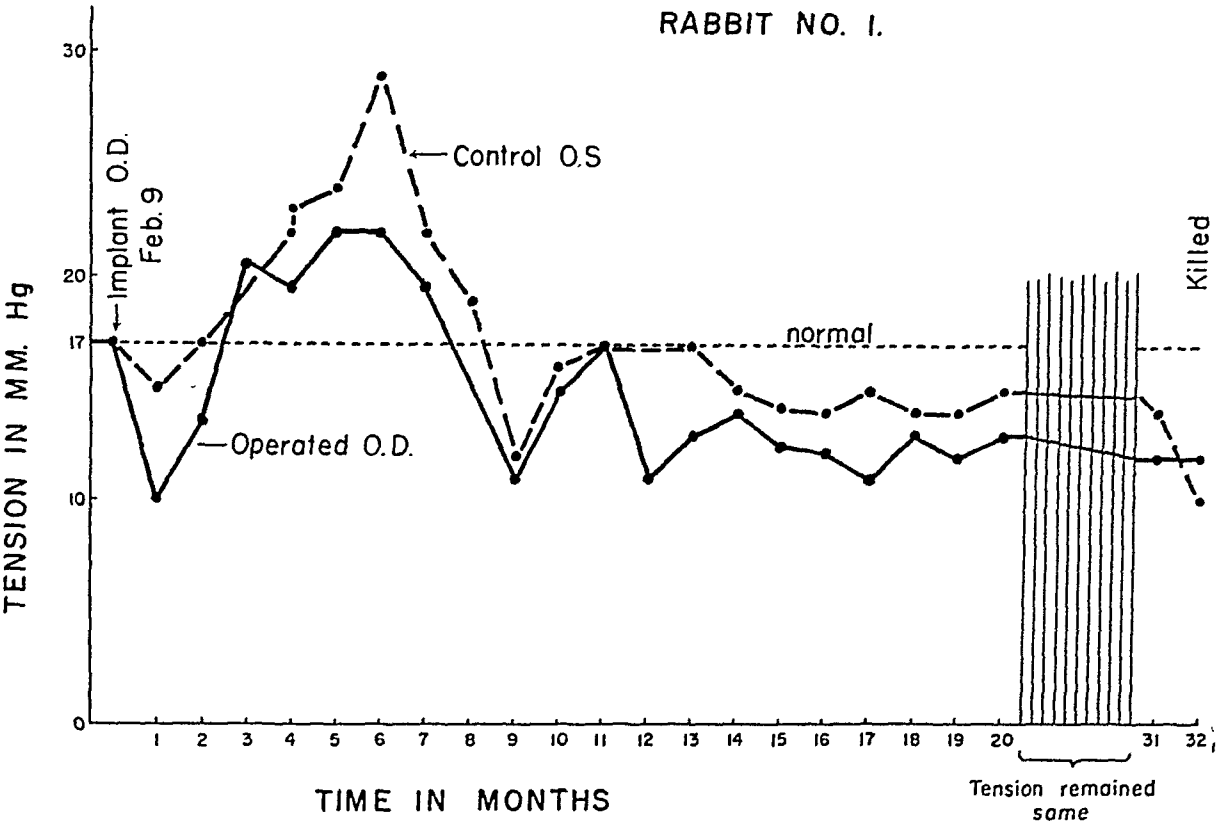
Fig. 1 (Troncoso). Curve of intraocular pressure after tantalum implant in anterior chamber. O.D.—the operated eye—has a full line. O.S.—unoperated eye—a dotted line.

In the middle of the second month, there was some reaction in the cornea which be-came turbid and vascularized in front of the implant. With the slitlamp microscope, fine white exudates were detected on the pos-terior surface of the cornea where the metal touched it. At that time the tension rose to

irritation or signs of sympathetic ophthalmia during the whole course of the experiment. Still, the curve of intraocular pressure (fig. 1—O.S.) followed closely the variations in the tension of the operated eye. When this became higher than normal, the fellow eye also showed a peak of hypertension and then became hypotonic again during the many months of observation.

Microscopic examination. The enucleated eyes were sectioned and sent to Dr. Parker Heath in Boston. His coöperation is grate-fully acknowledged here.

Right Eye: Sections show a few changes

in the cornea. At the limbus is noted a focal collection of lymphocytes and some blood pigment. There are a few fine vessels growing into the corneal substance about at its middle; and thin nebulous scarring. There are a few pigment deposits on the posterior surface of the cornea. The iris shows postmortem changes, and there is reduction in the lumen of the iris vessels due to exaggerated hyalin changes in their walls. The lens, choroid, retina, and vitreous appear normal. The ciliary body shows some pigment migration and some pigment profileration to a minor degree. There is no foreign body reaction in any of the ocular tissues.

In the left eye Dr. Heath did not find any departures from the normal state. The usual lesions of hypotony were missing and the nervous tissue of the eye was quite intact. We must conclude that the hypotony was only functional.

Comments. 1. A thick, heavy piece of tantalum stayed inside the eye for 2 years and 8 months, producing only a limited local reaction. No foreign body reaction was present.

2. Hypotony was marked all the time, except for a transient rise of tension in the 5th and 6th months.

3. No iritis, anterior synechia, lens opacity, or involvement of the inner membranes occurred as a result of the long stay of the tantalum in the anterior chamber.

4. The fellow eye never showed any sign of sympathetic involvement. However, this eye suffered from a long hypotony which was undoubtedly of a purely functional nature.

EXPERIMENT 2

Trephine operation. One of the drawbacks of the operation of trephining in glaucoma consists in the cicatrization of the conjunctiva and episcleral tissue around and over the hole and the transformation of the conjunctiva into a thick, fibrous tissue, which finally stops any outflow of aqueous into the episcleral tissues.

It occurred to me that perhaps this complication could be avoided by keeping the conjunctiva separated from the sclera over the hole and over the surrounding tissue. I used the tantalum suture, the finest obtain-
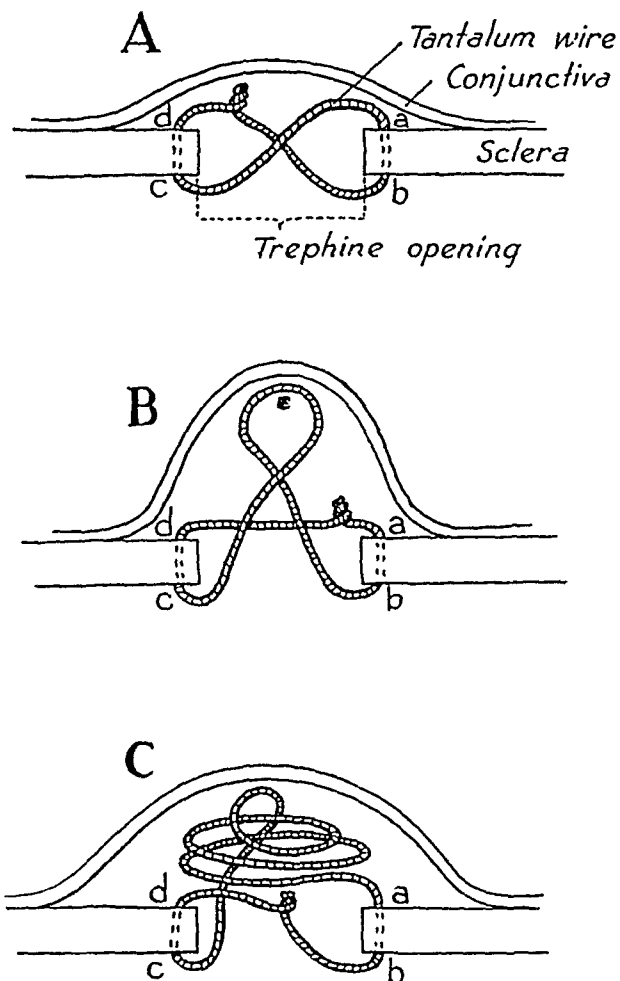
Fig. 2 (Troncoso). Semischematic sections of trephine holes, A, B, C, showing tantalum wire passed with a needle into the sclerocorneal lips, to raise the conjunctival flap.

able, 0.003 inch in size and threaded in an eyeless atraloc needle.

Technique. After cutting a conjunctival flap in the usual manner, a trephine hole, 2 mm. in diameter, was made at the upper part of the limbus. A needle was passed from within into the thickness of the sclera at the bottom of the hole at b (fig. 2A), brought out at the surface at a, then, crossing the hole, it was inserted, also from within, into the opposite side of the sclera at c, run through the membrane at d and cut through.

The two ends were twisted together over the hole. The flap was then sutured in place covering the wires.

Course. There was little reaction in the eye and two days after the operation the tension was 10 mm. Hg (Schiøtz). The flap cicatrized and the eye appeared normal. The metal loop could be seen with the slitlamp under the slightly raised conjunctiva. After

TIME IN MONTHS
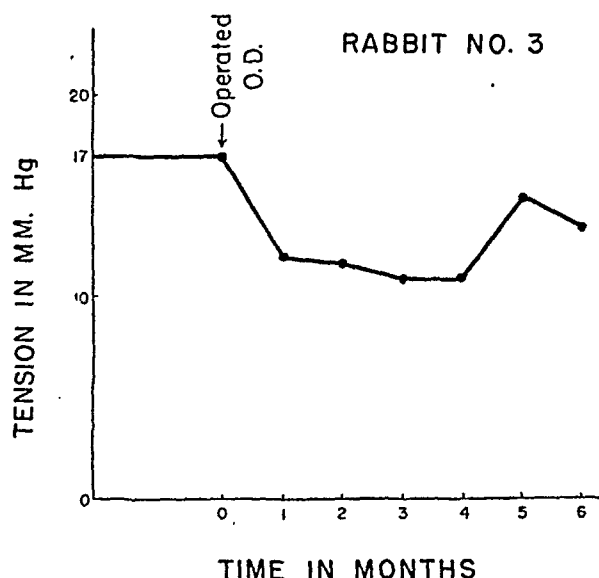
Fig. 3 (Troncoso). Curve of intraocular pressure in rabbit No. 3 after tantalum-wire implant.

two weeks the tension, in spite of gentle massages, came back to normal and the animal was killed.

Microanatomic examination with the slit-lamp microscope. The enucleated eye was examined first in front and then from the back of an equatorial section. The wire was clearly located entangled in a mass of cicatricial tissue, which entirely closed the hole, as shown by transparency. The twisted ends of the wire had been separated. One of them protruded from the scar and under the conjunctiva.

EXPERIMENT 3

Assuming that the wire loop had not been raised sufficiently over the sclera to avoid cicatrization, an experiment was made on another rabbit. After making a trephine hole

2 mm. in diameter, the wire was passed from a to b (fig. 2B) and then raised high at the center of the hole where it was twisted into a loop, e, about 3 or 4 mm. high. The needle was again run into the scleral lip from c to d and the two ends twisted together. The conjunctival flap was spread in a tentlike protrusion.

The eye did not show great reaction. The tension lowered to 10 mm. Hg (Schiøtz) and remained low. At the end of the first month after the operation, the metal loop could be seen clearly with the slitlamp under the raised and edematous conjunctiva. The hypotony persisted in this animal for six months at about the same level of 10 mm. Hg (fig. 3).

Unfortunately, a secondary infection supervened at this time and the eye became red. The conjunctiva was very much inflamed and secretion was very great. The tension returned to the normal level and the animal was killed.

Microanatomic examination. The globe was sectioned and placed in a glass jar filled with liquid. When illuminated by transparency with the beam of the slitlamp, it showed that the trephine hole was closed by a semitranslucent scar (figs. 4 and 5). The wires were located, entangled in a mass of cicatricial tissue. The loop was clearly seen, still raised above the level of the conjunctiva (fig. 5, front view). An equatorial section, examined from the back, showed the wires in place inside the hole (fig. 4). At the right, the small loop probably corresponded to a lateral portion of the wire which had cut through the thickness of the sclera.

EXPERIMENT 4

In order to provide more extensive and flat support for the raised flap over the hole, a tantalum wire was passed as follows (fig. 2C). The needle penetrated at the edge of the hole at b; then came to the outer surface of the sclera at a, and was rolled around a probe three times to form a spiral which

remained at a raised level not only over the hole but over the margins on the episcleral tissue. The wire was then run through the sclera again from c to d and finally the two ends were twisted together. The conjunctival flap was then spread out smoothly over the spiral. Reaction was slight in this animal, but the eye remained hypotonic for six weeks only.

Comment. The fact that a trephine hole was kept open and marked hypotony was pro-

EXPERIMENT 5

Tantalum Tube. Trephine Operation. In several operations, instead of wire, I used an implant made with the tantalum tube provided by the Ethicon Suture Laboratories. It has a lumen of 1 mm. and very thick walls. With shears, I made a small cylinder 1.5-mm. long. The tube was cut at the two ends and bent to form two lateral flanges or spurs. This implant was placed inside the trephine hole as follows: one spur was first intro-

Fig. 4 (Troncoso). *Microanatomic aspect* from equatorial section of eye of rabbit No. 3 seen from the back (×15).

Fig. 5 (Troncoso). The same eye of rabbit No. 3, seen from the front (×15).

duced in a rabbit's eye for a period of six months, while in normal eyes the trephine hole closes very promptly, shows that the tantalum wire can prevent cicatrization of the conjunctival flap over the aperture, keeping the episcleral tissue open for a long time. However, the results of these experiments were not uniform. In some animals the hole closed in 4 to 6 weeks, while in others they remained patent from 2 to 8 months.

duced into the aperture, and then the tube was pushed down into the hole, but it appeared too thick and bulky. The conjunctival flap was then sutured, covering the tube.

In rabbit No. 5 there was an infection after the operation and the next day the cornea was hazy near the implant and a posterior synechia appeared on the upper side of the pupil. The tension came down to 8 mm. Hg (Schiøtz).

Two weeks later, by the use of atropine

and sulfadiazine, the inflammation subsided, the pupil dilated, and the cornea cleared almost completely. Subsequently the eye returned to normal. The hypotony persisted for nearly two months, with the implant in place, as seen under the conjunctiva with the slit-lamp. Suddenly the tension came back to normal and stayed there in spite of massages of the eyeball and stretching of the conjunctiva over the implant. The animal was killed.

Microanatomic examination. With the slit-lamp the hole in the sclera appears opaque under transillumination. On dissection an anterior peripheral synechia was found below the place of the implant. This had been dislocated and was hanging inside the vitreous, attached to the trephine hole by one of the spurs and by several exudates. The implant looked too heavy and thick. It was probably displaced by the movements of the eyeball.

EXPERIMENT 6

Cyclodialysis operation with a thick tantalum tube. A cyclodialysis operation was performed on a rabbit's eye, making a scleral incision about 3 mm. from the limbus, with the purpose of reaching the cilioscleral sinus in front of the scleral spur. The implant consisted in a tantalum tube with a lumen of 1 mm. (thick walls) and 3-mm. long. One of its ends had been bent at right angles for 1 mm. The tube was introduced into the wound but the bent portion was left outside, in a vertical position, to provide a channel of outflow from the anterior chamber to the episcleral tissue under the conjunctiva.

The day after the operation the reaction was mild. There was some blood on the iris surface. The conjunctival flap was edematous. The tension taken on the fourth day was 5 mm. The eye was very soft and the tip of the implant could be seen under the flap. The eye became quiet. Twenty days later, however, the tension rose to normal. The animal was killed.

Microanatomic examination. In an equatorial section seen from behind, the heavy tantalum tube had been dislocated from its place and moved forward below the ciliary body. It was bound to the processes by white exudates. The scleral hole was closed, as seen by transparency.

THIN-WALLED TANTALUM TUBES

It being apparent that the heavy tantalum tubes were entirely unsuitable as implants inside the eye, I tried a new metal tube which I made with some very thin tantalum foil —0.00025-inch thick. This was rolled around a hypodermic wire once or twice. The foil being very pliable easily retained its shape.

Technique. I used the following technique. With ordinary scissors a band was cut in the foil, exactly 5-mm. wide for the length of the sheet. This band was rolled over the hypodermic wire. Then, pushing it to the end of the wire, a cut was made on each side in the direction of the axis of the cylinder for 1 mm. If two flanges were desired at this end, the metal was bent at right angles and the shape of the spurs was fashioned with scissors. If only one flange was intended, the other part was cut through. The same process was repeated at the other end of the tube. The implant, being tiny, was kept threaded on the hypodermic wire and placed inside a small glass tube for sterilization.

The tantalum tube could be made of any length and diameter and even when pressure was exerted outside with the thumb and index fingers it proved to be solid and resisted collapse.

The implant could be placed more easily, without risk of losing it, if it was kept threaded on the hypodermic wire until put into the wound.

EXPERIMENT 7

Reverse cyclodialysis with fine tube implant. A cyclodialysis operation, performed in the usual way, is difficult to do properly in rabbits. When the scleral incision is made 2 or 3 mm. from the limbus, the knife falls into the cilioscleral sinus and, if a com-

munication is needed with the suprachoroidal space, a spatula or a knife has to be pushed backward to cut the insertion of the ciliary body to the sclera. If the incision is made on this membrane, 4 or 5 mm. behind the limbus, in order to reach the anterior chamber the spatula has to cut or detach the spur. Because of these reasons I performed

on the forward end, and threaded in the hypodermic wire, was introduced with a forceps between the ciliary body and the sclera. When securely in place, the wire was withdrawn while the forceps kept the tube in place. Two sutures were placed on the corneal wound to keep the iris back. Eserine (1 percent) and sulfa salve were used.
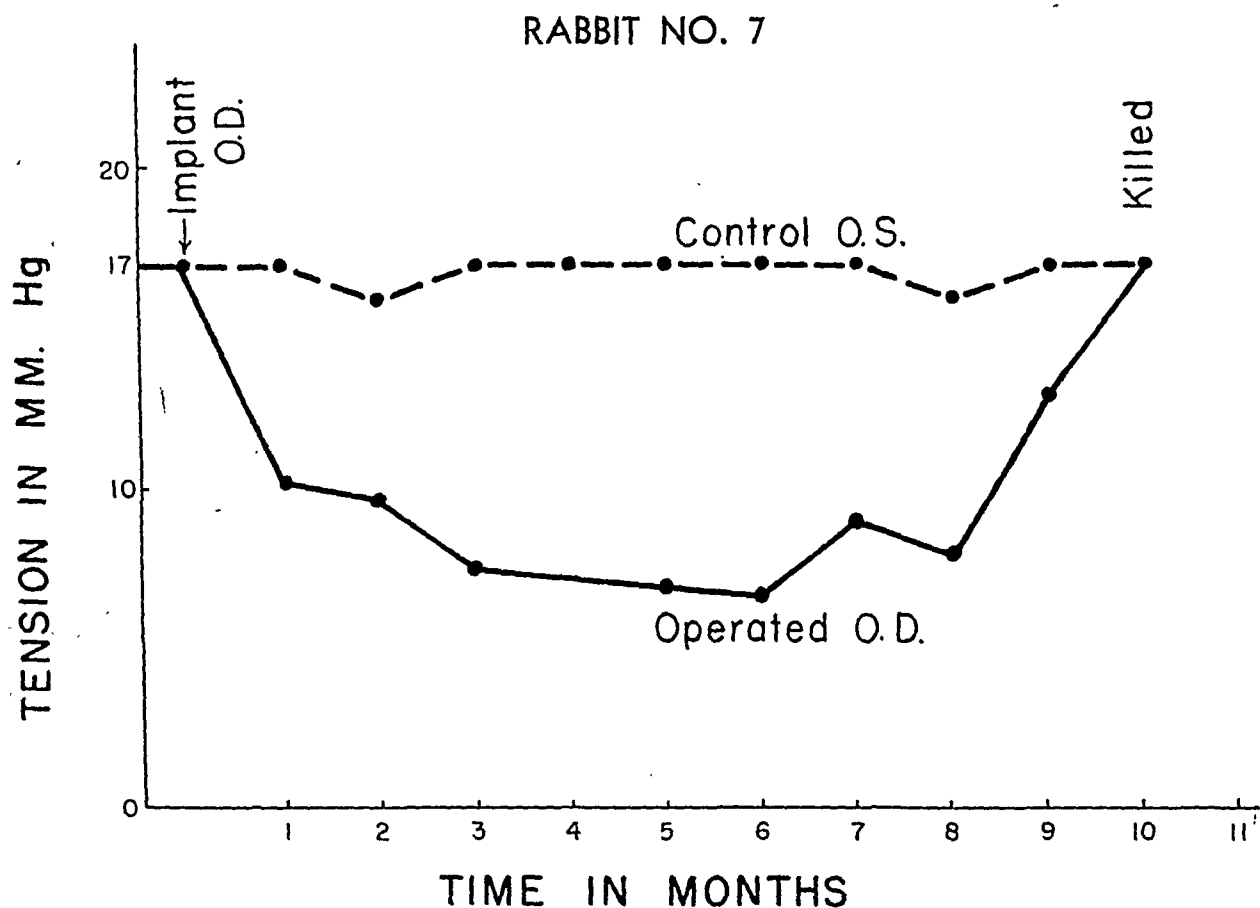
Fig. 6 (Troncoso). Curve of intraocular pressure in rabbit No. 7, after reverse cyclodialysis and implant of a thin-walled tantalum tube.

cyclodialysis from the anterior chamber backward.

An incision was made in the corneal limbus with a keratome and enlarged with scissors. In the rabbit, the iris protrudes immediately into the wound. No iridectomy was performed on this animal. Opening the corneal wound, a spatula was slid under the scleral lip, hugging it closely to break first the pectinate ligament fibers and then the scleral spur and to separate the choroid from the sclera. The implant tube, with two spurs

The reaction after the operation was moderate except that the lips of the corneal incision were infiltrated and there was some blood in the iris. One week later the sutures were removed. Tension was 11 mm. Hg (Schiøtz). The corneal wound, when viewed with the slitlamp, appeared hazy and vascularized; the pupil contracted by eserine. Three weeks after the operation, the eye appeared to be quite normal and the end of the implant could be seen in the anterior chamber. Two months later a small triangular,

white, corneal infiltration appeared and proved to be a scar where an anterior peripheral synechia had developed.

iris involvement. At the end of this time the tension started to rise until it returned to normal and the animal was killed. During
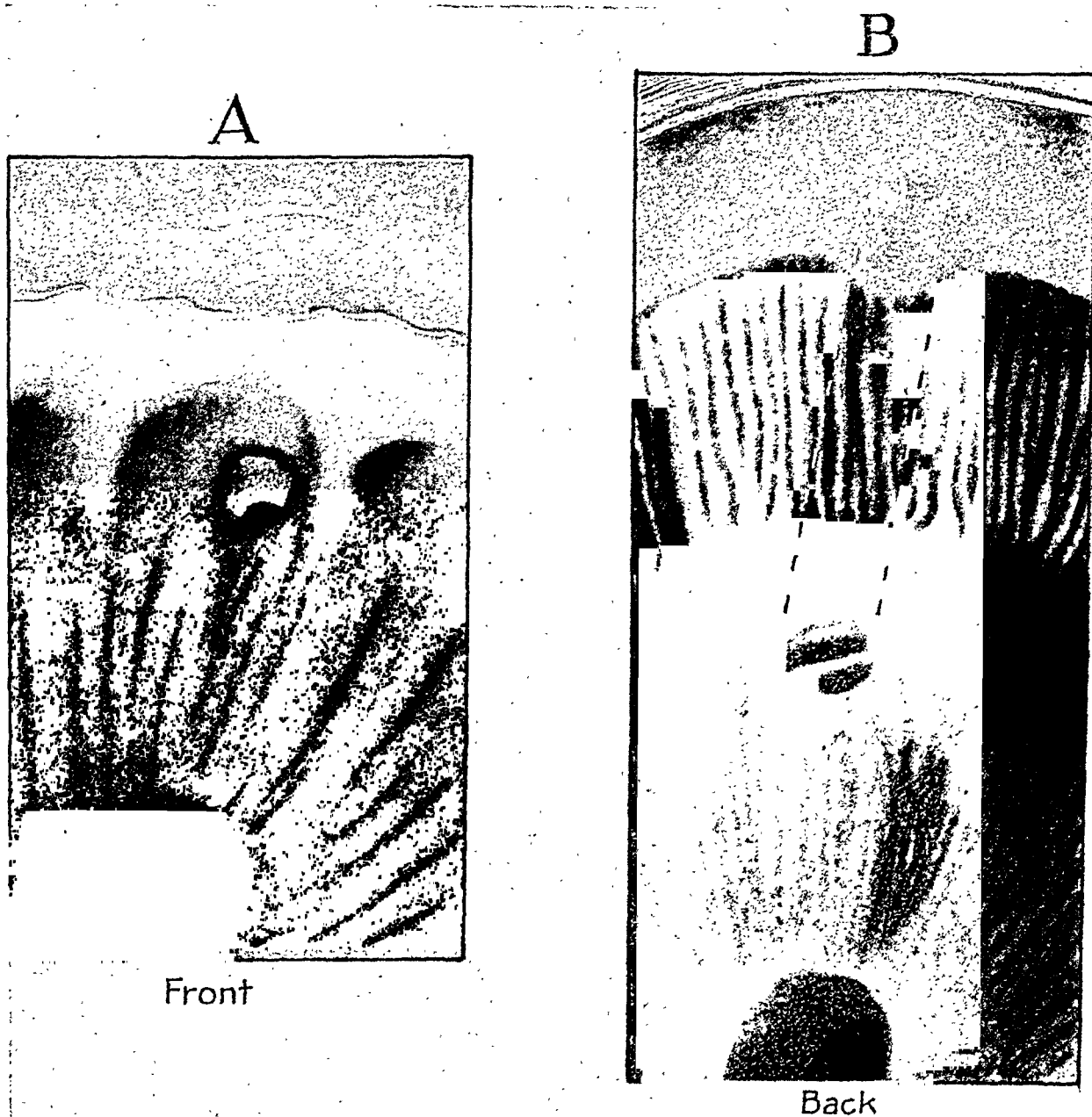
Fig. 7 (Troncoso). *Microanatomic examination of the eye of rabbit No. 7.* (A). The eye seen from in front showing in the iris the anterior end of a tantalum tube (×20). (B) The same eye seen from the back of an equatorial section showing (below) the anterior end of the tube and (above) the posterior end covered with a fine exudate in folds. The dotted lines represent the position of the central portion of the tube.

The intraocular pressure, which had become very low—about 7 mm. Hg (fig. 6)— was kept at this level for eight months without the eye showing any signs of irritation or

all this time tension in the fellow eye remained normal.

Microanatomic examination. The enucleated eye, seen from the front (fig. 7A)

showed, on the iris surface, a hole divided into two parts: the one above was the inside of the lumen of the tube, while the lower one was undoubtedly a metal spur.

In the equatorial section seen from behind (fig. 7B) the tantalum implant appeared clearly in two sections. The lower one was the tip of the tube with a spur which rested on pigmented cicatricial tissue. The upper end of the tube was located behind the ciliary processes and the ora serrata. With the light, the metal shone through white, translucent folds of exudates.

Fig. 9 (Troncoso). *Microanatomic examination of the eye of rabbit No. 8* showing tantalum tube in place between sclera and ciliary body.
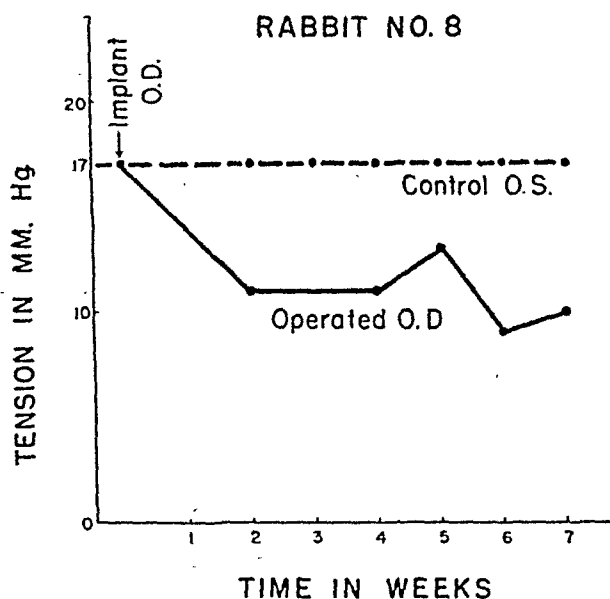
Fig. 8 (Troncoso). Curve of intraocular pressure in rabbit No. 8, after reverse cyclodialysis and implant of a thin-walled tantalum tube.

This tip of the tube lay under the retina and choroid, but no lumen was visible, being probably obtructed by exudates. This will explain the return to normal of the intraocular pressure after so long a hypotony. The processes appeared normal, but at the back of the iris there was a small atrophic spot. The lens was clear.

EXPERIMENT 8

Using the same technique as in former experiments an anterior cyclodialysis, without iridectomy, was performed and a tube implant was inserted from in front between the iris root and sclera. Two corneal sutures

were made and the bulging iris pushed back between the sutures with a spatula.

Inflammatory reaction after the operation was slight, but at the corneal scar there was some opacification and new vessels were present. An adhesion of the iris to the angle or a peripheral synechia drawing the pupil upward was disclosed 20 days after operation. With the slitlamp, the spurs of the implant could be seen on either side of this anterior peripheral synechia and under the conjunctival insertion.

Tension was low (fig. 8). At the end of the 6th week after the operation the animal became very sick with a pulmonary disease and had to be killed.

Microanatomic examination. The eye was sectioned meridionally on each side of the place of operation. A narrow peripheral synechia was seen clearly on the frontal view with the spurs on each side of the adhesion. Serial lateral sections were made until the implant was reached (fig. 9), and its continuity under the corona ciliaris was fully established. Some of the processes had been drawn forward with the iris into the synechia.

Comments. The fine tantalum tube proved handy, light in weight, and apparently inert as it did not provoke any important reaction on the inner structures. The drainage

from the anterior chamber into the suprachoroidal space was perfect as it kept the intraocular pressure low for 8 months in one rabbit and from 3 months to 6 weeks in others.

Apparently, tantalum induced a process of encapsulation with delicate, white, membranous exudates around the foreign body. The tubes, made of thin foil, were easy to shape and sterilize and stayed in position well.

CONCLUSIONS

Experiments in rabbits' eyes have shown that the metal, tantalum, is well tolerated by the inner membranes of the eye and may be kept in position for a long time after cyclodialysis operation and trephining. Tantalum sutures, foil, and tubes have been used. I favor the use of a fine tube made with thin tantalum foil rolled over a hypodermic wire and on which flanges can be fashioned. This tube used in a reverse cyclodialysis operation has produced a hypotony which, in some rabbits, has lasted as long as 8 months.

ADDENDUM

After this paper was written, I found, in the August, 1947, issue of the AMERICAN JOURNAL OF OPHTHALMOLOGY (Volume 30, page 1033, August, 1947), among the editorials, a brief mention that at the meeting of the Wilmer Residents Association, Dr. Malcolm W. Bick had discussed the subject of "Tantalum implants for glaucoma."

In a personal communication, Dr. Bick kindly wrote me as follows: "Dr. Alfred Maumenee, who is now in California, and I made a complete study of the use of various types of tantalum implants in rabbits and

the final phase of this work was completed last summer. It has not been prepared for publication.

"In humans, cases were confined to four patients in whom an implant had been placed in the suprachoroidal space and was permitted to remain there. In all four cases the tension was controlled for about two weeks at the end of which time the tension rose again. It was the feeling of Dr. Friedenwald that this was due to the fact that the cleft became lined with epithelium and no absorption could take place. These implants were buried in much the same manner as your magnesium implants but were sutured through the sclera by means of a 5-0 braided nylon suture which prevented the implant from slipping into the anterior chamber. In three of the eyes the implant was removed. In the fourth case, a patient who has had absolute glaucoma, the implant has remained for over a year and a half without causing undue irritation. The patient complains of ciliary pain from time to time. A small pannus has formed in the cornea adjacent to the area where the implant lies.

"The tantalum implant used in the four patients was a plate. The approximate size was 2-mm. wide, 7-mm. long, and 0.25-mm. thick. The edges were round and highly polished with jewelers' rouge. The implants in rabbits were also plates. However, in the rabbits the plates were brought out through the sclerotomy wound. The reason that this was not done in humans was that our microscopic sections showed a downward growth of episcleral fibrous tissue into the cyclodialysis cleft going forward toward the anterior chamber."

500 West End Avenue (24).

INVESTIGATION OF THE BLOOD-AQUEOUS BARRIER IN THE NEWBORN[*]

II. To Inulin

V. EVERETT KINSEY, PH.D., AND MARTIN B. WILLIAMSON, PH.D.

Boston, Massachusetts

The present study was designed to learn more about the nature of the blood-aqueous barrier in the eyes of newborn, and to aid in the interpretation of results obtained previously[1,2] in which the concentrations of ascorbic acid in the eyes of newborn were investigated as a function of age. In these earlier studies the concentration of ascorbic acid in the aqueous humor of human fetuses or in the eyes of rabbits or monkeys immediately after birth was found to be approximately that in the blood; that is, 1/10 to 1/25 of that in the adult aqueous humor.

Of the several explanations which might account for the difference in concentrations of ascorbic acid between the adult and infantile aqueous humor, the one considered to be the most likely was that the blood-aqueous barrier in the eyes of young animals and human fetuses was sufficiently permeable so that secreted ascorbic acid could readily diffuse out of the chambers of the eye into the blood stream.

The chief site of this assumed area of high permeability in the young eyes was thought to be the hyaloid system, since a close correlation was observed between the time at which the ascorbic-acid concentration begins to increase and the time at which the hyaloid system regresses, it being well known that the capillary endothelium surrounding the blood vessels in this system, unlike that in the iris, for example, is histologically like that in other parts of the body.

From the observation that the ascorbic-acid concentration in the aqueous humor of monkey eyes continued to rise for several months after the hyaloid system had regressed,[2] it seems probable that the permeability of other portions of the blood-aqueous barrier such as the iris or ciliary body may also be changing in eyes of some animals after birth.

EXPERIMENTAL

Albino rabbits varying from 6 to 14 days of age used in the experiments were obtained from a local dealer 2 to 6 days after birth and were kept with the does. Younger animals could not be employed since the quantity of aqueous humor was insufficient for quantitative analysis.

A solution of 1 gm. of inulin in 10 ml. of isotonic saline was prepared by heating in a water bath at 60° to 70° until clear. The solution could be cooled to room temperature and would not precipitate inulin for at least an hour.

The rabbits were injected intraperitoneally with 2 ml. of the inulin solution cooled to 37°C. The aqueous humor samples were drawn in a calibrated micropipette as previously described.[1] The samples from paired eyes were pooled and quantitatively diluted with 10 to 20 volumes of isotonic saline, depending on the size of the pooled sample. Blood, obtained by heart puncture, was heparinized and the red cells removed by centrifugation. The blood and aqueous samples were taken within 5 minutes of each other.

The inulin concentration in the plasma was determined by the method described by Alving and others[3] as modified by Harrison.[4] This method depends on the formation of a blue color by hydrolyzed inulin and diphenylamine in the presence of strong

acid after the removal of other carbohydrates by incubation with yeast suspensions. The aqueous-humor inulin was determined by the same method except that no dilutions were made before precipitating the protein. The amount of color developed was measured in a Beckman spectrophotometer at 620mμ and the concentration calculated

RESULTS

The results of measurements of the relative concentrations of inulin in the blood and aqueous humor at intervals after injection varying from 20 to 120 minutes are given in Figures 1 and 2. It will be seen that a steady state was reached within approximately 60 minutes, and also that the
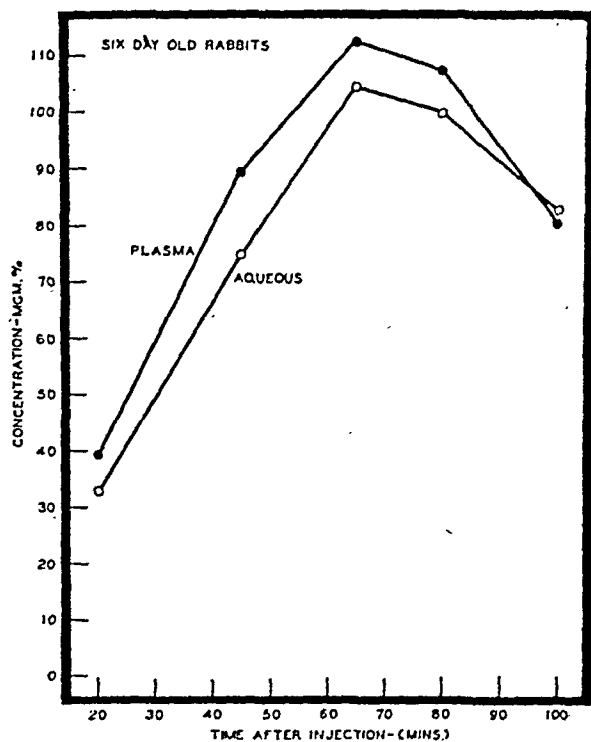
Fig. 1 (Kinsey and Williamson). The relative concentrations of inulin in the aqueous humor and plasma of 6-day-old rabbits at various periods following intraperitoneal injection.
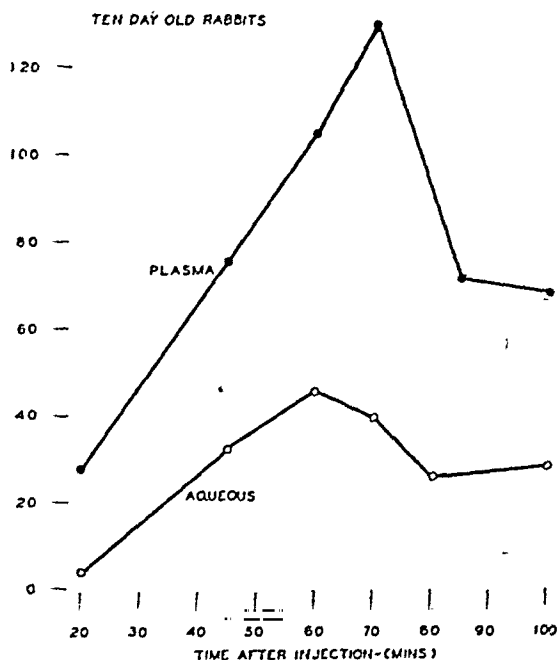
Fig. 2 (Kinsey and Williamson). The relative concentrations of inulin in the aqueous humor and plasma of 10-day-old rabbits at various periods following intraperitoneal injection.

from a standard calibration curve. Duplicate determinations checked within 4 percent.

To test directly whether the permeability of the blood-aqueous barrier changes after birth and whether any change in permeability is associated in time with regression of the hyaloid system, experiments were carried out using inulin as a test material. This substance is particularly suitable for testing changes in the permeability of the blood-aqueous barrier, since it is not metabolized and since it will not pass through the blood-aqueous barrier of the adult rabbit eye, presumably because of its relatively large size (molecular weight 5,000).

relative concentration in the aqueous humor is considerably higher in the 6-day-old than in the 10-day-old rabbits.

To relate more closely the change in the aqueous-blood concentrations with age, a series of experiments was performed in which samples were analyzed 60 to 70 minutes following injection into animals of varying ages. Using this time interval, the concentrations of inulin in the aqueous humor and blood from animals of varying ages were determined. The results of these experiments are presented in Table 1 and graphically in Figure 3. The latter shows that ratio of concentration decreases rapidly with increasing age of the animal until at

approximately 15 days of age no inulin is found in the aqueous humor.

DISCUSSION

The observation that inulin can diffuse freely into the anterior chamber of eyes of young rabbits clearly supports the idea that the blood-aqueous barrier in young animals is much more permeable than it is in older animals. The decrease in the ratio of concentration of inulin in the aqueous humor to that in the blood indicates that with increasing age there is a progressive decrease in the permeability of the blood-aqueous barrier or, at least, a decrease in the available surface area through which diffusion may take place.

The time period during which the steady-state ratio is changing corresponds with the time of regression of the tunica vasculosa lentis as observed both histologically and with the biomicroscope. The conclusion ap-

TABLE 1

CONCENTRATIONS OF INULIN IN THE AQUEOUS HUMOR AND BLOOD
FROM ANIMALS OF VARYING AGES

Age (Days)	Number Animals	Weight (Average)	Plasma Inulin (Average)	Aqueous Humor Inulin	Ratio Aqueous / Plasma
6	4	97	110	102	0.925
8	2	135	78	37.7	0.485
10	2	106	108	41	0.386
14	6	286	98	3.5	0.036

All corrected for small blank.
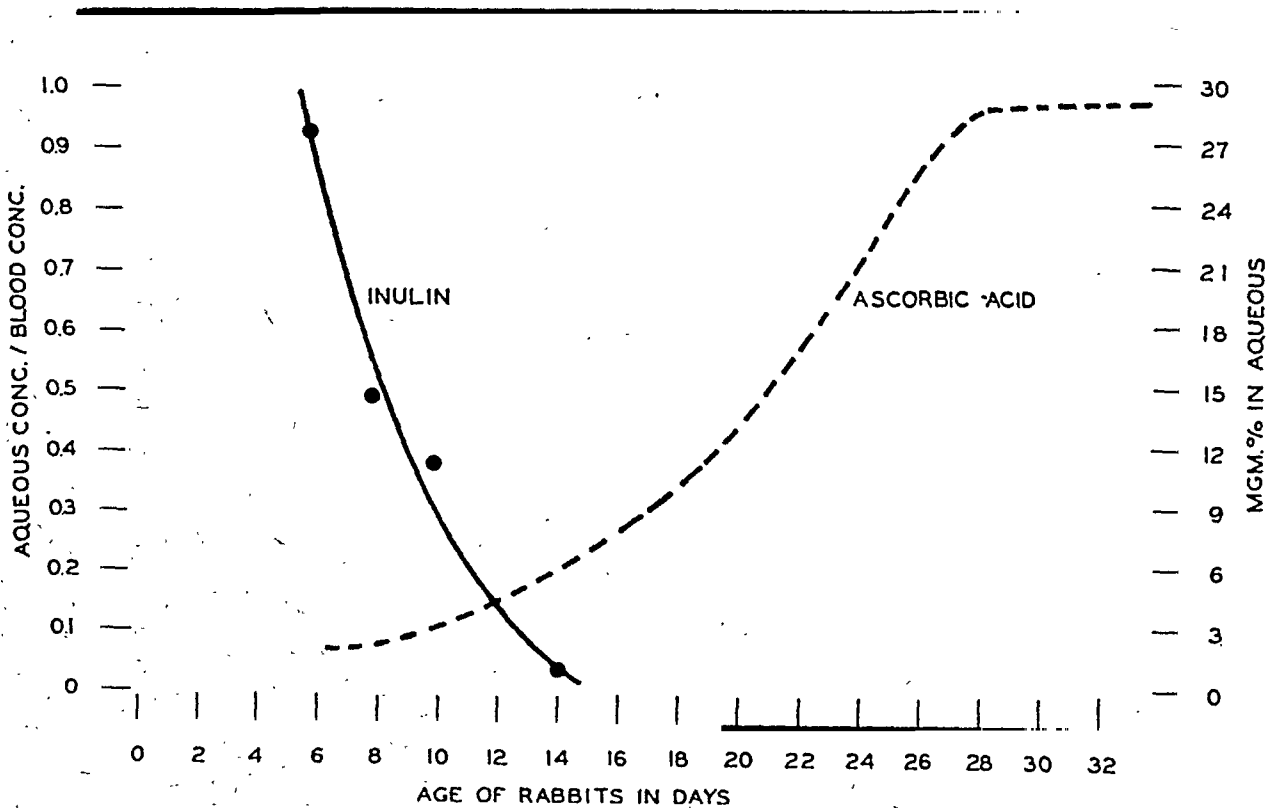
Fig. 3 (Kinsey and Williamson). (Solid line) —— The relative concentration of inulin in the aqueous humor to that in the plasma at steady state for rabbits of various ages. (Broken line) - - - The concentration of ascorbic acid in the aqueous humor of rabbits of various ages.

pears to be warranted therefore that the inulin passes into the eye through the capillary system of the tunica vasculosa lentis and probably not through any other portions of the blood-aqueous barrier.

In view of these results the explanation given previously[1] to account for the low concentration of ascorbic acid in the eyes of young animals appears to be correct; namely that any ascorbic acid secreted into the aqueous humor in concentrations above that in the blood would diffuse back into the blood stream.

It is interesting to consider the implication of the large change in permeability of the blood-aqueous barrier in the eyes of rabbits less than 15 days of age. It follows from the inulin results that in the young eye the concentrations of probably all water-soluble substances but protein are present in the same concentrations as they are in the blood; whereas, in the adult eye the blood-aqueous barrier is such that the concentrations of some of these materials are excluded from the intraocular fluids. Preliminary experiments with fat-soluble compounds, such as vitamin A, show that this difference does not occur.

SUMMARY

From a study of the relative concentrations of inulin in the aqueous humor and blood of young rabbits at various intervals after intraperitoneal injection it was found that a steady state was reached within approximately 60 minutes.

The ratio of the concentration of inulin in the aqueous humor to that in the blood under steady-state conditions decreased from 0.93 to 0.036 between the 6th and 14th day after birth.

The results are explained on the assumption that with increasing age the permeability of the blood-aqueous barrier is changing rapidly or the available surface area through which diffusion may take place is decreasing. This change is ascribed chiefly to the regression of the hyaloid system. The significance of these findings is discussed in relation to previous work in which the concentration of ascorbic acid was followed.

243 Charles Street (14).

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HARADA'S DISEASE*

Mary G. Bruno, M.D., and Samuel D. McPherson, Jr., M.D.
Baltimore, Maryland

In 1926, Harada[1] described an interesting and rare ocular syndrome which has borne his name since that time. The essential features of this syndrome are: (1) Prodromal symptoms of general malaise and meningeal irritation; (2) a bilateral uveitis of varying severity; (3) bilateral detachments of the retina with spontaneous reattachment; (4) disturbance of the pigmentary and hair systems, including vitiligo, poliosis, and alopecia; (5) lymphocytosis of the spinal fluid; and (6) dysacousia. The syndrome was incomplete in the 12 cases reported; the most common findings being the first three, and the least common the last three.

Since 1941, four cases of this syndrome have been observed in the Wilmer Institute. It is the purpose of this paper to present these cases, and to discuss their possible relationship to the Vogt-Koyanagi syndrome and sympathetic ophthalmia.

REPORT OF CASES

CASE 1

History. H. J., (J. H. H. No. 141208), a 24-year-old white woman, was admitted to the Wilmer Institute in August, 1941, with a history of malaise, anorexia, and fever of several days' duration. This was associated with severe frontal headache, redness of the eyes, and a progressive visual loss of two days' duration. There was nothing significant in the past history.

On physical examination the only positive finding was, a posterior cervical lymphadenopathy. Vision was limited to the perception of hand movements at a distance of one foot in both eyes. External examination of both eyes showed normal anterior segments, except for a moderate ciliary congestion.

Ophthalmoscopic examination revealed a few, fine vitreous opacities. The disc and blood vessels were normal. There were many gray, elevated nodules, scattered through the maculas and peripheral fundi. The patient underwent a diagnostic survey in an attempt to establish the etiology of her condition.[†]

Laboratory studies. This study showed an eosinophilia of 9 percent on one occasion, and 6 percent on another, for which no adequate explanation was found. One mg. of old tuberculin injected intradermally gave no reaction. Uveal pigment skin test was negative. The pathologic examination of a biopsied lymph node revealed hard tubercles, without caseation.

Lumbar puncture was performed. The spinal fluid was under normal pressure, and was clear. There was an increase in the protein content and in the cell count. There were 90 lymphocytes per cubic millimeter. Two subsequent lumbar punctures, done at weekly intervals, revealed 65 and 80 cells per cubic millimeter, all lymphocytes.

An audiogram was performed and showed a 15-percent loss of hearing for spoken voice.

Course. The patient ran an irregularly febrile course, with the highest temperature recorded as 100.9°F. The headache and general malaise persisted for two weeks after her admission.

Generalized subretinal edema appeared

[†] Diagnostic survey as performed on these patients included complete medical history, physical examination, hemocytology, blood chemistry including determination of the serum albumin-globulin ratio (for sarcoid), Wassermann reaction, urinalysis, X-ray studies of chest, Brucella agglutination, lumbar puncture and study of spinal fluid, otolaryngologic, gynecologic, and dental examinations, sensitivity to Old Tuberculin, bacterial hypersensitivity tests, uveal pigment skin test, and aspiration of subretinal fluid.

and increased until by the 28th day the retina appeared to come forward several diopters. Vitreous opacities obscured the fundi two days later. On transillumination only gray reflexes were seen in the lower part of the pupillary space. These were thought to indicate retinal detachments.

On the 14th hospital day, anterior uveitis of the granulomatous type was first noted. The patient was treated symptomatically. Two months after the onset of symptoms she was discharged.

Vision in the right eye was 20/200 and in the left eye, 10/200. At this time the media were clear, and it was possible to observe the fundi. There was a diffuse mottling throughout the retinas, most pronounced in the regions of the foveas. Absorbing exudates were seen, and pigment deposits were present along the blood vessels.

On slitlamp examination, the anterior uveitis was still present. There was iris atrophy, and the pupils were irregular and bound down with posterior synechias. The aqueous ray was strongly positive, bilaterally.

After a temporary exacerbation, improvement occurred. Over the course of the following year the patient attained a final visual acuity of 20/20 in each eye. There was no evidence of retinal detachments, and there were no changes in pigmentary or hair systems.

CASE 2

History. C. N. (J. H. H. No. 137131), a 38-year-old Negro woman, was admitted to the Wilmer Institute in May, 1946, because of an acute onset of severe headache, rapid loss of vision, and pain in both eyes of one week's duration. There was a history of syphilitic infection, treated 5 months with arsphenamine 5 years before onset of ocular symptoms. Physical examination was negative.

Eye examination. Vision was 4/200 in the right eye, and 2/200 in the left eye. The anterior segments were normal on external and slitlamp examinations. Ophthalmoscopic examination revealed 2 diopters of papilledema. There was marked generalized retinal edema and moderate venous engorgement.

Laboratory studies. The positive findings on survey included a corrected sedimentation time of 24 mm. per hour, a mild sensitivity to 0.01 mg. of old tuberculin injected intracutaneously, and a positive gonococcus complement fixation test. Wassermann reaction was negative. Gynecologic examination revealed an old chronic salpingitis and cervicitis. Uveal pigment skin test was negative. Cerebrospinal fluid showed a cell count of 86 lymphocytes per cubic millimeter and protein content was elevated. A subsequent lumbar puncture two weeks later revealed 46 lymphocytes per cubic millimeter.

Course. The patient's headache became more severe, and posterior cervical lymphadenopathy appeared. On the 3rd hospital day evidence of anterior uveitis was observed in both eyes. Both retinas were elevated about 5 diopters by subretinal and retinal edema. The fundi were a peculiar, waxy, yellowish color. The nerveheads were elevated 5 diopters, and bilateral retinal detachments were noted inferiorly for the first time. These progressed rapidly, and aspiration of subretinal fluid was done on the 5th hospital day, 0.2 cc. of greenish fluid being obtained. This was injected into the anterior chambers of rabbits' eyes, and intracerebrally into white mice. The results were negative.

By the 21st hospital day the anterior uveitis was severe. Vitreous opacities obscured the fundi except for a dim, red reflex. On the 23rd hospital day, there was no light perception in the left eye. The patient was discharged after 6 weeks.

At this time, fundi could not be visualized and anterior segments of both eyes showed an active, exceedingly destructive, granulomatous inflammation (fig. 1). Tension to fingers was very low. The patient showed some clinical impairment of hearing while in the hospital, and a 15-percent loss by audio-

gram. On discharge, large symmetrical areas of depigmentation were present on both shoulders (fig. 2).

When last seen on February 19, 1948, the patient's vision was limited to light perception. The uveitis was inactive. Both pupils were bound down by posterior synechias and occluded by vascularized membranes. The

Fig. 1 (Bruno and McPherson). *Case 2.* External view of anterior segment on discharge examination. Uveitis was active, and both pupils were bound down by posterior synechias and occluded by vascularized membranes.

irides were grossly atrophic and markedly depigmented (fig. 3).

CASE 3

History. A. W. (J. H. H. No. 141208), a 19-year-old Negro girl, was admitted to the Wilmer Institute in June, 1947, with the complaint of blurred vision and pain in both eyes of 4 weeks' duration. She had been seen in May, 1947, in the outpatient department where the diagnosis of episcleritis was made, but had not returned until the day of admission. Physical examination revealed a normal, young adult female, six months pregnant.

Eye examination. Vision in the right eye was 20/30 and in the left eye, 20/70. External and slitlamp examination of the right eye was completely negative. Ophthalmo-
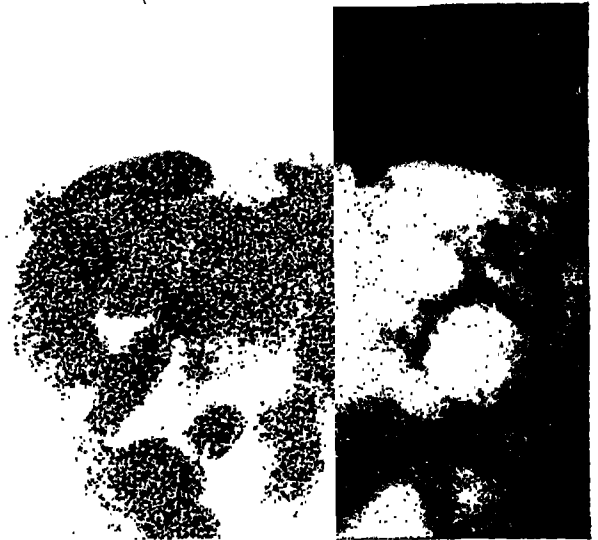
Fig. 2 (Bruno and McPherson). *Case 2.* Large, symmetrical areas of depigmentation on the back and shoulders.

scopically the disc was hyperemic and the macula appeared gray and edematous. The veins were somewhat overfilled.

The left eye showed moderate pericorneal injection and evidences of mild anterior uveitis. There was marked blurring of the neuroretinal margin, with loss of physiologic cupping. The edema of the nervehead extended into the surrounding retina. There was marked overfilling of the retinal veins and an elevated yellow nodule was present between the disc and macula.

A complete medical survey did not reveal any cause for the disease. The sedimentation
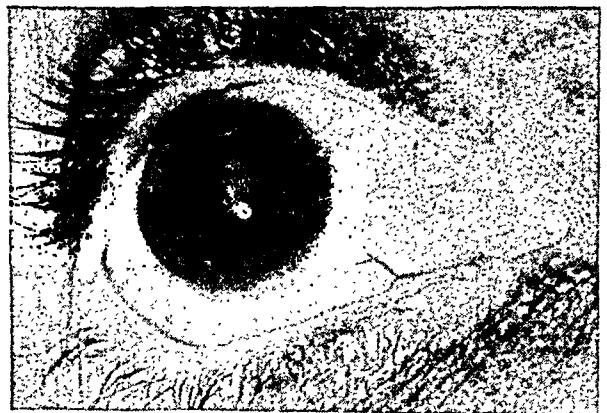
Fig. 3 (Bruno and McPherson). *Case 2.* External view of anterior segment one year later. Uveitis was inactive, pupils were secluded and occluded, and a depigmentation of the irides had occurred.

rate was increased. Uveal pigment skin test was negative and lymph-node biopsy showed only lymph-node hyperplasia. Lumbar puncture showed a normal spinal fluid with only two cells present.

Fig. 4 (Bruno and McPherson). *Case 3.* Bilateral poliosis, with patches of vitiligo involving the eyelids.

Course. The right eye developed a diffuse retinal edema similar to that in the left eye. Bilateral detachments of the retina appeared on the second hospital day. These progressed in both eyes to total detachments by the 17th hospital day. Four-and-one-half weeks after admission, only a dark reflex could be obtained in either eye. Vision in the right eye was restricted to hand motions and in the left eye to light perception temporally.

Because of the relentless course of the disease, it was decided to interrupt pregnancy. Hysterotomy was performed 18 days after admission. This had little apparent effect on the patient's ocular condition. Shortly after operation an intense anterior uveitis developed. As this cleared the elevated retina could be dimly seen in both eyes with a +20D. lens. Audiograms taken at this time showed a 15-percent and 18-percent loss of hearing in the right and left ears.

The patient was discharged and not seen again for three months. When she returned, the uveitis in both eyes was still active. Vision in both eyes was limited to perception of hand motions at one foot. The fundi could not be seen. Poliosis and vitiligo of both lower lids was present (fig. 4), and

there was an area of alopecia on the vertex of the skull (fig. 5).

CASE 4.

History. M. J. (J. H. H. No. 359518), a 19-year-old Negro girl, was admitted to the Wilmer Institute in October, 1947, with the complaint of poor vision in both eyes. The present illness began four weeks before admission when the patient developed a general malaise. Three weeks prior to admission vision began to fail and the patient developed severe frontal headaches. One week prior to admission she became febrile and vision failed rapidly.

Past and family histories were essentially negative. Physical examination on admission

Fig. 5 (Bruno and McPherson). *Case 3.* The area of alopecia which occurred at the vertex of the skull. The new hairs are growing in white.

revealed a healthy, young Negro female, two months pregnant.

Eye examination. Vision in both eyes was restricted to light perception. External examination of the anterior segments was negative. Both fundi showed a diffuse vitreous haze. The nerveheads were edematous and surrounding retinal details were ob-

scured by retinal edema. The veins were overfilled. Retinal detachments were present inferiorly.

Complete medical survey revealed no possible etiology for the ocular condition. Spinal-fluid examinaton was negative and there was no lymphocytosis. Uveal pigment skin test was negative. Audiometer showed a 10-percent loss of hearing in the right ear and a 15-percent loss in the left ear.

Course. Heavy vitreous opacities appeared shortly after admission. The retinal edema progressed, giving both fundi a yellow, waxy appearance. The detachments increased in height and size and by the 11th day of hospitalization the fundi could no longer be visualized. On the 9th day of hospitalization aspiration of subretinal fluid was performed. The fluid was inoculated on chorioallantoic

Fig. 6 (Bruno and McPherson). *Case 4.* Poliosis, with patches of vitiligo, involving both eyes.

membranes of chick embryos and cultured anaerobically. The results were negative.

The patient was discharged after 25 days of hospitalization with little change in her condition. Vision was 3/200 in both eyes. The

patient returned two months later. At that time there was little change in her ocular picture, but she had developed vitiligo and poliosis involving the lids (fig. 6).

Fig. 7 (Bruno and McPherson). *Case 4.* Left eye. The fundus showed irregular areas of pigmentation and widespread retinal atrophy.

The patient was seen on March 22, 1948, five months after discharge. The vitreous had cleared so that both fundi could be seen (fig. 7). Irregular areas of pigmentation were present and there was widespread retinal atrophy. The retina had reattached spontaneously in both eyes. Vision was limited to counting fingers at two feet. There was no active uveitis present, although moderate iris atrophy and posterior synechias were noted.

COMMENT

Case 1, H. J., demonstrates the symptom complex and clinical course which typify the "classical" cases described by Harada. The onset of an acute, diffuse, exudative choroiditis, associated with symptoms of cerebral irritation and the appearance of retinal detachments, is characteristic. It is true that the fundi were obscured before the retinal detachments could be observed, but the gray reflexes in the pupillary space seen at this time undoubtedly indicated detachments of

the retina occurring in the inferior aspects of the fundi. The increase in protein and the number and cell type in the cerebrospinal fluid point to meningeal involvement. Here, the anterior involvement was light, and the final visual acuity returned to normal.

Case 2, C. N., also showed the acute, characteristic onset of general and ocular
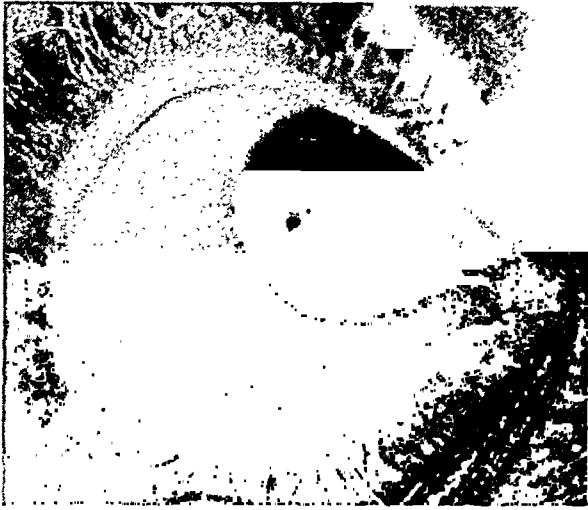
Fig. 8 (Bruno and McPherson). *Case 4.* Right eye. Transient hyphemia, occurring spontaneously, many months after the onset of original symptoms.

symptoms. Her course was complicated by the development of hypotony, severe anterior uveitis, and the formation of cataracts. The fundi could not be viewed to ascertain if the retinal separation ever receded. But the fact that the left eye had lost all light perception for a week or more, and that light perception and projection returned, indicates the probability that the retinas became re-attached. Vitiligo appeared in this patient after the onset of a severe anterior uveitis.

Case 3, A. W., too, was typified by the acute onset of an exudative chorioretinitis, with rapid loss of vision, and the appearance of bilateral retinal detachments.

This case is worthy of comment because pregnancy was interrupted. This was done on the possibility that the retinal detachments might be due to an atypical eclampsia, although the patient gave no clinical evidence of this state. Other forms of therapy had been of no avail and, in view of the rapid advance

of symptoms from bad to worse, it was felt that this might be of some benefit to the patient. The fact that this procedure did not appreciably alter the ocular picture indicates that eclampsia was not the factor.

Another point of interest in this case is the delayed onset of the anterior uveitis, which was severe and quite similar in its picture to that in Case 2. With the advent of the involvement of the anterior uvea, depigmentation took place in the skin and eyelashes. Alopecia occurred shortly afterward. It is interesting, too, that the patient presented no findings in the cerebrospinal fluid, as did Cases 1 and 2.

Case 4, M. J., is a transition between Case 1 and Cases 2 and 3, combining some features of each. The prodromal history was prolonged and intimately associated with the period of most rapid visual loss. This was prior to the outpatient department visits, and it is quite probable that, if she had been seen at that time, there would have been signs of meningeal irritation, as shown by increased protein and cells in the spinal fluid.

The onset of ocular symptoms was similar to that in the other three cases, but at no time was the anterior uvea more than mildly involved. The media are now clearing, and the patient has developed vitiligo and poliosis.

A tendency for spontaneous hyphemia has been observed in Cases 3 and 4 within the last few weeks, many months after the onset of the original symptoms. In Case 3 this has tended to persist, but this hemorrhage cleared rapidly in Case 4 (fig. 8). This patient was pregnant, as was the one in Case 3, but it is interesting to note that this apparently had little effect on the course of the disease and was not responsible for any retardation in recovery.

In the further evaluation of these cases, it is striking that three were seen in Negro women, all from the same city, within a period of one year. This is quite a high incidence of a relatively rare syndrome, unless we can presuppose that we have seen a

small epidemic due to some infectious process. Another interesting fact is the presence of a subclinical deafness in all four cases, as shown by audiometer readings.

This disease shows a wide geographic distribution, cases having been reported from Japan, Europe, South America, and the United States. It does not show a predilection for any specific race or sex. The patients reported in this series varied in age from 19 to 38 years; most of the previously reported cases have been in patients from 30 to 50 years of age.

ETIOLOGY

The specific etiologic factor in this disease is unknown. The four possible etiologies which have been proposed for this syndrome are: (1) Syphilis, (2) tuberculosis, (3) hypersensitivity to uveal pigment, and (4) a virus.

Serologic examination was carried out in all cases in the present series and found to be uniformly negative. In Case 2, in which there was a positive history of a luetic infection, there was a period of five months' treatment with arsphenamine, long before the onset of the ocular symptoms. Syphilis, therefore, cannot be considered as a causative factor in these patients.

Tuberculin tests were made on each patient as part of the diagnostic survey. Only one, namely, Case 2, was sensitive, and she gave a mild reaction to 0.01 milligram of old tuberculin injected intradermally. There were no other findings to substantiate the diagnosis of ocular tuberculosis in this patient. Chest X-ray studies were negative. This syndrome was ascribed to tuberculosis by Okamura.[2] His opinion was based on a histologic examination of one iris biopsy. Furthermore, the clinical course, the appearance of the fundi, and the final results of this process are not at all characteristic of ocular tuberculosis. In Case 1, the lymph-node biopsy showed hard tubercles with no caseation. The patient was insensitive to 1 mg. of old tuberculin and her chest X-ray film was

negative, findings which are more suggestive of sarcoid than tuberculosis.

Because of the clinical resemblance of Harada's disease to sympathetic ophthalmia, Weskamp[3] made use of Peters's[4] suggestion that hypersensitivity to uveal pigment may play some part in the production of the inflammation. This is simply an application of Elschnig's theory of the etiology of sympathetic ophthalmia to a disease which resembles it in many of its manifestations. Even if hypersensitivity to uveal pigment was present in these cases, it certainly seems that some other factor would have to be present to initiate the process. In the present series we were unable to demonstrate hypersensitivity to uveal pigment by skin biopsy in any of the cases.

A theory which has many adherents, but little proof for its support, is the virus etiology of Harada's disease. Takahashi's work strongly suggested this factor.[5] He studied both the vitreous and spinal fluid of patients in Harada's series.

Bacteriologically sterile vitreous was injected into the cisterna of 5 rabbits. In 2 rabbits an optic neuritis and uveitis developed; in 29 days in one case, and in 50 days in another case. The cerebrospinal fluid of a patient with Harada's disease was injected into the vitreous of a rabbit eye, producing an inflammatory reaction in both eyes within 12 to 16 days. The brain of a third rabbit which had been inoculated with human vitreous was injected into an uninfected rabbit. The latter developed an optic neuritis and an iridocyclitis within 2 days.

Controls inoculated with human serum and the cerebrospinal fluid of tabetics gave no reactions. From these experiments Takahaski concluded that the etiologic agent of the disease was probably a virus, and that it was transmitted by way of the optic nerve. He postulated a relation between this virus and the causative agent of herpes.

Tagami[6] injected the subretinal fluid of a patient with Harada's disease into the vitreous of rabbit eyes and produced a uveitis

Fig. 9 (Bruno and McPherson). A case of vitiligo in a patient with the Vogt-Koyanagi syndrome.

used for virus studies. Some of the fluid was injected intracerebrally into white mice. These animals were killed after varying intervals of time and transfers of infected brain tissue to uninfected mice was performed. The chorioallantoic membranes of 14-day-old chick embryos were inoculated with more subretinal fluid, and transfers were made to other embryos of varying age after a period of 5 to 7 days. The anterior chambers of rabbit eyes were inoculated with subretinal fluid and spinal fluid of patients. In all these experiments *no virus could be grown.*

This failure to confirm what other observers have reported may be explained in several ways. It is a well-known fact that a virus must be isolated early in the course of any disease in order to obtain positive results. Perhaps the inoculum was not obtained early enough in the cases of this series. Another explanation lies in the possibility that previous workers may have isolated a virus quite often found in the rabbit and transmitted this from animal to animal. None of the work reported is conclusive,

which he could transmit for three generations. Further, he studied some of these eyes histologically and observed a diffuse infiltration of the choroid, similar to that in sympathetic disease, but without the formation of giant cells. There was detachment of the choroid and retina by a serous or fibrinous exudate. The pigment epithelium was degenerated, but there were no changes in the neuroepithelium of the retina.

Malbran and Muhlmann[7] used vitreous of a patient with Harada's disease, injecting it into the subarachnoid space of rabbits, and produced optic neuritis and uveitis. Using the spinal fluid of the same patient, they inoculated one eye of a rabbit. *This resulted in an intraocular inflammation which appeared in the other eye in 12 days.*

Subretinal fluid was obtained from Cases 2, 3, and 4 of the present series. This was found to be bacteriologically sterile, and was

Fig. 10 (Bruno and McPherson). A case of vitiligo in a patient with sympathetic ophthalmia which followed an iridencleisis done for control of glaucoma.

since no agglutinins or other antibodies were ever demonstrated in experimental animals or in patients. However, the evidence for a virus etiology of this condition is the only evidence supporting any of the etiologies so far proposed.

What is the relation of Harada's syndrome to the Vogt-Koyanagi syndrome and to sympathetic ophthalmia? Certainly many Vogt-Koyanagi syndrome and occurred in all the cases of this series. It was present in 4 of Harada's 12 cases. This finding was reported by Komoto,[10] in 1912, in a case of sympathetic ophthalmia; also by Cramer, in 1913.[11]

Optic neuritis, retinal edema, retinal detachments, although rare, have been described in the Vogt-Koyanagi syndrome.[9]

TABLE 1

PHENOMENA PRESENT IN HARADA'S AND PRESENT SERIES OF CASES

	Harada's Cases	Case 1	Case 2	Case 3	Case 4
Bilateral uveitis	12	+	+	+	+
Bilateral retinal detachments	8				
A—With reattachment	8	+			+
B—Without reattachment	0		±	±	
Poliosis and vitiligo	8	−	+	+	+
Alopecia	*	−	−	+	−
Prodromal symptoms	5	+	+	+	+
Spinal fluid changes					
A—Lymphocytosis	5	+	+	−	−
B—Increase in protein	7	+	+	−	−
Dysacousia	4	+	+	+	+
Uveal pigment skin test		−	−	−	−
Race and Sex		WF	CF	CF	CF
Culture of subretinal fluid	not done	not done	negative	negative	negative

* Specific number of cases not given.

of the clinical signs of the three are similar and the syndromes frequently overlap. Poliosis and vitiligo are essential features of the Vogt-Koyanagi syndrome (fig. 9) and have been observed in sympathetic ophthalmia (fig. 10).

Nettleship[8] reported a case of poliosis in sympathetic ophthalmia, as early as 1884. Numerous other incidents of this occurrence have been reported subsequently. Two cases of the present series and 8 of Harada's original series developed this phenomenon (see table 1).

Alopecia is an integral part of the Vogt-Koyanagi syndrome and in 29 cases reported after Koyanagi's series up to 1941,[9] this finding was present in 13. This occurred in 1 of the present series and in 2 of Harada's cases.

Dysacousia is a frequent finding of the There are occasional findings of sympathetic ophthalmia. Spinal-fluid changes while more common in Harada's disease have been described in both of the other conditions.[12]

The bilateral granulomatous uveitis is characteristic of all three conditions. In the Vogt-Koyanagi syndrome and in sympathetic ophthalmia, it is identical in its cellular characteristics and clinical course. In Harada's syndrome, however, it tends to involve the posterior segment more severely than the anterior, and consequently leads to early retinal detachments which are relatively less common in the other two conditions.

Because of the many clinical resemblances of these three conditions and the tendency for them to overlap, it is possible there is some common etiologic factor in all but there is no indication what such a specific

factor may be. If it is a virus, it has not yet been recovered.

SUMMARY

Four cases of Harada's disease are reported. The etiology and relationship of Harada's disease to the Vogt-Koyanagi syndrome and sympathetic ophthalmia are discussed. It seems possible that there may be some common etiologic factor responsible for all three conditions.

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OPHTHALMIC MINIATURE

Nothing gives dexterity in the use of the ophthalmoscope so quickly and so effectively as an attempt to draw what is seen, and nothing gives ability to recognize details with accuracy and perceive every feature presented, as a habit of drawing does. Yet ophthalmoscopic drawing is hardly ever practised. It is supposed to be difficult, but it is neither difficult nor does it need any ability or facility for ordinary drawing. The process is within reach of every student.

Gowers, *Medical Ophthalmoscopy*, 1890.

OCULAR CYSTICERCOSIS*

Lech Junior, M.D.
Campinas, Brazil

Translated by Charles A. Perera,[†] M.D.
New York

Penido Burnier, on May 15, 1915, one year after the establishment of his eye clinic in the city of Campinas, forerunner of the institute which bears his name, diagnosed his first case of ocular cysticercus. Since then he kept his interest in this phase of ocular pathology and passed his knowledge and experience to his collaborators, assistants, and visitors, thus making possible the present study of 111 cases observed by the oculists and pathologist of the Instituto Penido Burnier. This work, therefore, represents the results of collective experience with ocular cysticercus.

This presentation is arranged in the following chapters: Historical survey, pathogenesis, casuistics, diagnosis, treatment, prognosis, pathology, prophylaxis, iconography.

HISTORICAL SURVEY

Human helminthiasis and porcine cysticercus have been known since times of greatest antiquity, as revealed by the celebrated Ebers papyrus and the writings of Hippocrates, Aristophanes, and Aristotle. The doctrine of spontaneous generation of worms in the intestinal mucosa was accepted until the middle of the 19th century. The Mosaic prohibition against eating pork must be considered as a prophylactic measure.

Although the preliminary studies of Stenstrupp (1842), Siebold and Dujardin (1845), and Wagner (1848) tended to demonstrate the relations between tenia and cysticercus and the similarity of their respective cephalic extremities, it was only in 1850 that

Van Beneden firmly established the origin and interdependence of the two parasites, throwing light on their evolutionary cycles.

The discovery of the first living cysticercus in the anterior chamber of the human eye by Schott and Sömmering of Frankfort, in 1829, must have created a great scientific furor and interest. However, Gescheidt, in 1833, still was defending the doctrine of spontaneous mucosal origin of the parasite, believing that morbid ocular changes preceded its appearance.

Thanks to the precious inheritance of Pereira da Cunha and Guedes de Melo, first teachers of Penido Burnier, and inspirers of his love for this specialty, the library of the Institute possessed the most important ophthalmologic literature of the last century dealing with the subject of ocular cysticercus, common enough especially in northern Germany in the second half of the last century, after the discovery of the ophthalmoscope. Thus it was possible to be familiar with the work of Sichel, Albrecht von Graefe, Alfred Graefe, Hirschberg, de Vicentiis, and other authors of experience who were skilled in the diagnosis and treatment of these cases without the resources of modern ophthalmology.

To Sichel, Sr., we owe not only perfect knowledge of subconjunctival cysticercus of which he made 7 personal observations of the 13 cases recorded up to that time (1859) but also a complete report of the first case of living cysticercus discovered in the anterior chamber of the human eye.

Sichel referred to the observations of Schott and Sömmering who followed the development of the parasite for 7 months and made instructive drawings. The patient, Helena Bauer, the 18-year-old daughter of a

shoemaker of Frankfort, concealed from Sömmering her previous visit to Schott, and thus permitted both investigators to publish separately this curious and unique case in the medical literature of that time. The parasite was easily extracted by Schott on July 17, 1829, in the presence of Sömmering and other notables of Frankfort. Hirschberg recorded that the pleased surgeon had the figure of cysticercus cellulosae engraved on his ring and published his daring operation in 1836 in the appendix of a paper on the umbilical cord.

In 1829, before the Congress of German Naturalists in Heidelberg, Sömmering emphasized that the above case represented not only the first case of cysticercus discovered in the human eye but also the first example of the living parasite in a living human. For several years it was considered a unique case, and even in 1859 Sichel said there had not been another such case in which the parasite was so minutely studied and depicted before and after extraction, with the naked eye and with the microscope. The description of Sichel, based on the publications of the two authors, the unpublished data and drawings furnished by Sömmering, and the sketches of Schott deposited in the Museum of the Faculty of Heidelberg, is superior to that of both observers separately.

In 1838, Siebold published the observation of Baum concerning the first case of cysticercus found under the human conjunctiva.

These two ocular localizations were observed on a few occasions in Germany, France, and England. Coccius described a cyst of the vitreous, resembling the cysticercus, barely two years after the discovery of the ophthalmoscope. In 1854, Albrecht von Graefe made the first undisputed observation of cysticercus in the retina and vitreous.

Among von Graefe's numerous writings on this subject, one important paper was published in the *Archiv für Ophthalmologie* (12:174(2)1866). This article refers to more than 80 cases observed during a period

of 13 years among 80,000 patients. He found the cysticercus 3 times in the anterior chamber, 5 times beneath the conjunctiva, once in the lens and in the orbit, and the remainder in the deep parts of the eyeball. He called attention to the frequency of the cysticercus in other organs, especially the brain, as recorded by pathologists. Virchow found the parasite in two percent of autopsies.

The famous Berlin professor was the first to extract the cysticercus from the vitreous by iridectomy, removal of the lens, and extraction of the parasite in 2 or 3 stages. To avoid delay which was often dangerous to vision, he later performed the three procedures at one sitting. When there was no probability of saving vision, he operated via an equatorial sclerotic incision. Von Graefe was always able to remove the parasite, but sometimes the operation was followed by atrophy of the globe and cataract. He judged as inoperable the subretinal cysticercus, even when some vision remained, because all of his attempts to remove the parasite in blind eyes were failures.

Arlt of Vienna, however, in 1866 succeeded in removing a subretinal cysticercus via a meridional sclerotic incision.

Later, Alfred Graefe, cousin and pupil of the great von Graefe, popularized the extraction of the cysticercus from the retina and vitreous through a meridional scleral incision. From 1877 to 1882, he performed 24 such operations, with success in 16 instances. To Alfred Graefe we are indebted for ophthalmoscopic localization, for this method served him well in localizing the cysticercus and other morbid retinal foci.

Hirschberg's article in 1855, in Eulenburg's *German Encyclopedia of Medicine and Surgery*, gave a good summary of the work of von Graefe and his pupils, and presented a large number of interesting observations.

Alfred Graefe collected about 70 cases of ocular cysticercus among 60,000 patients from his clinic at Halle, and Hirschberg in Berlin encountered 70 cases from a total of

60,000 patients. In the first five months of 1876, among 2,700 new patients, he found the parasite five times in the deep parts of the eyeball. As a result of progress in sanitation and popular education, Hirschberg could only find one new case from 1886 to 1889 among 30,000 patients.

In 1899, De Vicentiis called attention to

of the eyeball and suggested its destruction by the use of a solution of corrosive sublimate.

In 1918, the subject was propounded in Brazil by Abreu Fialho who published a case of subconjunctival cysticercus and referred to two others in which the parasite was encountered in the vitreous of enucleated

Fig. 1 (Lech Junior). Macroscopic appearance of a globe containing cysticercus. Ophthalmoscopic diagnosis impossible because of organized inflammatory process behind the lens (plastic choroiditis). Umbrella-shaped detachment of the retina. The irregular cavity was partially occupied by the vesicle of the parasite which was well preserved (probably alive). The reactive capsule was characteristic.
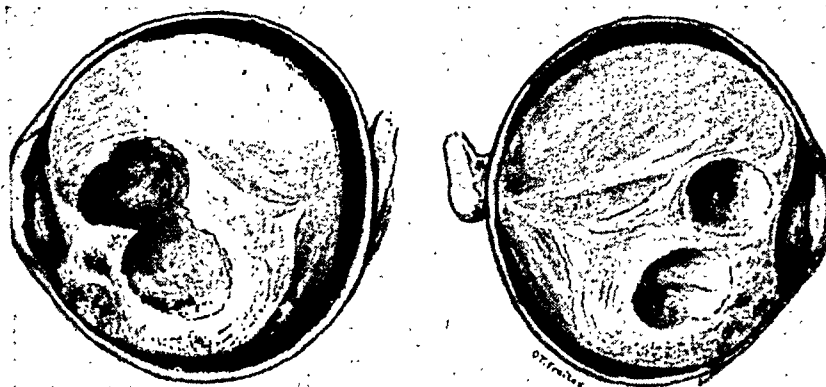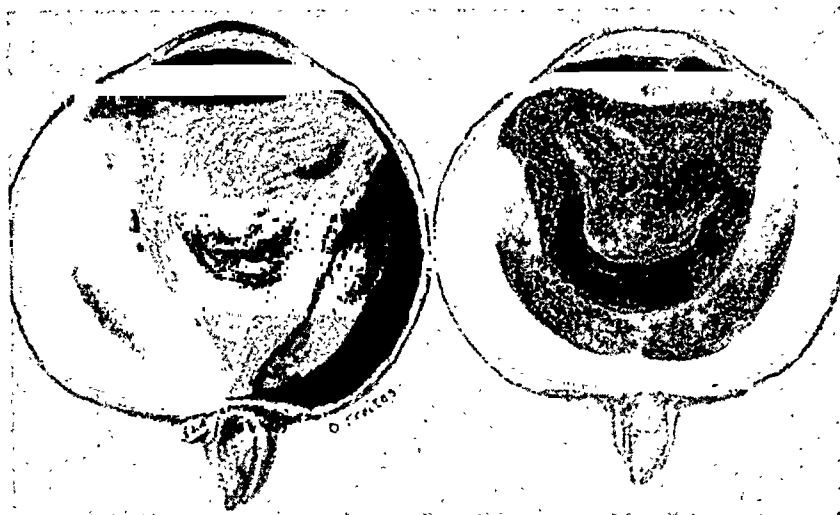
Fig. 2 (Lech Junior). Another macroscopic aspect of intraocular cysticercus. The retinal detachment here is more irregular and the cavity occupied by the parasite shows a bilobular appearance in one of the sections. The location was eccentric and the inflammatory process pulled the detached retina over to one side of the globe. In this case, ophthalmoscopic diagnosis was impossible.

his 26 cases observed in Palermo and Naples and stated that Hirschberg had informed him that no new cases had been found in Berlin during the previous 10 years among 100,000 patients.

In a paper on "Animal parasites of the visual apparatus," the treatise in Graefe and Saemisch Handbook, Kraemer of Zurich, who had studied the problem thoroughly, presented the entire bibliography up to 1898. Bardeli, in 1922, brought new and interesting observations on cysticercus in the deep parts

eyes. Soon after, there appeared the careful work of Pereira Gomes, "Two cases of intraocular cysticercus, operated upon with success." In the same year Penido Burnier reported his first 6 cases observed during a period of four years. After these reports, others followed, among them Belfort de Matos, in 1929, Pereira Gomes, Aureliano Fonseca, Nicolino Machado, Paula Santos, Abreu Fialho Filho, and other Brazilian authors.

Biancini, in 1923, in an erudite mono-

graph, claimed that a dead parasite is very dangerous to the ocular membranes. He advised postponing operation when the cysticercus is active and attempting extraction when the ocular reaction showed a decadence of the parasite.

Cosmettatos and Anargyros of Greece and Michail of Roumania reported an in-

Biancini, in 1913, considered cysticercus infection to be common in Italy, very rare in the Orient, Asia, Africa, and South America, and more frequent in North America. H. Ward disagreed with the idea, prevalent in Europe, that tenia and cysticercus in the United States were related directly to the extensive hog breeding. American statistics showed not more than a dozen cases of ocular cysticercus. On the other hand, the same
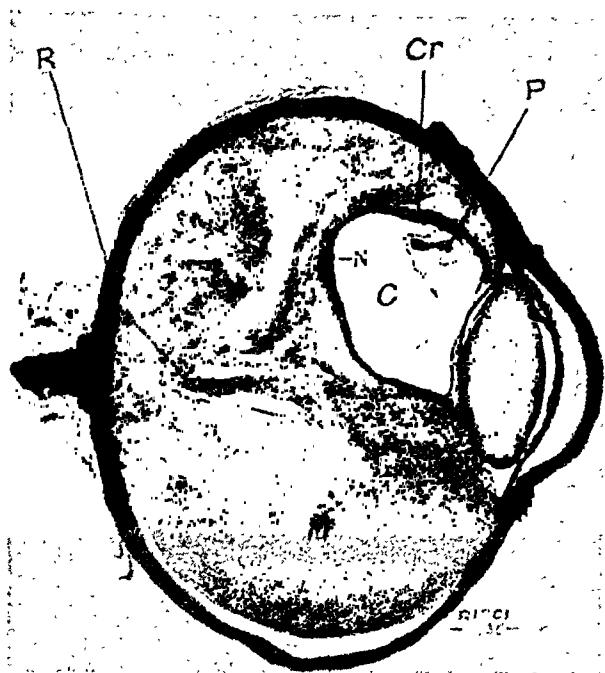
Fig. 3. (Lech Junior). Characteristic appearance of intraocular cysticercus. (Sectioned in celloidin, stained with V. Gieson.) The ophthalmoscopic diagnosis in this case was impossible. Patient was a 2-year-old child. The clinical picture was suspicious of retinoblastoma. Umbrella-shaped complete detachment of the retina, with extensive subretinal hemorrhages. The empty cavity was probably due to fixation fluids which collected as the parasitic vesicle retracted. The purulent and necrotic band (first zone) is wider on one side (N). (C) cavity occupied by the parasite. (P) cysticercus caught in a longitudinal section. (Cr) reactive capsule. (R) retina. (M) hemorrhage.

Fig. 4 (Lech Junior). Microphotograph of the same case as Figure 3.

creased frequency of cysticercus infestation in several regions of Europe during World War I. Up to 1935, several European authors published 18 new cases to which Michail added 12 more which were discovered in Roumania during the same period of time. When tenia solium exists, the cysticercus tends to be prevalent; both, however, are easily controlled by prophylaxis.

American author attributed, at least in part, the great richness of the German statistics to the accuracy of diagnosis in the well-managed and accessible clinics. At the same time he denied the rarity of the disease in other countries, believing this to be due to deficient observation rather than to absence of the parasite. Rafael Silva showed in his papers that cysticercus is not rare in Mexico, and Lech Junior is convinced that, if carefully investigated, the parasite would be found as frequently in other South American countries as in Brazil. Argentina is probably an exception to this statement, since in its splendid clinics the ocular cysticercus is rare according to the reports of Urrets Zavalia, Adrogué, and other learned colleagues.

ETIOLOGY

Tenia solium, whose larva is the cysticercus, belongs to the class of Cestoids, order of Cyclophyllidea, family Taenidiae, genus Taenia, and species Solium.

Its habitat is the small intestine. The definitive host is man, while the pig is its intermediary host, although there are other possible intermediary hosts such as the monkey, the dog, the cat, and even man.

EVOLUTION

Segments of the worm are found in the stools, and rupture to release 30,000 to 50,000 ova. The intermediary porcine host, eating contaminated vegetables or feces, ingests these eggs. The chitinous shell of the ovum is dissolved in the gastric or duodenal juices. The embryos with the aid of their hooks perforate the gastric or intestinal mucosa, and get into the capillaries, especially on the venous side. From there they are carried passively by the blood stream to the tissues and organs of the body. Once the embryos reach the liver or lung, they traverse the capillary network. The cysticercus, rarely found in the liver and lung, is thrown as a living embolus into the circulation where it comes to a halt in the capillaries. In the pig, the embryos localize in the interfascial connective tissue of the muscles, as for example in the pectoral muscles, subscapular muscles, sublingually, in the diaphragm, cardiac muscle, and also in the brain.

After coming to its resting place, the embryo loses its hooks, becomes vesicular, increases in size, and forms a head by evagination of one portion of its wall. Thus forms the mature larva during a period of three months, called the cysticercus cellulosae or cysticercus solium. The larva appears as a globular vesicle, the size of a pea or bean, measuring up to 15 mm. in length and 7 or 8 mm. in width. In color it resembles a transparent pearl in the interior of which is seen a yellowish firm formation called "receptaculum capitis," which consists of the scolex

and its neck invaginated like the finger of a glove. At the point in which the membrane is invaginated, is noted a small depression and in the center of this is an orifice through which the head appears when the cysticercus continues to evolve.

At a temperature of 35 to 40°C. the larva develops contraction movements. The head
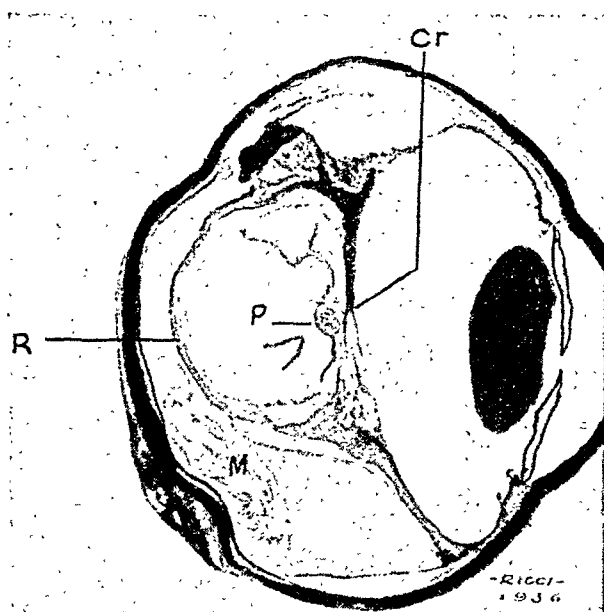
Fig. 5 (Lech Junior). Complete detachment of the retina (R) forming a pocket which involves the reactive capsule and which is closed anteriorly by this capsule (Cr) and by the hyaloid. (P) parasite in transverse section. (M) hyalin masses in the middle of the vitreous. (Section in celloidin, stained with V. Gieson.)

appears resembling the head of the adult worm.

When insufficiently cooked infested pig meat is eaten by a human being, the scolex of the parasite, freed by the digestive juices, becomes attached by its suckers to the intestinal mucosa. It then commences to form segments which are expelled in about three months as mature proglottids in the feces.

CYSTICERCOSIS

Infestation. Monteiro Sales stressed in his "New considerations concerning neurocysticercosis" several methods by which man may become infected.

1. INTERNAL AUTOINFECTION. Vomiting
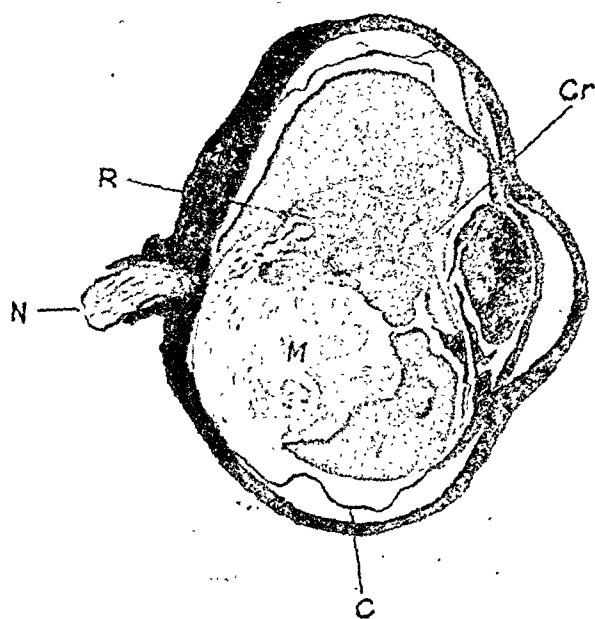
Fig. 6 (Lech Junior). Another case in which ophthalmoscopic diagnosis was impossible (retinoblastoma was suspected). Patient was a 2½-year-old child. The detached retina (R) was pushed to one side by a mass (M) formed by the parasitic vesicle. (Cr) reactive capsule. (C) choroid. (N) optic nerve. (V) vitreous. (Section in celloidin. V. Gieson stain.)

or antiperistaltic movements of the intestines may force mature proglottids into the stomach where digestive fluids may liberate the embryos. These perforate the stomach wall, get into the circulation, and invade different tissues of the body. Rarely, cysticercus and tenia may be found in the same individual. In most cases, cysticercosis does not reveal tenia and cysticercus together, because the intestinal form has been already expelled.

2. EXTERNAL AUTOINFECTION. In these instances the individual who harbors tenia ingests the ova or segments of his own parasite. This occurs in insane people and children.

3. HETERO-INFECTION. This is the usual method. The individual becomes infected by ingesting ova in polluted water, inadequately cooked vegetables, contaminated fruit, or on his own dirty hands, and so forth. In the history, it is important to ascertain the presence of infection in members of the family of the patient. There are cases where one spouse

harbored tenia and the other cysticercus.

Migration and Evolution. If an egg reaches the stomach by one of these methods, its shell is dissolved and the embryo passes into the circulation after perforating the gastric wall. The stomach represents the first means of defense against the parasites which are destroyed by prolonged action of the gastric juice. Even in the rare cases of massive infection, it is likely that the majority of the embryos do not survive. When the embryos get into the circulation they act like living, not inert, foreign bodies and come to a stop at points where the caliber of the vessel is narrow or where the flow of blood is slow.

In 1885, Hirschberg thought that infestations were mainly auto-infections, which we now know to be contrary to the facts. Among our 111 cases, only 25 showed tenia and ocular cysticercus simultaneously. We observed in 2 cases the presence of ocular cysticercus representing the larva of tenia solium and the coexistence of an intestinal parasite belonging to a different species (saginata).

Frequency. Ocular cysticercosis is a rare disease. Among 153,528 patients only 111 cases were observed, a proportion of 1:1,383 or a little more than 7 in 10,000.

Localization. The parasite was found in the ocular tissues as follows: 51 in the vitreous, 10 subhyaloid, 44 subretinal, 2 in the anterior chamber, 7 subconjunctival, 1 in the orbit, and 1 subcutaneous in the region of the lacrimal sac. The relative infrequency of the extraocular cysticercus may be influenced by the fact that the extraocular parasite is well tolerated and may exist for a long time before the patient notices its presence and seeks medical advice. When the parasite is located within the eye, the patient is likely to seek medical attention early because of reduced vision from turbidity of the ocular media. The rich vascular network of the choroid as compared with the conjunctival blood vessels may favor the intraocular localization of the parasite. In the

orbit only 1 case of cysticercus was found, in the supero-internal region above the lacrimal sac.

The 7 subconjunctival cases were distributed: 2 in the inferonasal portion, 2 in the external canthal region, 1 in the superior fornix, and 2 in the superonasal area of the conjunctival sac.

When subretinal, the parasite is usually

Fig. 7 (Lech Junior). Globe enucleated after operation for complicated cataract. Lens is absent. Anterior chamber very shallow and filled with exudate. Irregular retinal detachment. Parasite easily identified, free in the vitreous with its evaginated scolex resting on the internal surface of the retina. (Section in celloidin. V. Gieson stain.)

found at the posterior pole, particularly during the first months of infection before the retina is secondarily detached. This predilection may be a function of the diminishing caliber of the arteries which may prevent progress of the parasite toward the periphery. The following chart gives the percentages and locations of the subretinal cysticercus.

	Superior			
	7	0	14	
Nasal	0	39	7	Temporal
	11	11	11	
	Inferior			

After the secondary detachment of the

retina has developed, it is observed to be predominantly on the temporal side or inferiorly, because the cysticercus was originally located in the macular region. The same conditions do not hold for cysticercus located in the subhyaloid region or in the

Fig. 8 (Lech Junior). Same case as shown in Figure 7. Photomicrograph showing the scolex with two suckers and the characteristic crown of hooks lying upon the retina.

vitreous, because the parasite most often settles in the inferior hemisphere as shown in the following chart in which the percentages are recorded.

	Superior			
	0	0	5	
Nasal	2	5	2	Temporal
	15	42	29	
	Inferior			

The influence of gravity is the likely explanation for the localization of the parasite in the inferior portion of the eyeball when there is no obstacle to its movement.

The central or inferior localization of the

parasite in the anterior chamber is obvious (2 cases).

Vitality and Motility. The diagnosis of ocular cysticercus can only be made when the parasite is alive. Exudative or inflammatory disorganization of the fundus of the eye, when advanced, compromises the vitality and survival of the parasite. Among 97 clinically diagnosed cases of cysticercus, 88

subretinal site to beneath a fold of the secondarily detached retina, or from one sector of the vitreous to another, or migrating from the vitreous into the anterior chamber even without a vesicle as we had the opportunity to observe in the following spectacular case.

This was the case of a diabetic woman with cysticercus in each eye (Case 77, Chart
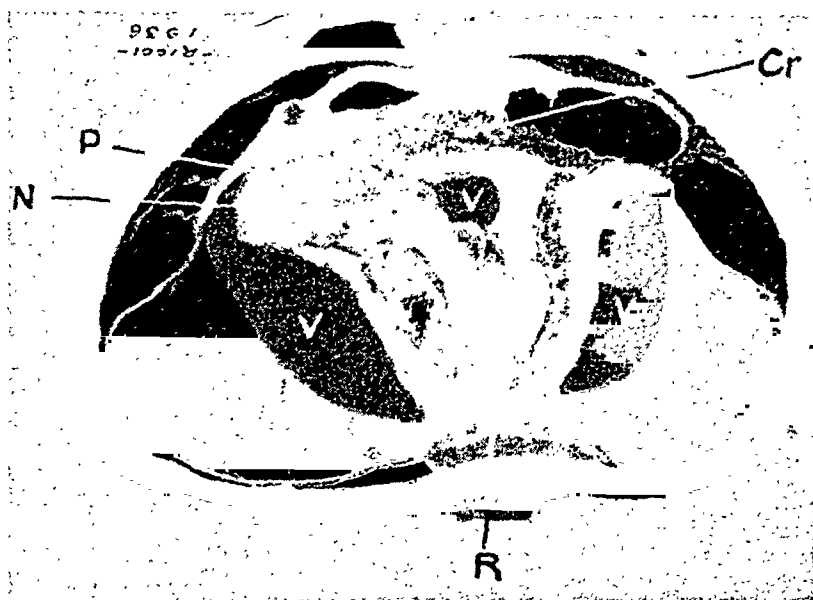
Fig. 9 (Lech Junior). Another case of altered globe with an old complete detachment of the retina (R) and a marked, organized inflammatory process. (Cr) reactive capsule. (V) vitreous. (N) zone of necrosis containing a small area (P) in which hooklets of the parasite were found. (Section in celloidin. V. Gieson stain.)

were intraocular. Its vitality could be verified in different ways:

a. Undulating movements of the vesicle.
b. Periodic evagination of the scolex.
c. Motility in relation to the vitreous.
d. Motility of the evaginated scolex.
e. Postoperative examination of the parasite.

The undulating movements, which are most evident when the parasite is in the vitreous, are very slight and can be seen at times only by long periods of observation when the media are sufficiently clear.

The movements of the scolex, on the other hand, are sufficiently noticeable when excited by light, although it is exteriorized only when the cysticercus is in the vitreous, subhyaloid region, or the anterior chamber.

Another evidence of its viability is its change of position within the eyeball during the course of time, moving from its original

108.436). The parasite of the right eye was successfully removed from the vitreous by the transcleral route. The cysticercus of the left eye, situated in the subhyaloid region and previously treated by diathermic cauterization by a colleague without destruction of the organism, was masked by a severe reaction.

While the patient was being treated to quiet the inflamed eye, she complained of severe pain in the eye and headaches. Examination showed the presence of a scolex in the anterior chamber attached to the posterior cornea by its suckers. The remaining portion of the scolex was emerging from its base in the iris, without a vesicle. The parasite moved upward by pseudopodlike movements of the sucking cups.

Before it disappeared from view at the opposite side of the iris it was possible to obtain photographs and extract the cysticercus with

forceps through a small corneal incision. During the operation it was possible to verify the strength of the suckers. When the caudal part of the scolex was pulled, the head remained attached to Descemet's membrane and tore loose, so that it was necessary to grasp this portion directly with forceps to remove it entirely.

The motility of the parasite within the

rarely in the first month (1 case).

b. More rarely, the cysticercus enters the vitreous directly. In this case, the remains of the retinal tear can be identified. When subretinal or in the retinal tear, the scolex has never been observed ophthalmoscopically to be evaginated.

Age. There is no immunity, although the parasite is less common in patients over the

Fig. 10 (Lech Junior). Photomicrograph of area (P) of Figure 9. The parasite is identified by its hooklets, of which three are seen in the area of necrosis.

eyeball depends upon the fluidity of the vitreous. Even then, the motility is so slight that its surgical removal is but little influenced by the position of the patient. When subretinal, the cysticercus usually remains in its original position for 3 (13 cases) and exceptionally up to 6 months (2 cases) from the onset of symptoms. After this, the parasite obtains the additional space needed for its development in one of two ways:

a. The retina offers some resistance and the parasite takes the path of least resistance in the subretinal space, provoking a secondary retinal detachment without retinal tear, occurring after 3 months (16 cases)

age of 40 years. The youngest patient was two years of age, the oldest was 66. The age incidence in our 111 cases shows:

Age	Number of cases
First decade	20
2nd decade	30
3rd decade	22
4th decade	24
5th decade	7
6th decade	5
7th decade	3

Sex. Contrary to von Graefe's figures (two thirds of the cases in males), we found that 64 of our patients were females and 47 were males. Probably there is no definite sex predilection.

TABLE 1

OCULAR CYSTICERCUS OBSERVED AT THE INSTITUTO PENIDO BURNIER BEFORE AUGUST, 1947

Case No.	Date	Chart No.	Age	Sex	Eye	Localization		Vision at First Exam.	Onset of Symptoms	Complement-Fixation	Carrier of Tenia
1	5/15/15	A.L.	18	F	O.S.	Vitreous	Inferior	C.F. at 1 M.	Unknown		—
2	4/11/17	2.336	30	M	O.S.	Anterior chamber	Central	H.M.	18 mos.		—
3	9/19/17	3.105	31	M	O.S.	Vitreous	Inferolateral	C.F. at 1 M.	6 mos.		+
4	10/13/17	3.251	25	M	O.S.	Subretinal	Not recorded	Nil	24 mos.		—
5	10/22/17	602	36	F	O.S.	Subretinal	Not recorded	Nil	24 mos.		+
6	6/21/18	4.600	9	F	O.D.	Subconjunct.	Superomedial		unknown		Brother
7	10/13/18	5.249	33	F	O.S.	Subretinal	Superolateral	C.F. at 1 M.	1 month		+
8	7/19/19	6.636	6	F	O.S. / O.D.	Vitreous	Not recorded / Superolateral	Nil / C.F. at 10 cm.	6 mos.		—
9	6/5/21	11.207	51	M	...... / O.S.	Subretinal	...... / Macula	...... / H.M.	12 mos.		—
10	1/31/22	12.932	32	F	O.S.	Vitreous	Not recorded	Nil	12 mos.		—
11	5/11/22	13.794	26	M	O.S.	Subhyaloid	Supermedial	H.M.	5 mos.		—
12	5/13/22	13.800	31	M	O.D.	Anterior chamber	Central	H.M.	8 mos.		—
13	7/11/22	14.246	42	M	O.D.	Subretinal	Paramacular	0.4	2 mos.		+
14	4/7/23	16.570	38	M	O.S.	Subretinal	Not recorded	C.F. at 2 M.	2 mos.		+
15	11/12/23	18.184	8	F	O.S.	Subretinal	Macula	H.M.	48 mos.		+
16	2/23/24	19.464	30	F	O.D.	Subretinal	Not recorded	C.F. at 2 M.	2 mos.		—
17	3/24/24	19.790	17	F	O.S.	Subretinal	Macula	0.5	3 mos.		—
18	8/26/24	20.920	38	M	O.S.	Vitreous	Inferomedial	C.F. at 2 M.	3 mos.		+
19	10/18/24	21.590	30	F	O.S.	Vitreous	Inferomedial	H.M.	5 mos.		—
20	1/14/25	22.975	60	M	O.D.	Subretinal	Not recorded	0.2	2 mos.		—
21	2/17/25	23.438	52	F	O.D.	Subretinal	Inferior	H.M.	12 mos.		+
22	3/27/25	24.012	17	M	O.D.	Subretinal	Inferolateral	0.5	3 mos.		—
23	5/11/25	24.605	63	F	O.D.	Vitreous	Inferior	H.M.	12 mos.		—
24	1/30/26	27.304	35	F	O.D.	Two in vitreous	Both inferior	C.F. at 1.5 M.	12 mos.		+
25	11/25/26	30.999	8	F	O.D.	Subconjunct.	Inferolateral		1 month		—
26	4/18/27	32.975	30	F	O.S.	Subretinal	Not recorded	H.M.	12 mos.		—
27	9/16/27	34.717	45	M	O.D.	Subretinal	Inferomedial	C.F. at 2 M.	3 mos.		+
28	11/23/27	35.671	9	F	O.D.	Subretinal	Inferior	C.F. at 2 M.	6 mos.		—
29	9/11/28	40.000	23	F	O.D.	Subretinal	Macula	H.M.	6 mos.		+
30	6/29/29	43.824	12	M	O.D.	Subretinal	Not recorded	H.M.	?		+
31	8/6/29	44.274	21	F	O.D.	Subhyaloid	Not recorded	H.M.	1 month		+
32	10/29/29	45.283	4	F	O.S.	Subconjunct.	Superomedial		?		+
33	12/6/29	45.626	9	F	O.D.	Subconjunct.	Inferolateral		1 month		+
34	1/29/30	46.223	14	M	O.D.	Subretinal	Inferior	H.M.	3 mos.		+
35	6/8/30	47.437	43	M	O.S.	Vitreous	Not recorded	C.F. at 1.5 M.	4 mos.		Father
36	1/27/31	49.531	18	M	O.S.	Subconjunct.	Superior		2 mos.		—
37	11/9/32	55.425	21	F	O.S.	Subretinal	Not recorded	L.P.	8 mos.		+
38	2/28/33	56.690	12	M	O.D.	Vitreous	Inferomedial	H.M.	12 mos.		+
39	5/12/33	57.374	27	F	O.S.	Vitreous	Inferior	C.F. at 2 M.	2 mos.		—
40	9/30/33	58.856	9	F	O.D.	Subretinal	Not recorded	Nil	7 mos.	++	—
41	1/24/34	60.273	26	F	O.S.	Subretinal	Parapapillary	0.5	4 mos.	+	—
42	2/8/34	58.381	66	F	O.D.	Subretinal	Superolateral	0.4	?	++	—
43	3/7/34	60.881	27	M	O.D.	Subretinal	Not recorded	H.M.	24 mos.		—
44	4/4/34	61.260	21	F	O.D.	Subretinal	Inferolateral	CF. at 2 M.	11 mos.	neg.	—
45	4/14/34	61.397	24	F	O.D.	Vitreous	Inferior	H.M.	12 mos.	++	—
46	5/5/34	61.598	24	F	O.D.	Subretinal	Inferolateral	L.P.	36 mos.	+	—
47	7/28/34	62.636	20	F	O.D.	Subretinal	Not recorded	H.M.	10 mos.	++	—
48	4/9/35	64.756	37	M	O.D.	Subretinal	Inferomedial	0.1	6 mos.		—
49	4/18/35	66.089	6	M	O.D.	Vitreous	Not recorded	Nil	?		—
50	6/21/35	66.907	32	M	O.D.	Subretinal	Parapapillary	0.5	2 mos.	++	—
51	6/23/35	67.345	6	M	O.D.	Subconjunct.	Lateral		?		—
52	9/19/35	67.374	24	M	O.S.	Vitreous	Inferolateral	C.F. at 2 M.	?	neg.	—
53	11/27/35	69.027	9	M	O.S.	Subretinal	Not recorded	Nil	12 mos.	+	—
54	3/2/36	68.611	11	F	O.D.	Subretinal	Not recorded	Nil	4 mos.	++	Sibling
55	3/23/36	70.785	7	M	O.S.	Subconjunct.	Lateral		24 mos.	+	—
56	6/6/36	71.787	12	M	O.S.	Subretinal	Not recorded	Nil	6 mos.	+	—
57	7/8/36	71.980	9	F	O.S.	Vitreous	Not recorded	Nil	?	++	Brother and sister
58	9/4/36	72.920	7	M	O.D.	Subretinal	Not recorded	Nil	11 mos.	+	—
59	10/15/36	73.725	11	M	O.S.	Subhayloid	Inferolateral	C.F. at 20 cm.	2 mos.	neg.	—
60	3/30/37	76.385	19	F	O.S.	Vitreous	Not recorded	Nil	12 mos.		—
61	7/7/37	77.858	34	F	O.S.	Vitreous	Inferolateral	C.F. at 3 M.	2 mos.		+
62	7/11/37	77.916	18	F	O.S.	Subretinal	Lateral	C.F. at ½ M.	3 mos.	++	+
63	8/24/38	57.346	25	M	O.D.	Vitreous	Not recorded	Nil	60 mos.	+	—
64	9/19/38	85.097	13	F	O.S.	Subretinal	Not recorded	L.P.	24 mos.		—
65	11/26/38	86.307	10	F	O.S.	Subretinal	Superolateral	H.M.	1 month		—
66	2/3/40	93.910	33	F	O.D.	Vitreous	Central	C.F. at 10 cm.	24 mos.	neg.	—
67	4/4/40	95.082	32	M	O.D.	Vitreous	Not recorded	H.M.	?	++	—
68	5/13/40	95.721	40	F	O.S.	Subretinal	Central	L.P.	6 mos.	++	—
69	9/14/40	97.830	10	M	O.S.	Subhyaloid	Superolateral	H.M.	?		+
70	2/14/41	100.407	17	F	O.S.	Vitreous	Not recorded	Nil	12 mos.	±	+
71	2/16/41	100.444	15	F	O.S.	Vitreous	Inferomedial	H.M.	2 mos.	±	+
72	5/27/41	102.306	11	M	O.D.	Vitreous	Macula	H.M.	1 month	neg.	—
73	6/25/41	102.815	9	M	O.D.	Vitreous	Inferior	Nil	?		—
74	7/24/41	81.719	2½	M	O.S.	Vitreous	Not recorded	Nil	48 mos.	+	—
75	10/8/41	104.509	16	M	O.D.	Subretinal	Lateral	Nil	1 month	++	+
76	5/6/42	108.168	8	F	O.D. / O.D.	Subretinal / Subhyaloid	Macula / Not recorded	C.F. at 2 M. / C.F. at 2 M.	9 mos.	neg.	—
77	5/25/42	108.436	50	F	O.S.	Vitreous	Inferolateral	C.F. at 30 cm.			

TABLE 1—(continued)

Case No.	Date	Chart No.	Age	Sex	Eye	Localization		Vision at First Exam.	Onset of Symptoms	Complement Fixation	Carrier of Tenia
78	5/27/42	108.484	11	F	O.S.	Subretinal	Macula	H.M.	3 mos.	±	—
79	7/28/42	109.258	18	F	O.S.	Vitreous	Not recorded	Nil	12 mos.	+	—
80	9/ 9/42	105.775	14	M	O.S.	Vitreous	Superolateral	Nil	9 mos.	+	—
81	5/10/43	114.464	25	F	O.S.	Vitreous	Inferolateral	C.F. at 2 M.	5 mos.	neg.	+
82	5/11/43	114.501	26	F	O.D.	Vitreous	Inferior	C.F. at 50 cm.	11 mos.	neg.	—
83	6/ 5/43	114.978	36	M	O.D.	Two in vitreous	Both inferior	C.F. at 50 cm.	12 mos.	±	—
84	7/ 2/43	115.502	10	F	O.D.	Vitreous	Inferolateral	C.F. at 2½ M.	9 mos.		—
85	7/27/43	116.018	48	F	O.D.	Subhyaloid	Inferomedial	0.6	3 mos.	++	—
86	11/13/43	118.208	24	F	O.S.	Subhyaloid	Inferior	H.M.	6 mos.	±	—
87	6/24/44	118.747	17	M	O.S.	Subretinal	Not recorded	Nil	24 mos.	+	—
88	7/18/44	124.032	28	F	O.D.	Subretinal	Superomedial	0.3	?	neg.	—
89	8/24/44	124.967	11	M	O.D.	Vitreous	Inferomedial	H.M.		neg.	—
90	9/30/44	125.902	6	F	O.D.	Vitreous	Inferior	H.M.		±	—
91	12/12/44	127.629	5	F	O.S.	Vitreous	Medial	Nil		±	—
92	3/ 8/45	130.093	23	F	O.S.	Vitreous	Not recorded	C.F. at 50 cm.		neg.	—
93	6/25/45	132.808	43	F	O.D.	Vitreous	Inferior	H.M.	6 mos.	+	—
94	8/22/45	134.163	23	F	O.D.	Subcutaneous lacrimal sac region			8 mos.	neg.	—
95	9/22/45	134.994	50	M	O.S.	Two in vitreous	Not recorded	0.4	1 month	±	—
96	4/25/46	33.465	50	M	O.S.	Orbit	Superomedial		?	neg.	—
97	7/11/46	142.053	14	M	O.D.	Subhyaloid	Inferolateral	C.F. at 1 M.	3 mos.	+	+
98	7/20/46	142.442	34	M	O.S.	Vitreous	Inferolateral	H.M.	6 mos.	neg.	—
99	8/22/46	143.314	39	F	O.D.	Vitreous	Inferolateral	C.F. at 50 cm.	18 mos.	±	—
100	9/ 9/46	143.761	35	M	O.D.	Vitreous	Inferior	C.F. at 20 cm.	3 mos.	++	+
101	9/17/46	105.859	18	F	O.S.	Subretinal	Inferomedial	0.2	2 mos.	neg.	—
102	9/25/46	144.233	16	F	O.D.	Subhyaloid	Lateral	C.F. at 2 M.	1 month	++	—
103	10/11/46	15.118	32	M	O.D.	Vitreous	Inferolateral	H.M.	6 mos.	±	—
104	1/16/47	147.178	49	F	O.S.	Vitreous	Inferior	H.M.	30 mos.		—
105	2/24/47	145.757	12	F	O.D.	Vitreous	Not recorded	H.M.	3 mos.		—
106	6/14/47	131.709	9	F	O.D.	Vitreous	Not recorded	L.P.	8 mos.	++	+
107	6/26/47	152.003	22	F	O.D.	Subhyaloid	Inferolateral	C.F. at 2 M.	2 mos.	±	—
108	6/29/47	43.824	12	M	O.D.	Subretinal	Macula	H.M.	3 mos.		+
109	8/ 6 47	153.322	33	F	O.D.	Vitreous	Inferior	0.3	3 mos.	+	—
110	8/ 8/47	153.421	22	M	O.D.	Vitreous	Inferior	C.F. at 10 cm.	1 month	+	—
111	8/12/47	153.528	15	F	O.D.	Vitreous	Inferior	L.P.	10 mos.		—

Occupation. All of our patients were laborers or farm workers with primitive concepts of hygiene, except for some Dutch workers, the daughter of a wealthy family, and a lawyer. The majority of patients come from rural areas; only exceptional cases arise in urban areas where standards of hygiene are higher.

Preference for the left eye. Our findings were at variance with this preference, as recorded by other observers. We found the distribution between the two eyes to be about evenly divided. Among 111 patients, 56 had cysticercus in the right eye, 50 in the left, 2 were bilateral, 2 had two parasites in the right eye, and 1 patient had two parasites in the left eye. Of the 116 parasites seen in 111 patients, 62 were found in the right eye and 54 in the left eye.

Trauma and site of least resistance. Although trauma was noted in 5 cases, it is probable that this drew the patient's attention to an already infected eye, and that there was no causal relationship.

Secondary inflammatory reaction. During the period of 1 to 3 months after onset of symptoms, the transparency of the media permits the diagnosis of cysticercus wherever it is located. But as time goes on, an exudative reaction develops and the vitreous becomes turbid. In our cases, there were 3 examples of simple iritis, 4 cases of posterior synechias, 11 patients with iridocyclitis, 3 with uveitis, 4 with purulent iridocyclitis, and 1 with endophthalmitis. At times (6 cases) there was so much intraocular disorganization that the attending oculist suspected tumor and advised enucleation, the diagnosis of cysticercus being made by the pathologist. In a few cases, a painful atrophic globe led to the same outcome.

Complications. In addition to the already mentioned complications, of other more or less serious complications, retinal detach-

ment is the most frequent (42 cases). This occurred from migration of the parasite subretinally, or as a consequence of retinal tear

was observed in 2 patients, although more or less hypotension is usually encountered. Atrophy of the globe was recorded on
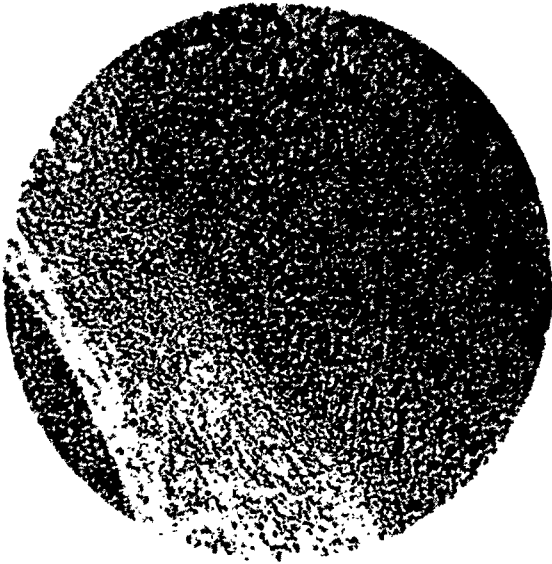
Fig. 11 (Lech Junior). Photomicrographs of paraffin preparations, stained with hematoxylin-eosin, to show the structure of the reactive capsule. (Left): choroid surrounded by the more external layer of the capsule (fibroblasts and mononuclear infiltration). The middle layer (histiocytes, young fibroblasts) can be seen as a dividing line separating it from the internal zone of necrosis. (Below at the left side): details of the middle zone. (Below at right side): another aspect of the reactive capsule in another preparation. (Upper picture, obj. 20 and ocular 5; lower picture, obj. 40 and ocular 5.)
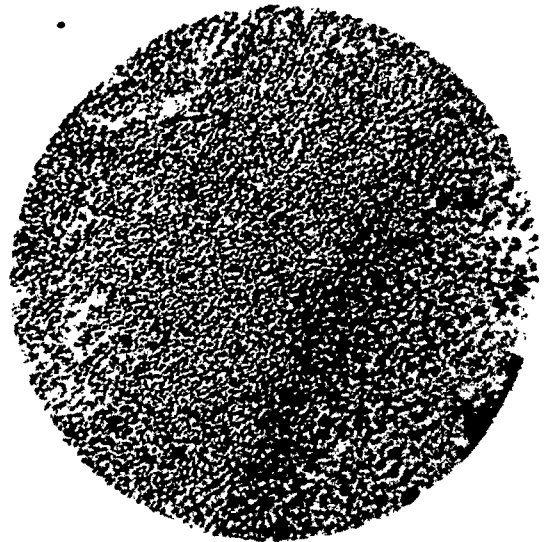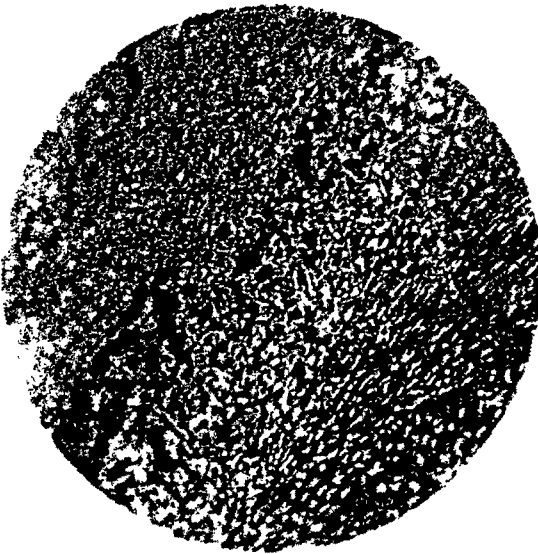
when the cysticercus moved from its original subretinal site into the vitreous, or as a complication of operation.

Less frequent were the cases (8 patients) in which the parasite migrated from its subretinal position and was observed before detachment of the retina developed. A late complication is cataract (16 cases). Glaucoma

3 occasions after the clinical diagnosis of cysticercus. The diagnosis was made only on pathologic examination in 12 cases. The above demonstrates how fatal intraocular cysticercus is for vision and even for preservation of the eyeball. In short, to leave the parasite in the eye is to condemn the eye to blindness or total loss.

Some oculists advise extraction of the parasite; others, fearing the surgical trauma, try to destroy the cysticercus *in situ* by corrosives, diathermic coagulation, radium, or ultraviolet light. Our experience shows that surgical removal of the parasite may restore vision, put a stop to or ameliorate the harmful process, and prevent further disorganization of the globe. Destruction of the parasite *in situ* does not

sist of disturbances of central or peripheral vision, depending on the location of the parasite. Since there is no pain, the patient often seeks the oculist only when secondary manifestations occur, such as muscae volitantes, the pains aroused by iritis, or marked reduction in vision from retinal detachment. In these circumstances, there is little probability of restoring vision; the oculist can only try to preserve the eyeball. Cysticercus

Fig. 12 (Lech Junior). *Chart No. 108.168.* Subretinal cysticercus in paramacular region. (a) Retinography on May 6, 1942, 15 days after the onset of the first subjective symptom (reduction of vision to finger counting at 2 meters). (b) Retinography one month later. (c) Retinography on August 5, 1942. Note the sphericity, the spot in the center of the vesicle corresponding to the scolex, and the iridescent reflex at the periphery, more accentuated in the second picture. Note also the growth of the parasite which has nearly doubled in size during the period of three months. Because of its paramacular location, the parasite was not accessible and surgery was postponed. On October 26, 1942, the cysticercus fell into the vitreous and it was extracted on November 3, 1942. On January 11, 1943, the vision was counting fingers at 3 meters, and there was a secondary detachment of the retina.

usually stop the progress of intraocular disorganization. The parasite is harmful, living or dead, as much from its toxins as from the secondary reactions it provokes.

CASUISTICS

Our observations have been gathered into tables. Table 1 contains the essential data recorded at the first examination. The complications, surgical results, and the evolution of the cases treated without operation will be summarized in the sections dealing with surgical therapy and prognosis.

DIAGNOSIS

Symptomatology. The subjective symptoms caused by cysticercus are few and con-

beneath the conjunctiva, in the subcutaneous tissues, or in the orbit is painless. In the first, there is often localized hyperemia.

Diagnosis. The diagnosis of ocular cysticercosis is difficult because of its rarity and unusual features. Schott was justified in having the figure of the parasite engraved on his ring after he identified the first human intraocular cysticercus and extracted it from the anterior chamber of the patient's eye on July 17, 1829. Another example of enthusiasm evoked by the diagnosis of the parasite is found in the account by C. Cockburn on page 65 of the February, 1946, issue of the *British Journal of Ophthalmology.*

The oculist without experience in this field may see the parasite and not recognize

it. From the histories given by our patients, it appears that exudative choroiditis (when the vitreous is turbid) and detachment of the retina are often diagnosed, and the presence of the parasite is not suspected. We know of a case where an experienced oculist mistook the parasite for leukosarcoma of the choroid and enucleated the eye. In one patient with the diagnosis of a malignant melanoma of
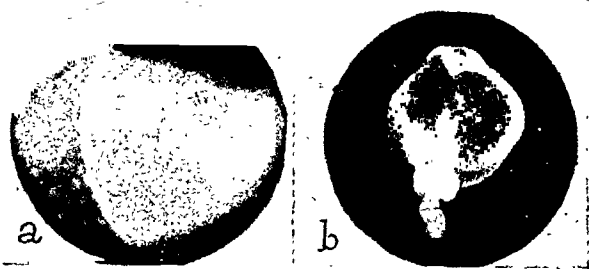
Fig. 13 (Lech Junior). *Chart No. 97.830.* Cysticercus free in the vitreous. (a) Its anterior position prevents view of the entire contour of the vesicle, but the visible sector permits diagnosis (sphericity, central spot corresponding to the scolex, marginal iridescent reflex). (b) The same parasite after extraction.

the choroid, a subchoroidal cysticercus was suspected because of the spherical shape of the lesion, a marginal rainbowlike reflex, and moderate scleral transillumination. A scleral incision in the region of the tumefaction uncovered a cysticercus.

The diagnosis is incontrovertible to the experienced oculist when the ocular media are transparent because of the characteristic appearance of the cysticercus—bluish white spherical vesicle with iridescent marginal reflections and endowed with slight, sometimes imperceptible, undulatory movements. When in the vitreous or in the anterior chamber the parasite may reveal an evaginated scolex. This structure is white, cylindrical and dense, thicker at its base. Under favorable circumstances it is possible to identify the sucking cups and hooks. When the scolex is invaginated it appears like a dense white spot at the center of the vesicle.

When subconjunctival, the parasite differs from a more voluminous lymphatic cyst, which it resembles, by having a central white

spot corresponding to its scolex. The diagnosis of the subcutaneous parasite can only be made after its surgical extraction. Our unique case of orbital cysticercus was diagnosed in an unexpected manner. The patient, a lawyer from Campinas, while in his office, felt some fluid running from his left eye down his face. Squeezing his eye with his fingers, a large cyst was forced out of the superomedial part of the conjunctival sac. This cyst was identified as a cysticercus.

The size of the parasite varies with its stage of development and with its location in the eye. It is smaller when situated deeply and early in its evolution. When in the vitreous, behind the lens, its apparent diameter seems much greater and at times its entire contour cannot be seen. The dimensions of the scolex vary with the stage of evolution, the depth of its position in the eye, and the amount of exteriorization of the segment.

At times it mobilizes more or less rapidly. The difficulties of diagnosis increase with the exudative and other secondary manifestations. The experienced oculist may make a definite diagnosis when he glimpses a small sector of the characteristic vesicle through the exudate or between folds of a detached retina.

Where there is much exudation, subconjunctival injections of hypertonic sodium chloride may clarify the vitreous sufficiently to identify the parasite. If the vitreous does not clear, one must observe the course of the ocular process which frequently goes on to atrophy, endophthalmitis, or suspicion of tumor, compelling the oculist to enucleate the globe. Then the pathologist will make the diagnosis.

Often, the suspicion of ocular cysticercus is accentuated when the complement fixation of the blood for cysticercus is positive. Monteiro Sales, our pathologist, says: "The biologic test, although liable to errors of reaction or technique, is sensitive enough to be of value. The blood showed a positive reaction in 89.9 percent of our proved cases of cysticercus (cerebral, subcutane-

ous, ocular). In the proved ocular cases the reaction was less sensitive (73.2 percent of 56 cases of proved ocular cysticercus). Curiously, the negative reactions were often found in eyes showing mild inflammatory or regressive changes. In these cases the diagnosis was easily made with the ophthalmoscope. On the other hand, the serologic reaction was usually positive in cases with advanced intraocular changes. In these the parasite could not be identified, but was found by pathologic study of the extracted tissue or by confirming the presence of the parasite after removing the complicated cataract.[1]

"It is possible that sufficient antibodies to produce a positive serologic reaction are not produced when the parasite is relatively free in the vitreous, or even subretinal, and does not react sufficiently with the host tissues.

"From our statistics 6 percent showed a positive reaction in patients having a positive reaction for syphilis by the Wassermann or Kahn test. Although some authors[2] consider this reaction in the blood of little significance, the possibility of associated luetic and cysticercus infection must be considered in these circumstances."[3]

TREATMENT

MEDICAL THERAPY

Medication useful in treating tenia infec-

Fig. 15 (Lech Junior). *Chart No. 116.018.* Cysticercus in the vitreous, adherent to the wall. Photograph of the fundus was made three months after the first subjective symptoms. The extraction was successful.

tion is valueless against ocular cysticercosis, for which surgery alone avails.

SURGICAL THERAPY

a. Orbital cysticercus. We have had no experience in this variety, because our only case (already described) resulted in spontaneous elimination.

b. Subconjunctival cysticercus. Surgical removal offers no difficulties. Care must be taken to avoid perforating the parasite since this makes its identification more difficult.

c. Cysticercus in the anterior chamber. Extraction of the parasite is relatively easy. The corneal section is made with a Graefe knife rather than with a keratome whose point may injure the vesicle. The incision should be limbal and sufficiently large to permit grasp of the parasite with a toothless forceps. We made an original observation in extracting a moving scolex from the anterior chamber (described under etiology).

d. Subretinal cysticercus. This will be studied in two categories: (1) When the parasite is in its original site; and (2) when, already mobilized, a greater or lesser amount of retinal detachment is present.
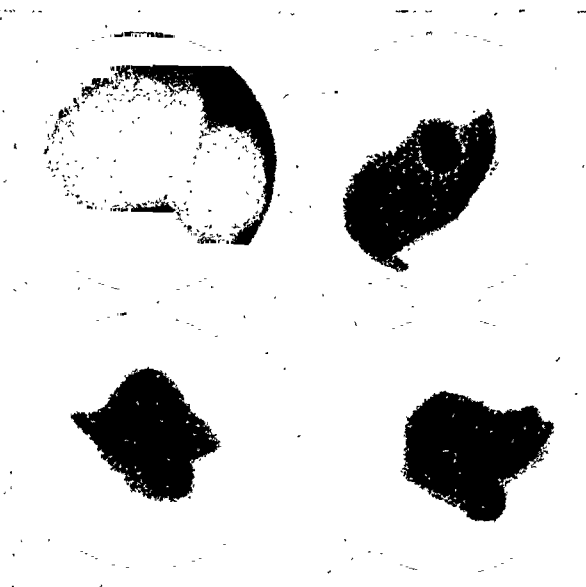
Fig. 14 (Lech Junior). *Chart No. 108.436.* Cysticercus free in the vitreous. Imperfect focus because of vitreous exudate. Diagnosis was made certain by the partial evagination of the scolex.

1. In its original site. Exact localization is necessary to assure a good surgical result, especially when the parasite is located peripherally enough to permit easy access. Since the small parasite measures only 1½ to 2 disc diameters, there is danger of incising the retina when the scleral incision is located away from the site of the parasite,

Fig. 16 (Lech Junior). *Chart No. 124.032.* A typical vesicular subretinal cysticercus in the nasal quadrant between the 2- and 3-o'clock positions in the right eye.

thus compromising the prognosis of this most favorable type of surgical extraction of ocular cysticercus.

This misfortune occurred in Case 13, Chart 14.246, dealing with a patient with a subretinal parasite, without retinal detachment, and with normal vision. The incision did not coincide with the location of the cysticercus, and the fruitless surgical attempt led to complicated cataract, cyclitis, and finally enucleation of the globe.

In order to avoid similar mishaps, we prefer to wait until the parasite enters the vitreous or moves more anteriorly under the retina. Thus the extraction has a better chance of success, although the prognosis as regards vision is worse. In 1944, Souza Queiroz evolved a very reliable localization technique, employing diathermic coagulation

to determine the exact position of the parasite, avoiding the margin of error involved in the perimetric localization, in a case of a small subretinal cysticercus located in the nasal sector of the fundus of the right eye. The following case demonstrates this technique.

Case report

Chart No. 124.032. E. V. S., a 28-year-old, married white Brazilian woman, resident of Guaxupe (Minas) was referred by Dr. Roberto Magalhães Gomes with a diagnosis of cysticercus. She entered the Institute on July 18, 1944. Vision was: O.D., 0.3; O.S., 1.0.

Examination of the right eye showed a typical vesicular subretinal cysticercus in the nasal quadrant in the meridian between the 2- and 3-o'clock positions. The parasite showed movements and an invaginated scolex. Its inferior border corresponded with a horizontal retinal vein. Its posterior border was 2½ disc diameters from the nervehead. The vesicle measured not more than 3½ mm. horizontally. Small hemorrhages were noted between the parasite and the disc. The vitreous, being transparent, permitted a good view of the fundus oculi (fig. 16). Complement fixation for cysticercus was negative.

Operation was performed on July 25, 1944, employing akinesia and anesthesia by retrobulbar and subconjunctival injection of 4-percent scurocaine. Instillations of neotulocaine were not employed, to avoid corneal desquamation and cloudiness. The bulbar conjunctiva was incised and dissected medially and superomedially, and a traction suture was placed in the medial rectus muscle. A transcleral diathermy puncture (bipolar, 50 ma.) was made in the 2-o'clock meridian. Ophthalmoscopic examination showed the area of chorioretinal coagulation to be peripheral and superior to the location of the cysticercus (fig. 17).

Second and third diathermy punctures

were made, the third one being close to the site of the parasite. At this point, the medial rectus was tenotomized. A fourth diathermy puncture was close to the upper border of

Fig. 17 (Lech Junior). (A) Diagram of operative procedure. (B) Showing localization of parasite by means of diathermy punctures.
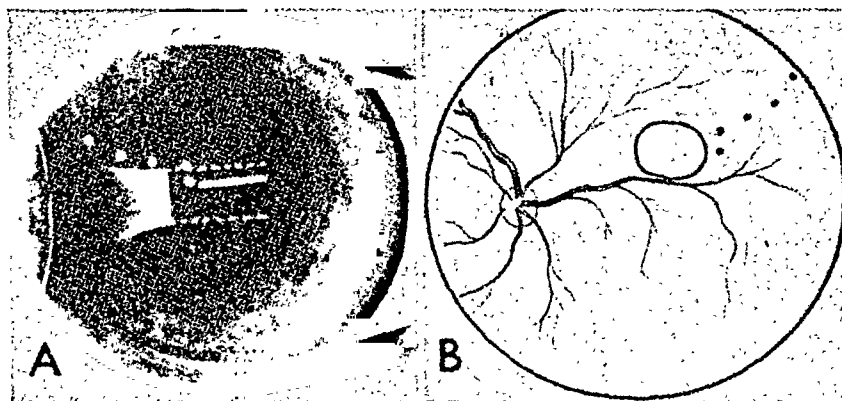
the vesicle, and a fifth one, placed 1 mm. inferior to the previous one, confirmed the exact position of the lateral border of the parasite.

A 6- to 7-mm. incision was made through the sclera behind the last diathermy puncture. Fixing the globe by grasping the insertion of the medial rectus, and having the assistant separate the scleral lips of the incision, the choroid was penetrated with the spatula. The cysticercus and a small amount of fluid were expelled when the intraocular pressure was increased by forced abduction of the globe. The medial rectus and conjunctiva were sutured. Ophthalmoscopic study revealed the absence of the parasite and very little choroidal disturbance. Atropine was instilled and a binocular dressing was applied. Laboratory examination confirmed the diagnosis of a cysticercus cellulosae measuring 3½ mm. in diameter. The sutures were removed after 7 days.

Result. On August 3, 1944, vision of the right eye was 0.7 improved to barely 1.0 with a − 1.0D. cyl. ax. 180°. The fundus (fig. 18) showed the diathermy punctures and a small scar at the site of the opening of the choroid. On February 3, 1945, a letter from Dr. R. Magalhães Gomes confirmed the excellent result, which we verified on reexamination of the patient on February 8, 1945.

In the case described above, we did not try to localize the cysticercus in the first punctures, in order to avoid perforating the vesicle. The tenotomy was performed when we verified the need of a more posterior incision. The diathermic coagulations were of weak intensity and little penetration to prevent perforation of the retina or a greater trauma. This technique is applicable in all cases of subretinal or subhyaloid cysticercus in which the parasite is not situated at the posterior pole of the globe. An exact localization of the parasite permits incision at the precise site and it further permits expulsion of the vesicle without the introduction of forceps.
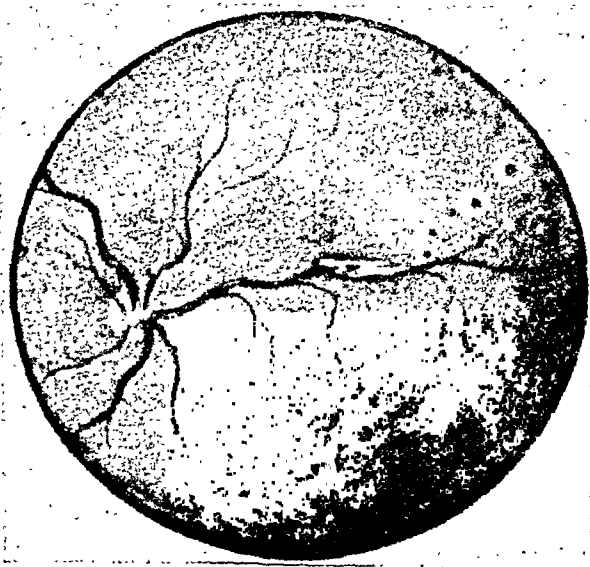
Fig. 18 (Lech Junior). Results obtained in the case shown in Figures 16 and 17. The fundus shows the diathermy punctures and a small scar at the site of the opening of the choroid.

2. SUBRETINAL, WITH SECONDARY DE-TACHMENT OF THE RETINA. The following general type of technique is employed. After asepsis and retrobulbar injection of 2- to 4-percent scurocaine, a subconjunctival injection of the same anesthetic is made in the region of the parasite. Instillations of a local anesthetic are to be avoided, so that ophthalmoscopic control can be carried out during the operation without cloudiness of the cornea.

After a conjunctival incision, a traction suture is placed at the limbus or in the nearest muscle. Lately, sutures have been

TABLE 2

OPERATED CASES OF SUBRETINAL CYSTICERCOSIS

Chart Number	Complications	Surgery	Vision Before	Vision After	Course
11.207	Exudates and detachment	Extraction with forceps	C.F. at 10 cm.	Nil Hemorrhage	Carrier of a cysticercus in each eye. Treatment given up with operation upon other eye. Epileptic attacks. ? cerebral cysticercosis
14.246	Iritis without detachment	Unsuccessful attempt	1.0	L.P.	Immediate hemorrhage. Atrophy of globe after 6 months. Complicated cataract. Enucleation.
16.570	Exudates without detachment	Spontaneous extrusion after incision	C.F. at 3 M.	0.2	Vision fell to C.F. at 2 M. 10 months later. Retinal detachment developed.
19.464	None	Extraction with forceps	C.F. at 2 M.	H.M.	Unknown.
22.975	None	Unsuccessful attempt	0.2	Nil	Immediate enucleation. Diagnosis confirmed at necropsy.
24.012	None	Spontaneous extrusion after incision	0.5	0.5	Good vision reported after 1½ years.
34.717	None	Extraction with forceps	C.F. at 1 M.	C.F. at 1 M.	Vision = C.F. at 2.5 M. 1 month later. Small hemorrhages and localized detachment.
35.671	Retinal detachment	Extraction with forceps	C.F. at 2 M.	C.F. at 3 M.	Vision = C.F. at 2 M. one year later. Slight exotropia.
43.824	Extensive detachment	Extraction with forceps	C.F. at 10 cm.	H.M.	Left hospital with quiet eye. Course unknown thereafter.
46.223	Retinal detachment	Extraction with forceps	C.F. at 0.5 M.	C.F. at 2 M.	Unknown.
55.425	Retinal detachment	Extraction with forceps	L.P.	L.P.	Vision Nil 15 years later. Quiet eye. Membranous cataract.
58.381	Synechias of iris	Unsuccessful attempt	0.4	H.M.	Eye quiet 9 years later. Exotropia. Complicated cataract. Hypotension.
60.273	Retinal detachment	Spontaneous extrusion after incision	0.5	0.5	Unknown.
61.260	Detachment. Suspected sarcoma of choroid	Spontaneous extrusion after incision	C.F. at 2 M.	C.F. at 2 M.	Unknown.
64.756	Exudates	Extraction with forceps	0.2	Nil	Detachment.
66.907	Without detached retina	Unsuccessful attempt	0.5	C.F. at 4 M.	Unknown.
86.307	Detached retina	Spontaneous extrusion after incision	C.F.	H.M.	Unknown.
104.509	Total detachment	Unsuccessful attempt	Nil	Nil	Unknown.
105.859	Small detachment	First operation not successful. Second led to extrusion after incision	0.2	0.4	Diathermic localization. Two months later, vision was 0.7 and there was no detachment.
108.168	Detached retina	Extraction with forceps	C.F. at 2 M.	C.F. at 3 M.	Extraction after parasite fell into vitreous. Vision = C.F. at 1 M. with extensive detachment 1½ years later.
124.032	Without retinal detachment	Spontaneous extrusion after incision	0.3	1.0	Diathermic localization, normal vision without detachment 7 months later. Case described in text.

TABLE 3

SURGERY OF CYSTICERCUS IN VITREOUS AND SUBHYALOID

Chart Number	Complications	Surgery	Vision		Course
			Before	After	
13.794	Detached retina	Extraction with forceps	0.1	H.M.	Unknown.
20.920	Exudates	Extraction with forceps	C.F. at 2 M.	H.M.	Retinal detachment.
24.605	Dense exudates	Extraction with forceps	H.M.	Nil	Hypotomy. Pseudoglioma.
27.304	Uveitis for 2 mos. Exudates	Two parasites extracted with forceps	0.2	C.F. at 2 M.	Complicated cataract.
44.274	Exudates	Extraction with forceps	H.M.	H.M.	Detached retina.
47.437	Exudates	Unsuccessful attempt	C.F. at 0.5 M.	H.M.	Detached retina
56.690	Detachment	Extraction with forceps	H.M.	H.M.	Unknown.
57.374	Exudates	Unsuccessful attempt	C.F. at 2 M.	H.M.	Unknown.
61.397	Exudates	Extraction with forceps	H.M.	H.M.	Unknown.
61.598	Complicated cataract. Previous operation	Extraction with forceps	Nil	Nil	Complete detachment.
67.374	Cyclitis	Extraction with forceps	C.F. at 2.5 M.	C.F. at 2 M.	Organized exudates in the vitreous.
73.725	Exudates	Extraction with forceps	C.F. at 20 cm.	H.M.	Detached retina.
77.858	Exudates	Extraction with forceps	C.F. at 3 M.	H.M.	Detached retina.
93.910	Cyclitis	Extraction with forceps	C.F. at 10 cm.	H.M.	Unknown.
95.082	Posterior synechias	Attempted successfully	H.M.	Nil	Detached retina. Quiet eye.
97.830	Exudate	Extracted with forceps	H.M.	H.M.	Unknown.
100.407	Extensive exudates	Extraction with forceps	Nil	Nil	Unknown.
100.444	Exudates. Detachment	Extraction with forceps	H.M.	L.P.	Detached retina. Quiet eye.
102.306	Detachment	Extraction with forceps	H.M.	H.M.	Unknown.
102.815	Detachment	Extraction with forceps	Nil	Nil	Unknown.
108.436	Diabetic exudates	Extraction with forceps	C.F. at 30 cm.	C.F. at 3.5 M.	Seclusion of pupil. Detachment later. Vision nil.
114.464	Exudates	Extraction with forceps	C.F. at 2 M.	C.F. at 3 M.	Later vision =C.F. at 2 M. Detached retina.
114.501	Exudates	Unsuccessful attempt	C.F. at 0.5 M.	Nil	Iridocyclitis and complicated cataract.
114.978	Localized exudates	Two parasites removed in two sessions	C.F. at 0.5 M.	L.P.	Quiet turbid vitreous. Outcome unknown.
115.502	None	Extraction with forceps	C.F. at 2.5 M.	0.8	Retinitis proliferans at site of incision.
116.018	Synechias of iris	Extraction with forceps	0.6	H.M.	Detached retina.
118.208	Exudates	Unsuccessful attempt	H.M.	H.M.	Unknown.
124.967	Detachment	Extraction with forceps	H.M.	H.M.	Quiet detachment.
127.629	Exudates. Detachment	Extraction with forceps	Nil	Nil	Detachment. Complicated cataract.
130.093	Exudates	Extraction with forceps	C.F. at 0.5 M.	H.M.	Unknown.
132.808	Exudates	Extraction with forceps	H.M.	C.F. at 1.5 M.	Unknown.
134.994	Cyclitis	Two parasites extracted in same operation.	0.4	0.2	Without detachment.
142.053	Exudates	Extraction with forceps	C.F. at 1 M.	H.M.	Unknown.
142.442	Exudates	Extraction with forceps	H.M.	H.M.	Unknown.
143.314	Exudates. Detachment	Extraction with forceps	C.F. at 0.5 M.	Nil	Cyclitis occlusion and seclusion of the pupil.
144.233	Exudates. Detachment	Extraction with forceps	C.F. at 2 M.	H.M.	Vitreous hemorrhage. Outcome unknown.
152.003	Exudates. Detachment	Unsuccessful attempt	C.F. at 2 M.	H.M.	Increase in detachment.
153.322	Exudates. Detachment	Extraction with forceps	0.3	H.M.	Vitreous hemorrhage. Detachment.
153.421	Exudates. Detachment	Unsuccessful attempt	C.F. at 10 cm.	H.M.	Vitreous hemorrhage. Detachment.

placed in the sclera at the sides of the proposed incision to aid in opening the incision during the introduction of forceps and extraction of the cysticercus. The incision of the sclerotic is made longitudinally between the sutures, layer by layer. The scleral cut must be long enough to allow opening the forceps in the interior of the globe. Curved smooth forceps are used to permit retrograde maneuvers with the globe in normal position for ophthalmoscopic control. The conjunctiva is sutured, whether the parasite is extracted or not, with or without previous diathermic cauterization of the scleral incision.

Extraction was attempted in 21 cases of subretinal cysticercus, with unsuccessful attempts in 6 patients, extraction with forceps in 8, and spontaneous delivery of the parasite after scleral incision in 7 patients. Thus, extraction was successful in about 70 percent of the cases.

e. Parasite in vitreous and subhyaloid. Extraction offers less difficulties, although spontaneous delivery cannot be expected after scleral incision. The parasite is easily seen and grasped when it is free in the vitreous, without interference of the retina.

OPERATIVE TECHNIQUE. This is identical with the preceding technique, except that

there is no need for special care in making the incision in the sclerotic. Since cysticercus in the vitreous is usually situated inferiorly, the patient should be in an almost sitting position.

Of all patients with cysticercus in the vitreous or in the subhyaloid region, 40 submitted to operation. Surgery was successful in 83 percent of the cases; 37 patients had a single cysticercus; 29 were re-

Thus, our results show 78 percent of successes in surgical removal of cysticercus within the posterior globe (excluding parasites in the anterior chamber, beneath the conjunctiva, and in subcutaneous sites). The outcomes reported by other observers using injections of corrosives or destruction of the parasites *in situ* by electrolysis or diathermy convince us that surgery is the preferred method of treatment.
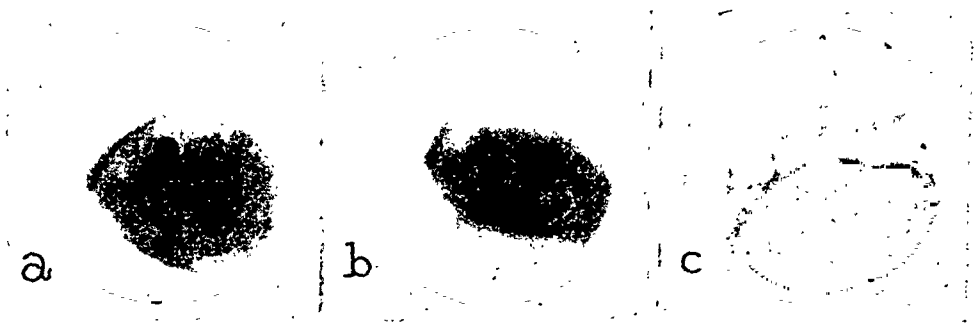
Fig. 19 (Lech Junior). *Chart, No. 108.484.* Subretinal cysticercus. Three months after the first symptoms in (c) is seen a secondary detachment of the retina. Exudates in the vitreous prevent more precise image. The vessels of the retina covering the parasite are seen. The patient refused operation. Posterior disorganization of the globe led to enucleation, and the diagnosis was confirmed by pathologic examination.

moved in one session, with 7 failures. One was removed in two surgical sessions. Three patients had 2 parasites in one eye. In two of these, both parasites were removed in one operative procedure. The third had two cysticercuses, one removed in each of two sessions because of hypotony and turbid media.

From the above, it is apparent that extraction is possible in a high percentage of cases, given good technique and a little luck. From the figures below, one sees that this surgical procedure gave more successes than disappointments to the surgeons who undertook this operation.

Surgeon	Operations	Failures
A	17	4
B	17	3
C	12	1
D	10	4
E	4	2
F	2	0
Total	62	14

PROGNOSIS

Extraocular cysticercus offers a good prognosis. It produces no reactions worthy of note, nor damage to the eye or its function. The same can be said of cysticercus in the anterior chamber, for the parasite can be easily extracted with little trauma. On the contrary, when the cysticercus is retrolental, the prognosis is poor, not only for vision but also for the integrity of the globe.

In Table 4 are summarized the results in all of the cases not included under "treatment," and records our observations in operated cases of subconjunctival cysticercus, in patients with the parasite in the anterior chamber and in the region of the lacrimal sac beneath the skin, as well as in patients who refused operation and those who required enucleation for some reason or other and had the diagnosis confirmed by pathologic anatomy or by necropsy.

We note that 7 subconjunctival parasites

TABLE 4

Results in all cases not included in Tables 2 and 3

Chart Number	Location	Complications	Vision at First Exam.	Course
A.L.	Vitreous	Exudates	C.F. at 1 M.	Unknown. Refused operation.
602	Vitreous	Cyclitis. Atrophy of the Globe	Nil	Enucleation.
2,336	Anterior Chamber	None	H.M.	Operation in S. Paulo. Course unknown.
3,105	Vitreous	Detachment	C.F. at 1 M.	Operation in S. Paulo. Larger detachment.
3,251	Vitreous	Iridocyclitis. Complicated cataract	Nil	Enucleation.
4,600	Subconjunctival	None		Operation. Uneventful course.
5,249	Subretinal	Exudates in vitreous	C.F. at 1 M.	Atrophy of globe 3 years later. Enculeation. Clinical diagnosis confirmed by necropsy.
6,636	Vitreous	Absolute glaucoma	Nil	Enucleation.
11,207	Subretinal	Iris synechias. Detachment	H.M.	Unknown. Refused operation.
12,932	Vitreous	Cyclitis. Atrophy of the globe	Nil	Enucleation.
13,800	Anterior Chamber	Cyclitis	H.M.	Preexisting corneal opacity. Operation. Vision =0.2.
15,118	Vitreous	Exudates. Detachment	H.M.	Unknown. Refused operation.
18,184	Subretinal	Detached retina	H.M.	Unknown. Refused operation.
19,790	Subretinal	Exudates with detachment	0.3	Unknown. Refused operation.
21,590	Vitreous	Exudates	0.1	Refused operation. Detached retina 1 year later, with Vision =H.M.
23,438	Subretinal	Exudates and detachment	H.M.	Unknown. Refused operation.
30,999	Subconjunctival	Hyperemia		Uneventful operation.
32,975	Subretinal	Exudates and detachment	H.M.	Unknown. Refused operation.
33,465	Orbit	None		Spontaneous expulsion.
40,000	Subretinal	Exudates. Macular localization	H.M.	Complicated cataract 9 years later.
45,283	Subconjunctival	None		Uneventful operation.
45,626	Subconjunctival	None		Uneventful operation.
49,531	Subconjunctival	None		Uneventful operation.
57,346	Vitreous	Atrophy of globe	Nil	Enucleation. Anatamopathologic diagnosis.
58,856	Subretinal	Purulent iridocyclitis	Nil	Unknown. Refused operation.
60,881	Subretinal	Seclusion	H.M.	Refused operation. Developed complicated cataract later.
66,089	Vitreous	Cyclitis. Pseudotumor	Nil	Enucleation.
67,345	Subconjunctival	None		Uneventful operation.
68,611.	Subretinal	Purulent iridocyclitis	Nil	Enucleation. Diagnosis confirmed by pathologic studies.
69,027	Subretinal	Purulent iridocyclitis. Detachment	Nil	Refused operation. Developed complicated cataract later.
70.785	Subretinal	None		Uneventful operation.
71.787	Subhyaloid	Suspected tumor. Detachment	Nil	Enucleation. Pathologic diangosis.
71.980	Vitreous	Uveitis	Nil	Enucleation. Pathologic diagnosis.
72.920	Vitreous	Pseudotumor	Nil	Enucleation. Pathologic diagnosis.
76.385	Vitreous	Iris synechias. Detachment	Nil	Unknown. Refused operation.
77.916	Subretinal	Exudates and detachment	C.F. at 1.5 m.	Unknown. Refused operation.
81.619	Vitreous	Pseudotumor	Nil	Enucleation. Pathologic diagnosis.
85.097	Subretinal	Cyclitis. Iris synechias	L.P.	Refused operation. Complicated cataract and atrophy of globe later.
95.721	Vitreous	None	L.P.	Unknown. Refused operation.
105.775	Vitreous	Endophthalmitis	Nil	Enucleation. Pathologic diagnosis.
108.484	Subretinal	Exudates without detachment	C.F. at 30 cm.	Developed pseudotumor. Enucleation. Pathologic exam. confirmed cysticercus.
109.258	Vitreous	Cyclitis. Complicated cataract	Nil	Enucleated. Pathologic diagnosis.
118.747	Subretinal	Cyclitis. Complicated cataract	Nil	Enucleated. Pathologic diagnosis.
125.902	Vitreous	Exudates	Nil	Unknown. Refused operation.
134.163	Subcutaneous in region of lacrimal sac	None		Uneventful operation.
143.761	Vitreous	Exudates	C.F. at 20 cm.	Unknown. Refused operation.
145.757	Vitreous	Cyclitis. Detachment. Pseudotumor	Nil	Enucleation. Pathologic diagnosis.
147.178	Vitreous	Exudates and detachment	H.M.	Unknown. Refused operation.
151.709	Vitreous	Plastic choroiditis. Suspected tumor	Nil	Enucleated. Pathologic diagnosis.
153.528	Vitreous	Exudates and detachment	L.P.	Unknown. Refused operation.

were extracted uneventfully. Two were removed from the anterior chamber, one by Pereira Gomes in São Paulo and the other in our Institute. In the latter case, vision improved from hand movements to 0.2 notwithstanding preëxisting corneal opacities. One cysticercus was removed from the region of the lacrimal sac without sequela, and another, located in the orbit, was expelled spontaneously.

Fifteen patients rejected operation and the outcome was not known. In some patients who refused operation and were followed we found: increase in retinal detachment in 1, development of complicated cataract in 3, one atrophy of the globe followed by enucleation and confirmation of the clinical diagnosis. In one patient with a surgically inaccessible parasite in the macular region, a complicated cataract developed 9 years later.

In 18 cases, the diagnosis was made exclusively by immediate postoperative necropsy or by pathologic examination. Enucleation was indicated for different reasons: 7 because of suspicion of tumor; 4 for atrophy of the globe; 3 for iridocyclitis with complicated cataract; 1 for uveitis; 1 with endophthalmitis; 1 for absolute glaucoma;

ficed to reduce the frequency of this disease to a negligible amount of the German morbidity statistics. Prophylaxis consisted in inspection of meat, the use of efficient disposal of contaminated feces, and education in personal hygiene and eating, so as to prohibit ingestion of poorly cooked or inadequately smoked meats.
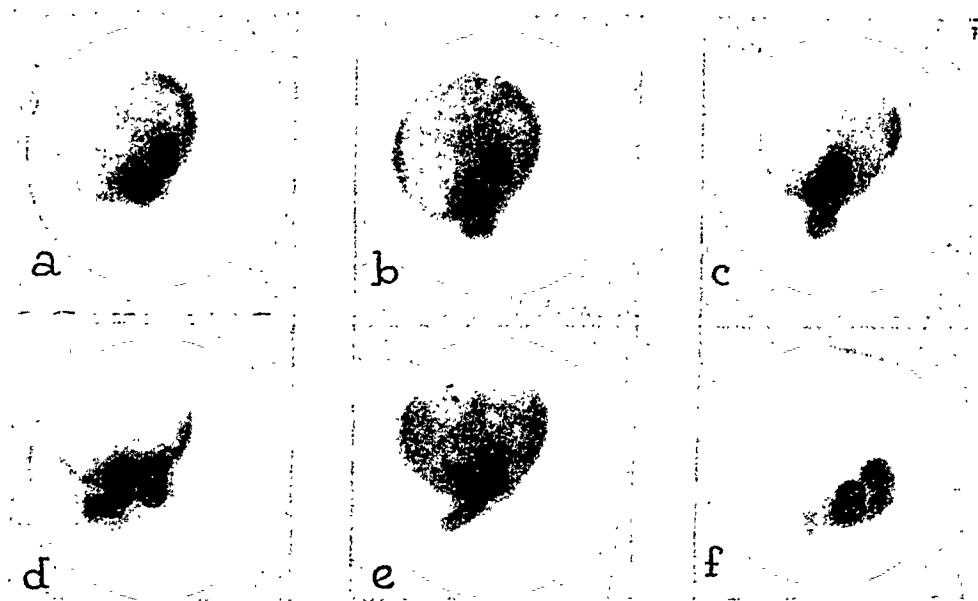
Fig. 20 (Lech Junior). *Chart No. 47.437*. Cysticercus free in the vitreous. The succession of photographs (a, b, c, d, e) shows the motility of the scolex. In (f), a photograph of the same case, it is possible to see two sucking cups on the head of the scolex.

and 1 because of purulent iridocyclitis.

As we see, the eyes containing a parasite suffer a wide variety of pathologic changes, showing destruction in about 80 percent of the cases in which the cysticercus was not extracted at an opportune time.

Comparison of the various tables convinces us that the involved eye stands a better chance if submitted to the earliest possible surgical therapy.

PROPHYLAXIS

This is simple and has demonstrated its efficacy. At the end of the last century, cysticercosis was widespread in Germany according to Biancini. The prevention of teniasis, from which cysticercosis is derived, suf-

The public authorities should be more concerned with rural areas where human cysticercosis is more frequent. The rarity of the disease should not permit relaxation in efforts at prophylaxis, for this will also eliminate other organic affections, especially the very serious cases of cerebral cysticercosis.

From our statistics, the disease is not decreasing in São Paulo. During the past two years, we have observed 18 cases among about 20,000 patients. This proportion of 1:1,000 parallels the highest incidence recorded in northern Germany. Among a total of 150,000 patients examined in 30 years, we found 111 cases of ocular cysticercus, although it is likely that other cases were missed or undiagnosed.

PATHOLOGY

The histologic diagnosis of cysticercus is not difficult when the parasite can be observed in microscopic sections, but good slides are not always easy to obtain. Certain features of the inflammatory capsule suggest the presence of cysticercus which should be sought for in serial sections. Sometimes the complete parasite can be demonstrated, or else certain of its parts when inflammatory and degenerative changes have caused disorganization. The cysticercus is characterized by (a) the scolex, with its suckers and crown of hooks, (b) the gland-shaped folds of the neck, and (c) the membrane of its vesicle. When degenerative processes involve the parasite it may not always be possible to identify these structures. The diagnosis, then, may be confirmed by encountering even a single hook, which as a rule lies in a necrotic mass.

The reactive capsule is made up of three more or less distinct layers, consisting from within outward of the following: (a) a zone
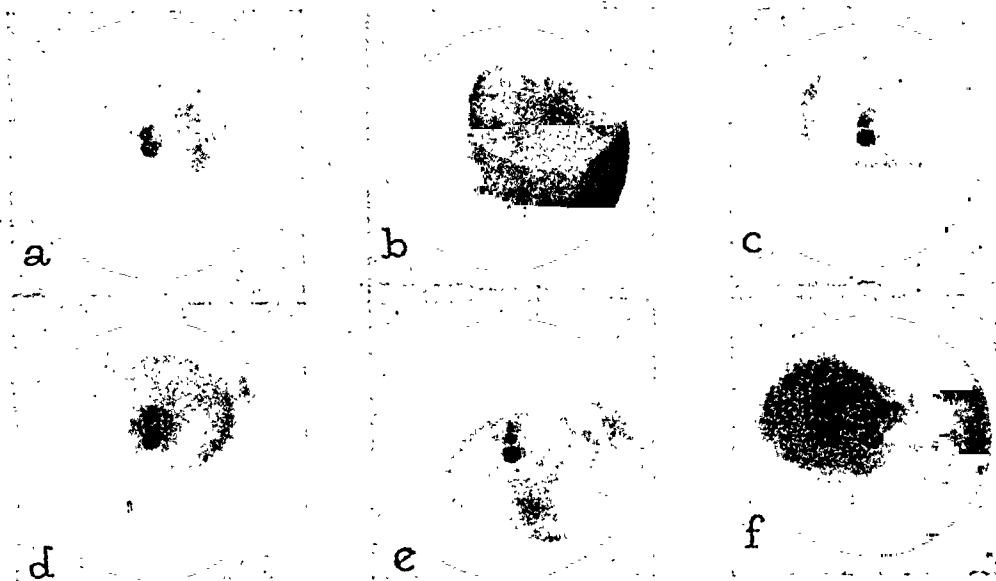
Fig. 21 (Lech Junior). *Chart No. 102.306.* Subhyaloid cysticercus. This series of photographs shows the undulatory movements of the wall of the vesicle and the slight motility of the partially evaginated scolex. In (f) is seen subretinal parapapillary fibrous tissue at the original site of the parasite whence it migrated into the subhyaloid space.

Fig. 22 (Lech (Junior). Subconjunctival cysticercus is revealed in three photographs. In (b) we note the central condensation which differentiates cysticercus from lymphatic cyst, as well as the hyperemia which is the only reaction provoked by the parasite.

of purulent exudate with a more or less wide band of coagulation necrosis; (b) a zone of histiocytes, young fibroblasts, and an occasional rare giant cell of the Langhans type: and finally (c) a wider zone of sclerosis with a diffuse and intense mononuclear (lymphocytes and plasmocytes) exudate, with or without eosinophils.

by his knowledge of the literature and of Sichel's illustrations. Cockburn evolved his diagnosis through his knowledge of the evolutionary cycle of tenia infestation.

Illustrations help to engrave in our memories the multiple aspects of this ocular parasite. Therefore, we have illustrated this paper freely. Many opportunities for obtain-

Fig. 23 (Lech Junior). *Chart No. 108.436.* Stereoscopic photographs of the scolex moving in the anterior chamber. The patient was a diabetic married woman with a cysticercus in each eye. The parasite in the right eye was extracted from the vitreous. Diathermic cauterization of the subhyaloid cysticercus in the left eye by a colleague failed to destroy the parasite, and the eye became inflamed. The exudates and reaction prevented immediate surgical extraction. While under treatment to quiet the eye, the patient complained of severe pain in the eye and headache. Examination showed the parasite in the anterior chamber with its suckers attached to the posterior cornea. By pseudopodlike movements of the suckers, the parasite moved toward the opposite side. Extraction was performed with forceps through a small corneal incision. When the caudal part of the scolex was grasped, it tore, leaving its head attached to Descemet's membrane. It was necessary to grasp the head of the scolex directly to effect its removal.

In this last zone we can find the remains of ocular structures (retina, sclerotic) showing various regressive changes (detachment, edema, hemorrhages, deposits of cholesterin, and even bone formation in some of the oldest cases). We have observed more than once the development, in this inflammatory area, of an abscess cavity in which serial sections made posteriorly revealed the parasite.

DESCRIPTION

Ocular cysticercosis is a rare disease, and its identification is difficult for those who have not studied it in specialized clinics and who have not paid attention to this subject in the literature. I am convinced that this diagnosis has been given many different and extravagant labels by observers who were ignorant of the existence of this nosologic entity.

Penido Burnier recognized his first case

ing pictures were lost because of the lack of photographic material during the last war.

SUMMARY

This work represents the experiences of the ophthalmologists and pathologist of the Instituto Penido Burnier with 111 patients bearing 116 ocular cysticerci. The parasites were situated as follows: 51 in the vitreous; 10, subhyaloid; 44, subretinal; 2 in the anterior chamber; 7, subconjunctival; 1 in the orbit; and 1, subcutaneous in the region of the lacrimal sac. The youngest patient was aged 2½ years, the oldest was 66 years of age. The greatest frequency was found before the age of 40 years (96 cases). There was a slight predominance in women (64 female patients, 47 males). In 56 cases, parasites were in the right eye; in 50, in the left; 2 were binocular; 2 were double in a right eye; 1 was double in the left eye. In 101

eyes the diagnosis was made clinically, and in 15, it was made after necropsy (of these, 12 were examined pathologically).

History. Schott and Sömmering (in Frankfort, in 1829) independently observed the same cysticercus in an anterior chamber. The former extracted the parasite. Siebold (1838) published a report of the subconjunctival cysticercus observed by Baum. Two years after the discovery of the ophthalmoscope, Coccius saw a cyst in the vitreous resembling a cysticercus. Only in 1854 were the first indisputable observations of cysticercus in the vitreous and under the retina made by von Graefe, who, by 1866, had seen more than 80 cases among 80,000 patients.

Etiology and Pathogenesis. Ocular cysticercosis obeys the same laws of general infestation as cysticercus cellulosae, the larva of tenia solium. Heteroinfection is more common than autoinfestation. The parasite is encountered in all the tissues of the eye except the lens. When intraocular, cysticercus provokes an exudative inflammatory reaction (exudates, iritis, uveitis, purulent iridocyclitis, and even panophthalmitis). Among the complications are: detachment of the retina, synechias of the iris, complicated cataract, and atrophy of the globe.

Diagnosis. Ocular cysticercosis is a rare disease (116 in 54,000 patients, or 1:1,383). When intraocular, the first symptom is reduction in vision. During the first months of infestation, if the media are clear, the cysticercus can be positively identified: by its bluish-white spherical vesicle with peripheral iridescent reflexes and slight undulatory movements at times; and by its scolex which, when evaginated, reveals the sucking cups and, when invaginated, appears as a denser white spot in the center of the vesicle.

When the media are more turbid, diagnosis is more difficult. Penido Burnier has taught us that we must be alert to the possibility of cysticercosis. It is not enough to see a white spot through the exudates of exudative choroiditis, or to note a detachment of the retina which is a complication of the parasitosis. The inferior vitreous, where the parasite is more often encountered, must be explored. We have to pay greater attention when the complement fixation reaction in the blood is positive, for it is positive in 73.2 percent of cases—a valuable aid in diagnosis. The subconjunctival cysticercus resembles the lymphatic cyst from which it can be distinguished by the denser white spot in the center.

Treatment. Medical therapy and destruction of the parasite by caustics, diathermy, and electrolysis are ineffective. The organism must be extracted by the transcleral route when it is behind the lens. The parasite, living or dead, is destructive to the eye, and must be removed to preserve the globe. In 40 attempts, 34 extractions from the vitreous or from the subhyaloid area were successful. In 21 trials, 15 parasites were removed from beneath the retina, 7 of these being spontaneous extrusions after incision of the sclera and choroid. Extraction may preserve vision in the early cases of subretinal cysticercus by using diathermic localization under ophthalmoscopic control.

Prognosis. Extraocular cysticercus is benign, but the intraocular disease leads to blindness with rare exceptions.

Prophylaxis. Control and inspection of meat, and personal and dietary hygiene are essential, especially in rural areas, where almost all of the carriers of cysticercus live.

Pathology. Sometimes the diagnosis is difficult especially when careful search reveals only a single relic of the parasite such as its hooks or the typical histologic reaction.

Description. A knowledge of this is of great value, particularly for those who are not familiar with the diagnosis. Many must have seen the parasite without recognizing it. Where tenia solium is found, there must be a certain proportion of ocular cysticercus.

Instituto Penido Burnier.

DISCUSSION

MANUEL URIBE TRONCOSO, M.D.
New York

I consider the paper of Dr. Lech Junior of importance because it gives new data about the frequency of cysticercosis in Brazil and also because of the successful results obtained with surgical treatment in the preservation of the eye and the improvement of visual acuity. Dr. P. Burnier and Dr. Sales in their paper, in 1935, state that the frequency of cysticercosis in Brazil was about 62 cases among 70,000 patients of eye diseases.

Dr. Lech Junior asserts that in the Instituto Penido Burnier the proportion in later years has been 1 case in about 1,383 patients. In these new statistics he observed 111 cases of which 51 were in the vitreous, 10 subhyaloid, and 44 subretinal. He also observed 2 in the anterior chamber and 9 under the conjunctiva, the skin, and in the orbit.

During the first years of my practice in Mexico City, I had the opportunity of seeing 3 or 4 cases of intraocular cysticercosis, while during my whole practice in New York I have not been able to see a single case.

The appearance of the vesicle of cysticercus and its movements in the vitreous are one of the most striking and beautiful views that can be observed with the ophthalmoscope. The spheric vesicle has a bluish iridescent coloration, contrasting with the white aspect of the body and head of the parasite, the latter especially visible when it has moved outside of the vesicle.

The literature about this disease in Mexico is abundant. Many observers—Ramos, 1887; Lopez, 1903; Chavez, Montaño, 1902; Silva, 1928, and lately Puig Solanes, 1946, have minutely described the clinical symptoms of cysticercosis and emphasized the importance of an early operation to remove the parasite.

Chavez found in Mexico 1 case of cysticercosis in about 4,000 patients of eye diseases, a proportion lower than that of Dr. Lech Junior.

Montaño, as early as 1902, used electrolysis for the destruction of the parasite in the vitreous. Other surgeons have used caustics, diathermy, and radium. The consensus of opinion, however, is that the parasite should be removed from the eye; for even when destroyed and dead it is able to elicit great inflammatory reaction.

Dr. Lech Junior's statistics of 34 successful extractions from the vitreous in 40 cases, or 85 percent, are impressive; as the average of successful operations mentioned by other authors is only 60 to 70 percent of the cases (Duke-Elder). In 21 subretinal cases he was able to remove the parasite 15 times. I believe the method he describes, of making accurate localization of the parasite with nonperforating diathermic cauterizations, nearer and nearer to the vesicle, until its exact place has been accurately found by ophthalmoscopic examination, may have contributed materially to the success of his operations.

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APPARENT ROTATION OF A FIXED TARGET ASSOCIATED WITH LINEAR ACCELERATION IN FLIGHT*

BRANT CLARK,[†] PH.D.

San Jose, California

AND

ASHTON GRAYBIEL,[‡] M.D.

Pensacola, Florida

INTRODUCTION

This study is one of a series of investigations which have been designed to establish factors that are important in proper orientation during flight. The original stimulus for these studies came as a result of a series of airplane accidents that occurred under peculiar circumstances. These accidents were characterized by the fact that the pilot became confused or disoriented at the time of the crash. The pilots reported difficulties which fell into several categories: (1) States of confusion, (2) disturbances in equilibrium; (3) undue fascination on objects, and (4) various types of visual illusions.

Orientation in space during flight has been found to be subject to a number of illusions even under normal conditions in the daytime.[12] However, when visual cues are reduced as in night flying, additional illusory effects appear.[1, 4-9] One of these is known as autokinesis or the autokinetic illusion.[4] This refers to certain illusory perceptions of movement of a fixed object in the visual field when other visual references are meager or lacking. Autokinesis is most prominent in the case of an isolated light in the dark when it is experienced universally by normal persons. It has been found to occur not only in the laboratory but also in flight and can

be considered to be a factor contributing to disorientation in pilots.

A still more important factor in causing visual disorientation during flight is the effect of acceleration on the nonacoustic labyrinth. Here, it is necessary to distinguish between the effect of angular acceleration on the semicircular canals and the effect of linear or radial acceleration on the otolith organs. Previous studies both in the laboratory and in the air have served to define the chief characteristics of the associated illusory effects.[1, 3, 6-11]

If a person is subjected to angular acceleration in the dark, while viewing an object which rotates with him, this object will appear to move in a characteristic manner which we have termed the oculogyral illusion.[6, 7] This apparent movement is due, in large part at least, to ocular nystagmus which is produced reflexly following stimulation of the semicircular canals. The eye movements produce a tracking of the image across the retina which, during the slow phase of the nystagmus, is perceived as movement of the object rather than of the eyes. This effect is observed following angular accelerations of as small as 0.2 degree per second per second,[10] but the illusion is displayed in the most striking fashion when the observer is subjected to strong angular acceleration while viewing a moving object.

If, for example, the real movement of the object is clockwise and the apparent motion counterclockwise, a paradoxical situation is created in which the observer must keep turning his head to the right in order to keep in view an object which appears to be rushing in the opposite direction.[7] The chief

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characteristics of the oculogyral illusion in the horizontal plane are: (a) the direction of motion is related to the direction of acceleration; (b) the lag between the onset of acceleration and the maximum illusion of motion is short; (c) objects appear to move rapidly but are displaced relatively little from their original position; and (d) following a strong stimulus there are prolonged after effects in which the apparent motion may reverse itself one or more times.[6, 7]

The effects of radial acceleration in causing visual disorientation differ markedly from those of angular acceleration and, although the exact mechanisms mediating the effects are unknown, they are caused in part at least by stimulation of the otolith organs.

If, for example, a person is rotated at constant speed on a human centrifuge, the perception of the vertical, in the absence of visual cues, will tend to coincide with the direction of the resultant of the centrifugal force and the force of gravity.[8] If now the observer regards an object in the dark which does not provide adequate cues for orientation to the earth, this object will be projected in space in accordance with the apparent vertical direction.

Thus, when a subject faces toward or away from the line of resultant force, an object on the horizon will appear to be, respectively, above or below it. If the subject is at right angles to the force, the object will appear to rotate clockwise if the direction of force is from the left, and counterclockwise if the force is from the right.

The characteristics of this phenomenon, which has been termed the oculogravic illusion, are as follows: (a) the direction of the displacements bears a constant relation to the resultant force; (b) under constant acceleration the object may not appear to move but simply to be displaced in space; (c) a considerable lag is observed between the onset of the stimulus and the maximum illusory effect; and (d) there are no after effects following cessation of the stimulus.[1, 8, 9]

It has been pointed out elsewhere[2] that

a clear distinction must be made between three types of acceleration which affect a pilot's orientation during flight; namely, angular acceleration, radial acceleration, and linear acceleration.

Angular acceleration is a change in the velocity of rotation and is the adequate stimulus to the semicircular canals. Reflex connections to the extraocular muscles produce ocular nystagmus and resultant illusory effects.[6, 7]

Radial acceleration or centrifugal force results when the pilot rotates about an axis at some distance from his body, for example in a normal turn. This accelerative force is a stimulus to the otolith organs and causes generalized changes in bodily pressure. It is invariably associated with rotation but not necessarily with angular acceleration. This force results in the apparent displacement of stationary objects in the dark.[1, 8, 9]

Linear acceleration is a change in velocity from point to point without a change in direction. Linear acceleration and deceleration acting in the horizontal plane as the aircraft changes velocity combine as a vector with the force of gravity to produce a resultant force which is greater in magnitude and acts in a different direction from the force of gravity. The change in magnitude and direction of this resultant force and its effect on visual perception are the primary factors with which this report is concerned.

APPARATUS AND PROCEDURE

An experimental procedure which was used in studies of the effects of angular and radial acceleration on visual orientation was adapted for use in this study.[9] The subjects observed a collimated "star" while they were seated in the rear cockpit of an SNJ-6 aircraft during flight. The star consisted of a central luminous point with six symmetrically placed radiating lines and was observed in complete darkness which was made possible by a light-proof goggle mounting attached to the instrument and a covering for the head. Head movements were minimized by a biting

board. Trials were run while the subject faced 85° to the left of the forward motion of the aircraft. The three subjects* were experienced observers, having made many similar observations both in flight and in the laboratory.

Each observer gave a running account of the illusory motion of the star by using a throat microphone which was connected to an airborne wire recorder. Hence, the subjects' verbal reports were automatically recorded for future study in the laboratory after the flight. As each verbal report was given the subject simultaneously pressed a switch which marked the accelerometer record. This made is possible to relate each report of the movement of the star to the changes in the acceleration of the aircraft. All measures of temporal relations were therefore made directly on the accelerometer records.

In order to obtain a measure of the accelerative forces in operation during the observations, an accelerometer which measures the force of acceleration was set on shock mounts in the luggage compartment of the aircraft just back of the observer.[†] The instrument consists of three independent accelerometer units, one for each of the major planes of the aircraft. The individual accelerometer mechanisms consist of a weight supported between two metallic bellows and guided in the direction of its action by means of a central rod passing through the bellows and through the weight. Radial ball bearings mounted on the weight reduce the friction between the weight and the central rod to a negligible value.

Air damping is used. When the weight moves along the rod, one of the bellows is compressed while the other is extended and

air is forced from one to the other through a hole in the center of the supporting rod. The amount of damping is adjustable. Motion of the weight is transmitted to a stylus by means of a simple linkage system.

A record of the accelerative forces is obtained on a special aluminum-backed paper by means of a small electrical charge passing between the stylus and the recording drum. Two solenoid markers are also available to be used as signal devices. The range of measurable accelerations is 2G. in planes other than the vertical where it is +6 to −3G.[‡]

Measurements at any point on the record are read directly by placing a calibrated celluloid mat over the chart. This device made it possible to measure the force of acceleration in all of the three major axes of motion of the aircraft. When these records were taken simultaneously with a subject's reports of his perceptual experiences, it was possible to correlate the accelerative stimuli with the illusory reports of motion and displacement of the target.

Linear acceleration and deceleration occur in flight as a result of the increase and decrease in the power used or the raising and lowering of the flaps which have a braking effect on the aircraft. In this experiment all of the observations were made at altitudes ranging from 4,000 to 7,000 feet.

Accelerative forces of different magnitudes were produced by setting the initial air speed at 90 m.p.h. and using various combinations of flap positions and increase in throttle setting to raise the air speed. For the maximum accelerative force full throttle was applied and the flaps were raised simultaneously. Decelerative forces were produced by reversing this procedure. Thus, accelerative forces having maximum values ranging from 0.03 to 0.20G. and decelerative forces having maximum values from 0.04 to 0.44G. were produced.

A typical series of experimental trials

* The subjects were the authors and Richard C. Snyder, PhM/1c, U.S.N.
† This instrument is a special modification of the Hathaway Type AR-1 Flight Analyzer and was designed to measure accelerative forces within the range known to affect visual perception. It was designed and made by the Hathaway Instrument Company, Denver, Colorado.

‡ In this paper G. will be used to refer to the force of acceleration measured in terms of the force of gravity as unity.

was conducted as follows: The pilot would select the most desirable altitude and level off the plane at a prearranged speed. The subject prepared the equipment and set the recording devices in operation. The subject then said, "Trial one" and simultaneously pressed a switch to mark both the wire recorder and the accelerometer record. The pilot waited from 5 to 15 seconds and applied the accelerative or decelerative force by appropriate manipulation of throttle and flaps.

Throughout the trial the observer gave a running account of any motion or displacement of the star and for each report simultaneously pressed a switch and thus marked the accelerometer record. The pilot reported when the plane had been flying without change in speed for 20 seconds, and the observer marked the record indicating the end of the trial.

This sequence was followed for 12 to 24 trials for each flight alternating accelerative and decelerative stimuli. The magnitude of the stimuli was prearranged to be in random order and was unknown to the subject. Rest periods occurred after each series of six observations.

The principal effect reported by the subjects was rotation of the "star" about the central point in the plane of the radiating lines. They reported the illusory rotation of the star indicating whether it was clockwise or counterclockwise and the onset and offset of rotation. They also estimated the extent of rotation and displacement in degrees from the "true" position in which one set of radiating lines was horizontal.

The data from the two recording devices were combined in the laboratory. The data from the wire recordings were transcribed onto the accelerometer records. All determinations of the stimulus-response relationships were then made by measurements directly on the accelerometer record, the temporal measurements being made to the nearest second.

The magnitude of the linear accelerations involved was determined by the use of an "interpretation mask" supplied with the accelerometer. The calibration of this "mask" was checked by producing known forces on a human centrifuge and was found to be accurate within the error of measurement of the forces on the record.

The description of the linear accelerative forces produced by the aircraft presented certain unique problems because the accelerative force was far from constant throughout any trial. In the typical psychophysical experiment, stimuli of constant intensity are presented to the observers for a prearranged period of time. These controls were impossible in this experiment because the forces were a function of the accelerative or decelerative characterstics of the aircraft. Therefore, the accelerative and decelerative forces used were constant for only a brief interval of time.

The force in each case has been described in terms of three variables involved: (1) the duration of the force, (2) the maximum acceleration or deceleration produced during the trial, and (3) the time required to reach this maximum force. It was not possible to take completely into account the significance of the variations of changing accelerations during the interval the stimulus occurred.

The distribution of maximum decelerative forces, the mean time to reach this force, and the mean time the force was acting on the subject are shown in Table 1. There is no regular or significant difference between the two temporal variables for the different maximum forces reached. The trend was for the force to increase rapidly to its maximum value within approximately 5 seconds; this maximum force remained only for a short period (2 to 3 seconds) after which there was a slow reduction to zero. The total duration of the force averaged approximately 28 seconds. The typical pattern was a rapid increase to a maximum followed by a gradual reduction over a prolonged period. Correlations among the three measured stimulus variables were negligible.

The accelerometer records were also

TABLE 1

THE TABLE SHOWS THE DISTRIBUTION OF THE MAXIMUM ACCELERATIVE AND DECELERATIVE FORCES ATTAINED IN THE VARIOUS TRIALS, THE MEAN TIME REQUIRED TO REACH THIS MAXIMUM FORCE, AND THE MEAN TOTAL DURATION OF THE FORCE FOR THE THREE SUBJECTS

Maximum Decel. Force in G.	N	Mn Time to Max. G. (In. Sec.)	Mn Duration of G. (In Sec.)	Maximum Accel. Force in G.	N	Mn Time To Max. G. (In Sec.)	Mn Duration of G. (In Sec.)
.04–.06	9	7.1	23.1	.02–.03	8	7.3	27.4
.07–.09	22	8.6	32.5	.04–.05	21	5.8	28.9
.10–.12	10	4.8	25.9	.06–.07	17	5.2	30.9
.13–.15	11	4.0	25.9	.08–.09	12	4.7	28.8
.16–.18	14	4.3	28.9	.10–.11	11	2.6	30.6
.19–.21	20	5.5	25.6	.12–.13	4	5.5	25.5
.22–.24	6	6.7	26.7	.14–.15	11	5.4	25.4
.25–.27	7	5.7	26.7	.16–.17	14	5.2	28.9
.28–.30	10	5.5	22.6	.18–.19	8	5.9	33.4
.31–.33	5	4.2	23.8	.20–.21	1	8.0	45.0
.34–.36	1	6.0	28.0				
.37–.39	3	5.5	31.0				
.40–.42	2	3.5	26.5				
.43–.45	1	5.5	31.0				
Total	121	5.8	27.2		107	5.1	29.6
Stand. Dev.	—	3.2	6.7		—	2.4	7.8

studied to determine whether there were forces evident in the other two major planes of the aircraft. Lateral forces (slipping and skidding) were not evident on any of the records. The sensitivity of the accelerometer was 0.02G. so any lateral force was less than this value. Some vibration was evident but this was constant throughout all trials and appeared in all three planes.

The accelerometer which recorded the vertical component of force registered accelerations and decelerations of measurable amounts (that is, greater than 0.10G.) during some of the trials. During accelerations greater than 0.13G. and during decelerations greater than 0.21G. the average positive component was less than 0.10G.

In other words the aircraft lost altitude for a few seconds during acceleration and gained altitude for a few seconds during deceleration due to the operation of the flaps. This component of force was greater during deceleration than during acceleration, but in each case the average duration of this force was less than the time required for acceleration or deceleration as recorded by the fore and aft component to attain its maximum value.

The effect of this change in altitude was either to increase or decrease the vertical component of the force for a short period. This modified the pattern of increase of the resultant force acting on the body without affecting the maximum force reached or the duration of the change in force.

The net result of the linear accelerative forces was to change both the magnitude and direction of the resultant force acting on the body. During normal straight and level flight, the force of gravity was acting on the body in a vertical plane. During acceleration the added forces produced changes in the magnitude of the resultant force varying from 1.0004G. to 1.0218G. and changes in direction from 1.7° to 11.9°. During deceleration the resultant force varied between 1.0008G. and 1.0925G. while its change in direction varied between 2.3° at lower intensities to 23.7° at higher intensities.

Angular accelerations were kept subthreshold during these maneuvers by appropriate operation of the aircraft. The pilot kept the wings level, kept on a constant heading, and kept the nose of the plane on the horizon. The loss of altitude during

certain trials may have produced small angular accelerations about the horizontal axis of the plane. These stimuli appear to have been subthreshold because the pattern of response was the same even during the deceleration runs where the change in altitude was greatest.

EXPERIMENTAL RESULTS

Illusory effects during deceleration. Although in this experiment the forces were at or near the threshold and of short duration, clockwise rotary motion and displacement occurred at all levels of stimulus intensity used. The rotation observed in these trials involved a rotary displacement about the central point of the star to a new position. This was usually accompanied by motion but occasionally the displacement would appear suddenly without any apparent motion. As the accelerative force decreased, the star rotated slowly back to its original position.

The percent occurrence of rotary motion and displacement of the target during deceleration is to be found in Table 2. On several trials the subjects reported rotary motion without accompanying rotary displacement. When these data were plotted typical S-curves resulted, the motion curve being displaced slightly to the lower stimulus values. The group limen for motion determined by linear interpolation was found to be 0.067G. while the group limen for dis-

placement was found to be 0.078G. Motion was reported in all trials above 0.22G. while both motion and displacement were reported in all trials above 0.30G.

The mean duration of the illusory rotation and the mean maximum rotary displacements showed a progressive increase with increasing force of deceleration (table 2). The average displacement reported for decelerative forces from 0.03 to 0.06G. was 1.4° and this increased to 10.0° for decelerations from 0.43 to 0.46G. The maximum report of rotation was 15°. There were five such reports by two subjects.

The average duration of the rotary effect varied from 9.2 seconds to 22.0 seconds; its duration was on the average less than half the total duration of the stimulus (tables 1 and 2). On 16 trials, however, the three subjects reported that the illusory rotation lasted beyond the point where the decelerative force had been reduced to zero.

This suggests the possibility of a positive after-effect, although it may have been a result of a delay in reporting the termination of the effect which presented a difficult subjective judgment.

Illusory effects during acceleration. Counterclockwise rotation and accompanying rotary displacement of the fixation object occurred during acceleration (table 3). All of the stimulus levels used were above threshold since both rotary motion and dis-

TABLE 2

PERCENT OCCURRENCE OF ILLUSORY EFFECTS, MAXIMUM DISPLACEMENTS, AND TEMPORAL RELATIONS FOR VARIOUS MAXIMUM DECELERATIVE FORCES

Maximum Decel. Force in G.	.03–.06	.07–.10	.11–.14	.15–.18	.19–.22	.23–.26	.27–.30	.31–.34	.35–.38	.39–.42	.43–.46
N	9	25	14	18	23	7	13	5	4	2	1
% of Motion Reports	33	64	71	72	96	100	100	100	100	100	100
% Displacement Reports	22	56	71	67	87	100	92	100	100	100	100
Mean Max. Clockwise Displacement in Degrees	1.4	2.4	5.1	3.6	7.5	8.5	7.4	5.7	9.0	10.0	10.0
Mean Duration of Motion in Sec.	9.2	12.8	15.2	13.9	16.8	21.3	16.6	14.0	15.8	22.0	22.0
Lag to First Report in Sec.	5.7	6.1	5.5	4.8	5.0	3.9	4.3	6.2	6.3	4.5	5.0

TABLE 3

THIS TABLE SHOWS THE EXTENT, LAG IN TIME TO FIRST REPORT, AND DURATION OF ILLUSORY
ROTATION OF THE STAR FOR VARIOUS MAXIMUM ACCELERATIVE FORCES

Maximum Accel. Force in G.	.02– .03	.04– .05	.06– .07	.08– .09	.10– .11	.12– .13	.14– .15	.16– .17	.18– .19	.20– .21
N	8	20	18	12	11	4	11	14	8	1
Mean Counter-clockwise Rotation in Degrees	6.0	10.0	8.8	10.0	10.1	9.8	11.0	10.2	9.8	10.0
Mean Duration in Sec.	30.6	29.4	29.9	27.2	26.8	25.8	29.9	25.9	27.6	25.0
Lag to First Report in Sec.	5.6	5.4	5.2	4.6	4.2	4.8	5.0	4.4	3.9	6.0

placement were reported during 105 of 107 trials for the three subjects. Within the range of accelerative forces used, there was very little relation between the degree of force and the amount of reported rotary displacement.

Although the mean value in the lowest group of forces was notably less than the mean scores for greater forces, this difference was not significant at the 10-percent level by the chi-square test, although it approached this level. The maximum rotation was 15° reported by two subjects during 30 trials distributed throughout the complete range of accelerative forces. There was no uniform change in the duration of the rotation for the various stimulus intensities, but the time lag from the beginning of the accelerative force to the first report of motion decreased as the accelerative force increased.

Illusory effects with the subject facing forward. Some additional trials were also run with the subjects facing forward rather than to the side. On the basis of the forces involved the star could be expected to rise during acceleration and fall during deceleration.[1, 2, 8, 9] However, these displacements did not occur with the expected regularity in the case of all subjects.

This may be attributed to two factors: (1) The short duration of the strong part of the accelerative force, and (2) the judgments of the degree of displacement are much more difficult to make than the judgments of the rotation of a horizontal line;

this is particularly true with regard to judgments of the initial reference level. An additional investigation will be made of this problem in a future study.

DISCUSSION

The data reported here show clearly defined changes in the apparent position of an isolated target in the dark when the subjects were exposed to linear acceleration or deceleration during flight.

The characteristics of the illusory effects were similar to those found for radial acceleration on a human centrifuge in the following ways:[8] (a) the direction of the apparent rotation bore a constant relation to the direction of the linear acceleration, and the illusory effect was uniformly shorter in duration than the stimulus; (b) there was a lag in time of from 4 to 6 seconds between the onset of the stimulus and the first report of rotation; (c) the displacement of the target to a new position usually occurred with accompanying motion but sometimes appeared suddenly with little or no motion; (d) after effects were not regularly observed.

In general, the orientation of the subject with respect to the isolated visual target was in accordance with the resultant of the force of the linear acceleration and the force of gravity acting on the subject; however, the extent of the rotation of the target was less than the change in the direction of the resultant force.

These data lend support to the hypothesis

that the disorientation of the subject is a result of the stimulation of the otolith organ, although sensations of increased bodily pressure and change in bodily position may contribute to the total perception.

The results of this experiment show that accelerations and decelerations such as may be encountered in the normal operation of an aircraft produce the illusion of rotation of an isolated target in the dark if the subject is facing toward the side.

These illusory effects may result from linear acceleration as reported here, from radial acceleration acting in the same direction as the forces in this experiment,[8] from angular accelerations which affect the vertical semicircular canals,[3] or from combinations of these factors. In normal flight all three commonly occur simultaneously and to isolate them requires particular care in the operation of the aircraft.

When the rotary displacement of the target is judged as real, or if the rotation is referred to the subject himself, the result will be disorientation on the part of the pilot. The practical significance of such effects is emphasized by the fact that pilots flying at night have reported rotations of the visual field which subsequently proved to be illusory.[12, 13]

Reports of illusory motion and displacement were made at all stimulus levels used for both acceleration and deceleration, but there was a substantial difference in the threshold levels of the two forces. The explanation of this difference is not immediately apparent from an analysis of the subjects' reports or the nature of the accelerative and decelerative forces. The reports of rotation were basically the same in the two situations and the general patterns of the records of the forces were closely similar both on the basis of inspection and a comparison of the various parts of the curve of force.

SUMMARY

The purpose of this study was to determine the effects of linear acceleration and deceleration on the visual perception of a target in the dark. Three subjects observed a collimated "star" in the dark while the pilot of an SNJ-6 aircraft executed various degrees of linear acceleration. The subjects gave a running account of the behavior of the "star" using a throat microphone connected to a wire recorder.

The forces produced represented the range of accelerations and decelerations occuring in the normal operation of the aircraft. The forces were measured by a three component accelerometer which showed that accelerative and decelerative forces built up to a maximum in approximately 5.5 seconds and within 2 to 3 seconds began to drop off slowly to zero.

The net result of these accelerations and decelerations was to change both the magnitude and the direction of the resultant force acting on the subject. The magnitude of the maximum resultant forces varied between 1.0004G. and 1.0925G., and its change in direction varied between 1.7° and 23.7°.

When the subjects faced to the left in the aircraft, the radiating lines of the star appeared to rotate about the central point to a new position. This rotation was clockwise during deceleration and counterclockwise during acceleration. As the force became smaller, the star appeared to rotate back to its normal position. This illusory rotation occurred at all stimulus levels.

The thresholds of linear deceleration for motion and displacement were 0.067G. and 0.078G., respectively. All of the linear accelerations used were above threshold. The mean maximum rotation during deceleration increased as the decelerative force increased, the maximum estimated rotation reported being 15°.

There was also a positive relation between the maximum force and the duration of the illusory effect. The accelerative effects did not show a consistent variation with the maximum change in the accelerative force.

The results are similar to those observed on a human centrifuge and show that linear

acceleration and deceleration during flight have a marked influence upon visual perception in the dark. Although the observed rotation were small, they were clearly defined and may be considered to be factors contributing to disorientation in pilots.

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SPASTIC ENTROPION CORRECTION: WHEELER'S ORBICULARIS ADVANCEMENT*

M. PAUL MOTTO, M.D., AND ROBERT L. ALEXANDER, M.D.

Cleveland, Ohio

The following case, representative of a series of entropion, is of interest because of its relative infrequency and for the reason that it is a good example of what the proper surgical technique and management can be expected to accomplish in similar cases.

Entropion is less common than ectropion and not as easily nor as permanently corrected. Most operations for this condition depend for their effectiveness on a downward pull, calculated to unroll the inverted lower lid, and on downward traction to prevent turning in of the margin. But not all of these meet the requirements set forth by Spaeth[1] that: "(1) It must relieve the faulty position of the cilia; (2) it must prevent the subsequent recurrence of this faulty position; and (3) it must fulfill the foregoing requirements with the least amount of disfigurement and loss of position of the normal lid border." The last requirement is the most difficult to fulfill.

The problem of spastic entropion has been approached by the application of adhesive strips or adhesive substances and buried sutures, as suggested by Snellen, Gaillard, and Arlt. Others have used skin incisions as suggested by Calsus, von Graefe, Gasson,
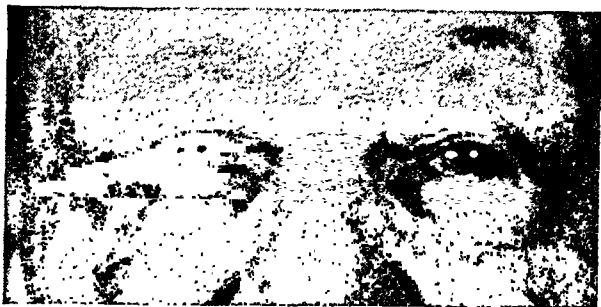
Fig. 1 (Motto and Alexander). Entropion present. Mascara has been placed at the abnormal lid borders.

Panas,[2] and others. Ziegler's[3] method of cauterization, introduced in 1909 and so well advocated by Wiener and Alvis,[4] has become quite popular.

There have been other procedures for correction of spastic entropion not dependent on the downward pull of the lid. Pocnisov[5] advised canthotomy and severance of the attachment of the outer part of the eyelid to the orbital margin. Goldzieper[6] and Blaskovics[7] made lateral traction on the skin of the lower eyelid by removal of a triangle of skin over the zygomatic region. A free canthotomy and a readjustment of the edges at the outer canthus with sutures to hold the lower flap outward during the healing was suggested by Vogt.[8] The injection of 95-percent alcohol into the muscle at the outer canthus was advocated by Hughes[9] in that it weakened the action of the orbicularis.

These means of attempting to correct the problem often result in failure to meet

Fig. 2 (Motto and Alexander). Left lower lid is everted under tension. Pathologic lid border marked by mascara.

Spaeth's criteria. The condition tends to recur or correction results in disfigurement and loss of normal lid-border position.

It was thought by one of us (P.M.) that the technique advocate by Wheeler might most satisfactorily fulfill these requirements. The operation has been performed on 7 patients, 4 private and 3 from the clinic service. The sixth case is being presented at this time.

CASE REPORT

P. E., a white man, aged 81 years, received a diagnosis of spastic entropion. Ocular tension was 20 mm. Hg (Schiøtz) in both eyes, and the fields were normal. The muscle bal-
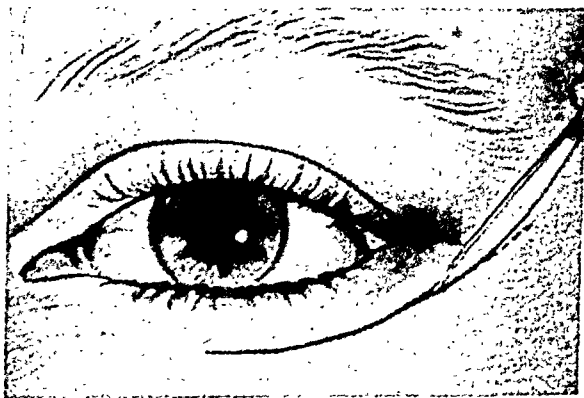
Fig. 3 (Motto and Alexander). Site of primary skin incision. (From *The Collected Papers of John Martin Wheeler.*)

ance was within the physiologic range of normal.

The upper lids were in good position as to cilia and lid border, but senile atrophy of the skin surface was present. The lid border and cilia of the lower lids were turned inward against the conjunctiva (fig. 1). This eliptical area measured 7 mm. at its greatest width from the normal to the pathologic lid border (fig. 2). The lid could be easily everted with finger traction, but on release of traction and gently closing the eye, the lid border again turned inward.

The condition of the palpebral conjunctiva was not remarkable, but the bulbar conjunctiva had slight and superficial injection. The corneas were clear. The anterior cham-

bers were clear and without flare upon slit-lamp examination. The iris stroma were of good quality. The pupils were symmetrical, reacting to light and accommodation.

Slitlamp examination of the lens showed opacities that were cortical in position. The media were clear. Fundus examination showed normal discs but marked arteriolar sclerosis. Both maculas showed degenerative changes that extended on to the surrounding retinas.

The patient's uncorrected visual acuity was: O.D., 6/12; O.S., 6/15. His subjective refractive error was: O.D., +2.0D. sph. ⊃ 0.5D. cyl. ax. 180° = 6/7.5; O.S.,

Fig. 4 (Motto and Alexander). Section of muscle dissected from orbicularis oculi. (From *The Collected Papers of John Martin Wheeler.*)

+2.25D. sph. ⊃ 0.75D. cyl. ax. 180° = 6/7.5; with a +2.75D. sph., he read J1.

OPERATION PERFORMED

An operation for the correction of the entropion was advised, and the patient consented. Wheeler's operation for spastic entropion without modification was performed. Local anesthesia was obtained by infiltration of the field of operation with a mixture of procaine and adrenalin. The injection was placed in front of the tarsus and tarso-orbital fascia so that the lid was in good position before operation. The anesthesia was carried out over the periosteum at the outer orbital margin.

Fig. 5 (Motto and Alexander). Muscle strip in position and sutures in place. (From *The Collected Papers of John Martin Wheeler.*)

The primary incision was made 6 mm. below the normal lid margin through the skin only (fig. 3). The incision was started a little nasally to the center of the lid. Following the direction of the lid margin and parallel to it, the incision was carried about 1 cm. beyond the orbital margin out into the zygomatic region. The skin overlying the orbicularis was dissected free from the incision border up to near the cilia and downward 4 mm. from the incision border.

Following this, a strip of muscle, 4 to 5 mm. wide, was dissected free from the orbicularis oculi, starting at the innermost edge of the skin incision, extending out to the outer orbital rim, and ending at an area opposite the canthus. The dissection swept out and upward, following the anatomic arrangement of the orbicularis fibers. The

Fig. 6 (Motto and Alexander). Postoperative results, one year later.

strip of muscle was then severed at the outer terminal edge of the dissection (fig. 4).

The important placement of the muscle strip was then accomplished by putting it on a stretch and bringing it upward and outward to be attached to the periosteum slightly superior to and lateral to the orbital tubercle. The muscle was attached by two 3-0, chromic gut sutures, one at the end of the muscle and a second a little beyond the orbital margin (fig. 5). The first suture is important for positioning and directing the muscle strip; the second makes its attachment more secure.

The skin wound was closed by fine, interrupted black silk sutures. The lids were covered by a protective tissue. A thin ointment and a secure pressure bandage were placed over the operative site for five days. On the seventh postoperative day one half of the sutures were removed; the remaining sutures were removed on the ninth postoperative day.

RESULTS

The result of this procedure is a permanent correction of the spastic entropion without appreciable scarring or other dis-

figurement (fig. 6). The lid, well supported in a normal position, is kept from future ectropion or sagging by the muscle strip. The operation has fulfilled the three requirements as outlined by Spaeth: (1) the faulty position of the cilia is corrected; (2) it prevents recurrence; (3) there is little disfigurement and no loss of normal lid-border position.

SUMMARY

1. We have operated on seven cases of spastic entropion according to the method of Wheeler. One case, the sixth, is presented as an illustration.

2. The results have been excellent in all cases and to date there have been no recurrences.

3. We feel that the Wheeler procedure should be employed more frequently because it offers, in our opinoin, the best, the safest, and the most conservative operation for correction of this condition. The lid is well supported. Future recurrence or sagging is prevented by the muscle strip, resulting in normal position of the lid border.

650 Rose Building (15).
2065 Adelbert Road (6).

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HIGHER REFRACTIONAL ANOMALIES

Their frequency in different groups and countries

Ernst Schmerl, M.D.
Toledo, Ohio

I. Introduction

The higher refractional anomalies do not fit into the pattern of the mathematical curve of a normal frequency distribution. They are not variations within the normal range. The majority represents abnormal conditions. Comparative studies of these anomalies with regard to exogenous as well as endogenous factors are not available.

The purpose of this contribution is to present some data on this subject and to compare them with respect to sex, national characteristics, constitution, and geographic conditions.

II. Method and Materials

This study considers as higher refractional anomalies hyperopias in which +5.0D. and more were prescribed and myopias with a prescription of −7.0D. or more.

The material was obtained from two groups of records.

Group in Nauen. The first group consisted of the records of my former office in Nauen near Berlin, Germany. About 8,000 men and 8,000 women patients of all age groups were examined. The second group of records was studied in New Orleans, Louisiana, thanks to the kindness of Dr. Charles A. Bahn. Files of 4,420 men and 1,570 women patients of all age groups were checked.

The results obtained in Nauen and in New Orleans are considered representative for these areas, not for other parts of the two countries. (A. Statistical findings: Graphs 1, 2, and 3. B. Clinical observations: Table 1.)

A family history of higher refractional anomalies, especially in the cases of myopia, was not unusual. Excessive myopia was associated with the asthenic as well as with the lateral dysplastic habitus.

TABLE 1
Clinical observations in the Nauen group

	Hyp. ♂	Hyp. ♀	Myop. ♂	Myop. ♀
I. Both eyes affected	111 out of 114 Cases	59 out of 60 Cases	220 out of 265 Cases	274 out of 332 Cases
II. Very large temporal conus or pronounced peripapillary changes		1	68 times in both eyes 12 times in one eye	97 times in both eyes 15 times in one eye
III. Large conus pointing downward	1		6 times in both eyes 8 times in one eye	6 times in both eyes 4 times in one eye
IV. Coloboma of the optic nerve Coloboma of the iris	1	1	3 3	4
V. Signs of phlyctenular, keratoconjunctivitis, maculas, corneas (1)		1	19	18
VI. Muscles: Strabismus convergens Strabismus divergens Nystagmus	13	9	5 4 3	3 8 1
VII. Signs of syphilis Signs of tuberculosis			6 3	4 5

Other observations were: High hyperopia appeared rather stationary from the beginning in early childhood,[2] high myopia was progressive for many years.[3] The extreme degrees of myopia were found more often in women than in men.[3] The youngest patient examined under atropine was a girl, aged 3 weeks, having a myopia of −18.0D. The highest degree of myopia[4] found in
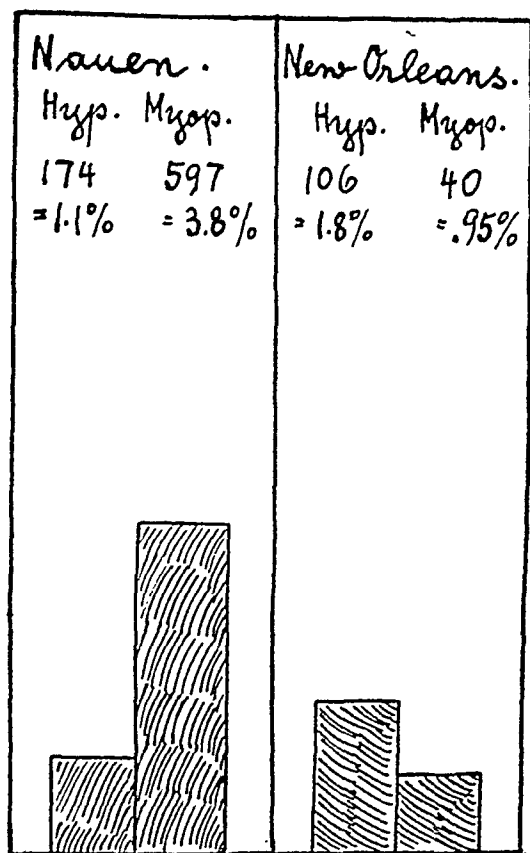
Graph 1 (Schmerl). Representation in percentages of the frequency of higher hyperopia in comparison with higher myopia in Nauen, Germany, and New Orleans, Louisiana.

boys under 8 years of age was −14.0D. (atropine); in girls under 8 years of age, −20.0D. (atropine).

The higher hyperopics showed less outspoken deviations from both the normal linear and the normal lateral type of Stockard.[5] However, sometimes mental abnormalities were noticed.[6] High hyperopics frequently were difficult to handle. The population around Nauen consisted of Germans markedly mixed with Slavs (Wenden).

Group in New Orleans. Fourteen cases of high myopia were seen during 18 months

as assistant to Dr. Bahn. They included 3 male and 11 female white patients. Six patients did not show any abnormalities of the fundus; 2 twin girls had practically the same refractive error and presented coni of medium size. In another patient a nasal conus was observed, and in 2 more patients, coni pointing downward. Only 3 of the 14 cases showed major peripapillary changes. A family history of myopia was extremely rare. The constitutional types of progressive myopia seemed to be the same as in Nauen. Among the hyperopics, body types were seen as described by Hooton.[7] This will be discussed later on.

As to nationality, the practice predominantly consisted of patients of French, English, and Irish extraction, and of smaller groups of German, Italian, and Spanish origin. In both groups, in Nauen and in New Orleans, the number of Jews was negligible. This is mentioned because higher myopia is rather frequently seen among the Jewish population; for instance, in New York.

III. DISCUSSION

At the beginning of the discussion it has to be repeated that the findings reported here do not permit any generalization. In other geographical zones with other national groups, different results are probable. However, some of the statements of this study might find confirmation, such as the observation that excessive myopia occurs in the asthenic as well as in the lateral dysplastic habitus. So the problem of refraction and constitution might be discussed first.

1. Refractional anomalies and constitutional types. Stockard mainly considered two groups of normal bodybuild—the linear and the lateral type. The asthenic and the lateral dysplastic habitus would represent the pathologic extremes of these two groups. In many cases the excessively myopic eye, no less than the glaucomatous eye, is a diseased organ in a diseased body. It is not surprising to find it in the body of any extreme constitutional type.

The literature on the subject of high re-

fractional anomalies and constitution is somewhat confusing. National differences and the differences between the normal and the pathologic constitutional types are not sufficiently taken into consideration. The difficulty in differentiating between normal and pathologic variates of refraction further confuses the issue.

This in part explains why Stockard, in this country, enumerated as characteristics of the linear type: Dolichocephaly, short interpupillary distance and frequent farsightedness; and as characteristics of the lateral type: Brachycephaly, wide interpupillary distance and frequent nearsightedness.

E. Francke[8] (Berlin, Germany), however, found myopia more often in the leptosomic (linear) type; hyperopia more often in the pyknic (lateral) type. Excessive myopia was often encountered in dysplastic types.

Similar results had been obtained by Incze;[9] and Steiger,[10] in Switzerland, had found an increase in the corneal curvature combined with a decrease in the interpupillary distance. Further data relating to this problem can be found in Erggelet's[6] contribution.

In the hyperopics of New Orleans a constitutional type was rather frequently seen as described by Hooton[7] who refers to the children of European immigrants saying: "One gains the impression that the squat build of the parent associated with a broad
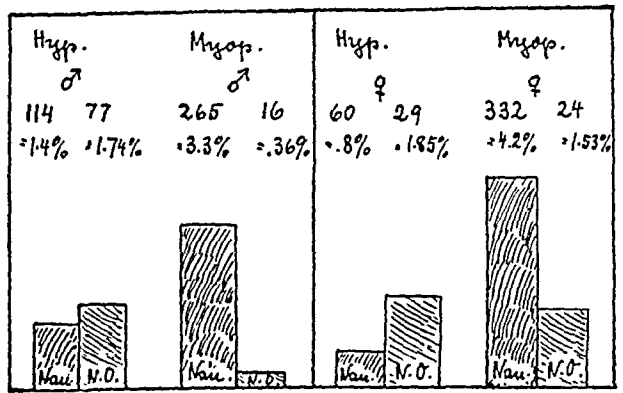
Graph 3 (Schmerl). Representation in percentages for each sex of the frequency of higher refractional anomalies in Nauen, Germany, in comparison with New Orleans, Louisiana.

short face has been transformed into a more weedy and linear body type in which horizontal dimensions have been compressed and vertical diameters stretched." It is this type of linear bodybuild which, derived from the more lateral habitus, remarkably often shows high hyperopia.

Bourgeois and Tscherning[11] have noted a decreasing corneal curvature combined with an increase in body size and skull circumference, and, according to Steiger, hyperopia more often combines with less curved, myopia with more curved, corneas. With Hooton's views in mind, a correlation between change in body type and increased frequency of hyperopia in New Orleans becomes understandable.

2. High refractional anomalies and sex. Although off and on the opinion was expressed that high myopia occurs more often in the female than in the male, few quantitative statements can be found. Jackson[4] in Denver, Colorado, had seen high myopia in 2 boys and 7 girls. Blegvad[3] in a large Danish eye clinic found myopia of —6.0D. and more in 1.14 percent of men and 2.64 percent of women. Our own material shows that the differences in both sexes are marked. In New Orleans this difference is due mainly to the fact that high myopia is practically nonexistent in males.

Instead of offering an explanation for this difference in frequency encountered in males and females, it might suffice to bring to mind that in keratoconus and in glaucoma similar
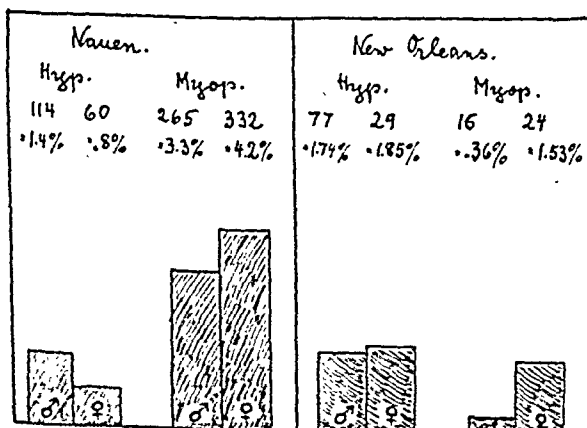
Graph 2 (Schmerl). Representation in percentages of the frequency of higher refractional anomalies in males in comparison with females in Nauen, Germany, and New Orleans, Louisiana.

conditions exist. Reports of positive Asch-heim-Zondek reactions[12] found in high myopia and in keratoconus point to endocrine disturbances.

The prevalence of high hyperopia in males as found in Nauen has not been described before. This difference was missing in New Orleans.

3. *High refractional anomalies and national and geographical factors.* The national differences between the populations in Nauen and in New Orleans were mentioned above. It seems that excessive myopia occurs rather frequently in the German-Slav group, as seen in Nauen. It is also rather often found among Jewish people. Finally, I have seen a number of cases of progressive myopia among the Irish population of this country.

No doubt, it is difficult to evaluate to what extent refractional anomalies are due to national characteristics, how far they are due to constitutional, geographic, or pathologic circumstances. Steiger, for instance, had his doubts about national differences with regard to myopia, and, as an illustration for his belief, he mentioned the Irish and the German nationalities. However, these are just two groups in which myopia seems to occur more frequently.

Kronfeld and Devney[13] also did not seem to be inclined to ascribe much importance to the fact that they had found more myopia of a slight and moderate degree in Chicago than Scheerer and Betsch[14] had found in Tuebingen, Germany. But southern Germans differ markedly from northern Germans among whom the pyknic type, as described by Kretschmer,[15] is rather common, and, as Francke and others had found, this type usually combines with hyperopia. Therefore, small as the difference between Kronfeld's and Scheerer's values is, it seems to be of biologic significance.

In agreement with our findings Kronfeld[16] states that high myopia is more prevalent in Europe than in America, and Novak[17] has found more hyperopia in Iowa than in Vienna.

4. *High refractional anomalies and malformations and general diseases.* In a number of cases of excessive myopia, errors of development seem to be the causative factors. For instance, in cases in which a coloboma of the optic nerve or a large conus pointing downward occurs in but one eye, the myopia was probably caused by an accident in utero.

Among the general diseases connected with excessive myopia, tuberculosis has been mentioned repeatedly.[18] Our own observations justify the statement that, in addition to constitutional, national, and many other factors, tuberculosis and other diseases play a part in the production of progressive myopia in a number of cases.

The rather frequent occurrence of phlyctenular keratoconjunctivitis in high myopia, general signs of tuberculosis, and positive family histories are in favor of this view. It should also be remembered that the asthenic habitus predisposes to tuberculosis as well as to excessive myopia.

Several times the progress of myopic conditions could be observed while a congenital syphilitic keratitis developed.

IV. SUMMARY AND CONCLUSIONS

A number of statistical statements and clinical observations are presented for the purpose of demonstrating: (1) The correlations which exist between higher refractional anomalies and the factors of nationality, constitution, and sex, and, (2) the differences in frequency of higher refractional anomalies which exist in different parts of the world.

It is hoped that this contribution will stimulate better and more specific studies in the field of constitutional ophthalmology.

401 Irving Street (2).

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OCULAR MYASTHENIA GRAVIS*

REPORT OF TWO CASES

JACK V. LISMAN, M.D.

New York

The majority of reports on myasthenia gravis have been made by neurologists, but since the disease may start with purely ocular manifestations, the ophthalmologist is often the first to be consulted. Indeed, as in one of the two cases about to be reported, the disease may remain localized to the eyes for many years. The ophthalmologist must, therefore, be familiar with and always suspicious of the transient, evanescent, and extremely variable manifestations of this rare illness.

Myasthenia gravis was described by Erb, in 1878, and Goldflam, in 1893, but was first named by Jolly,[1] in 1895; the modern era of diagnosis and treatment began in 1935 with the discovery of the striking efficacy of prostigmin by an English ophthalmologist, Mary B. Walker.

DESCRIPTION OF DISEASE

The disease is clinically characterized by a syndrome which comprises marked weakness and fatigue and, in some cases, actual wasting of muscles without any characteristic pathologic changes. There is no predisposition for sex and the disease may occur at any age with the greatest frequency in the third and fourth decades. The onset of the disease has been reported in persons as young as 11 months and as old as 75 years of age. Heredity plays no role. The symptoms may be alleviated by pregnancy and the disease does not interfere with normal labor. Very often the affection first manifests itself after a respiratory illness and such an infection is prone to intensify the symptoms in an established case.

ETIOLOGY

The causation of myasthenia gravis is unknown, but it is believed that there is an

insufficiency of acetylcholine or a similar substance at the myoneural junction. The motor impulse is therefore not transmitted across the junction. The inadequacy of the cholinelike substance at the motor end-plates is due either to underproduction or to rapid destruction by an overabundance of acetylcholine esterase, a substance whose normal function is to destroy acetylcholine.

Walker[2] recognized the similarity between the paralysis of mild curare poisoning and the symptoms of myasthenia gravis and first used eserine and later prostigmin because of their decurarizing effects. These two closely related substances have a protective influence on acetylcholine by rapidly breaking down cholinesterase.

SYMPTOMATOLOGY

The diagnosis rests upon the demonstration of rapid fatigue and weakness of muscles. This is easily accomplished in patients suffering from myasthenia gravis by repeated opening and closing of the eyes or mouth, opening and closing the hand, leg raising and similar movements designed to tire an affected muscle. Recovery occurs on resting that muscle.

OCULAR SIGNS

There appears to be a predisposition for involvement of groups of muscles innervated by cranial nerves. The extraocular muscles together with the orbicularis oculi and the levator palpebral superioris are usually involved. The functions of the extraocular muscles are particularly sensitive to the acetylcholine mechanism.[3] Their sensitivity to acetylcholine is unlike that of any other skeletal muscle. It is not surprising, then, that a general disturbance in acetylcholine utilization should first manifest itself and most profoundly in the extraocular muscles.

In Mattis's[4] series of cases, 96 percent manifested ocular symptoms at some time during the disease. Of importance to the ophthalmologist is his figure of 65 percent of cases manifesting the presenting symp-

tom in the eyes. Presumably, therefore, 65 percent of persons affected with myasthenia gravis present themselves to the ophthalmologist with their initial complaints.

Ptosis is most frequently the first symptom, being present in 46 percent of all cases. Diplopia is the initial complaint in 34 percent of cases.

Occasionally, there are cases that exhibit *no signs or symptoms other than those referable to the ocular apparatus.* Of note is the case reported by Gavey[5] in which the disease remained localized in the eye over a period of 25 years, during which time the diagnosis was in error. Although, statistically, ocular signs and symptoms are most frequent, their correct etiologic basis is often not recognized until other unmistakable concomitants have appeared. One could speculate as to the frequency of cases of monosymptomatic ocular myasthenia gravis that are erroneously diagnosed as neurasthenia, psychosomatic aberrations, neurosyphilis, organic oculomotor palsy, and similar neurologic conditions.

DIPLOPIA

Double vision may be present even when there is no visible evidence of limitation in the ocular excursions. In mild cases there is danger of the condition being considered functional. The extraocular muscle involvement may be so mild as to affect only one muscle. On the other hand, it may be so extreme that a *picture of complete external ophthalmoplegia is produced with complete paralysis of rotations in all directions.*[6]

Limitation of movement of the eyes may be unilateral or bilateral and in any direction. Sometimes, there is a close resemblance to supranuclear paralysis of conjugate movement.

Muscle balance tests vary from time to time. The diplopia is so variable that classification is not possible except in a few cases of the most stable involvement. Cases with minimal diplopia may persist for a long time. When cases of this nature with *obscure*

etiology are encountered, attempts at mapping out the diplopia produce an increasing separation of images due to fatigue; this so called myasthenic reaction is the clue to the correct etiologic diagnosis.

In those cases of pronounced limitation of ocular motility, ptosis is invariably severe and bilateral. These cases of myasthenic ophthalmoplegia exhibit a pronounced resistance to improvement when prostigmin is administered. While the ptosis is invariably improved by prostigmin, the extraocular muscle palsy improves slightly, if at all. It is possible that, in such cases of almost complete external ophthalmoplegia, permanent structural changes may have occurred.

The most constantly observed defect in proved cases is the presence of convergence insufficiency. Mattis[4] coined the terms "drifting phoria" and "transient tropias" to illustrate the variability of deviations when measured by prisms.

The variability is due to fatigue and prevents accurate measurements. Once the deviations are corrected by prisms, active deductions are no longer needed, recovery from fatigue occurs, and reversals from exophoria to esophoria or visa versa occur.

Prosis .

This may vary from complete to mild ptosis and increases rapidly on successive attempts on looking upward. After repeated attempts at elevating the lids, the ptosis becomes more marked. Characteristically, the ptosis becomes most marked when the patient is fatigued. It is, therefore, most marked at the end of the day and minimal on arising in the morning.

Lid retraction in one eye associated with ptosis in the fellow eye has been described by Walsh.[7] This is regarded as evidence that the smooth muscle fibers of the upper lid are not involved in myasthenia gravis. Walsh describes cases of abnormal movements of the upper lid associated with ocular rotations similar to cases of regeneration of the third nerve with misdirection of fibers.

The strength of the orbicularis oculi also fails rapidly. Inability to close the eyes tightly is frequently present and increases on repeated squeezing of the lids. Lagophthalmos with exposure keratitis has been reported.

In spite of the imbalance of the acetylcholine mechanism, there are no abnormalities of the pupils or their reactions. There are likewise no changes in accommodative power.

Facial weakness, usually bilateral, is frequently present. This produces a flattening of the face and the so-called myasthenic snarl, since the retractor muscle at the corners of the mouth are more severely affected than the elevators. Weakness of the jaws, soft palate, and pharynx produces difficulties in speech and swallowing.

Weakness of the chest muscles and diaphragm may cause dyspnea and respiratory embarrassment. Weakness of the muscles of the trunk and extremities are frequent. Aside from the weakness there are no focal neurologic signs. Tiring of the knee jerk is said to occur and to recover after a brief rest.

DIAGNOSIS

Electromyographic, electroergographic methods and such other tests as the Jolly reaction can be used to ascertain the state of skeletal muscle function.[8] However, as Moore[9] points out, all these methods are either unsuitable for testing ptosis or require cumbersome and elaborate apparatus. Fortunately, the prostigmin test is much more reliable, simpler, and more practical.

The use of prostigmin for diagnostic purposes has been extensively studied by Viets, Schwab, and Mitchel.[10] This simple test consists of the intramuscular injection of 1.5 mg. of prostigmin methylsulphate plus 0.6 mg. of atropine sulphate to overcome the abdominal cramps. The observation of subjective and objective improvement is observed at 10-minute intervals for one hour.

The test is absolutely diagnostic for myasthenia gravis alone and will not produce

improvement in muscle power in any other disease. No apparatus other than a syringe and needle is needed for the test. The symptoms of myasthenia are intensified by quinine which may be used to substantiate the diagnosis.

TREATMENT

While prostigmin methylsulphate is rapid in its action, its effect is of brief duration. The bromide salt taken orally is more suitable for maintenance therapy and can be taken in 15-mg. tablets. Sufficient tablets are taken to produce a remission and from 3 to 25 tablets may be taken daily.

Viets[10] emphasizes the importance of prescribing adequate amounts of prostigmin ("what is usually called developing a tolerance to the drug is merely an acknowledgment of inadequate dosage"). As a rule, the oral dose is about three times that by injection.

That this therapy is not without danger is indicated by the report by Nielson[11] of a death due to bromidism in a patient taking 16 tablets daily. Other antimyasthenic drugs that may be used in conjunction with prostigmin are potassium chloride, ephedrine sulphate, and quanidine hydrochloride.

While most patients are benefited by increased muscle power, many are still bothered by intermittent diplopia or ptosis. It is not possible to correct the diplopia with prisms because of the extreme variability.

REPORT OF TWO CASES

CASE 1

History. A. M., a 43-year-old Italian woman, was first observed on April 24, 1947. Her presenting complaint was double vision which had been present for one month. There had been one previous episode of double vision 14 years earlier, at which time the patient had been told that she had had a "stroke." With the administration of eye drops, the double vision had subsided in a few weeks. There were no recurrences until the present episode.

No history of fatigue or weakness, or of articulation, mastication, or swallowing difficulties could be elicited. There was no history of temperamentality, hysteria, or emotional upset. She did not complain of discomfort in her neck or chest or of chronic cough or sputum. Her daily work, in a factory, caused no unusual fatigue of the muscles of the extremities.

Her diet had been excessive in carbohydrates. She took no alcohol or tobacco. There had been a weight gain of 100 pounds since a pregnancy 16 years previously. She had had pleurisy 15 years ago, a left mastoidectomy as a child, and a laparotomy for "internal adhesions" at the age of 30 years.

Menstruation had been normal, although the menarche was at the age of 9 years; no symptoms of menopause had yet appeared. The Wassermann reaction had been negative in 1946.

Ocular examination. There was no ptosis and no wrinkling of the brow. The ocular excursions were full with no evident restrictions. There was no weakness of the orbicularis oculi and no undue fatigue on squeezing the lids.

Diplopia was present in the field of the left superior oblique muscle only; there was no diplopia except on looking down to the right. On attempting to chart the diplopia field with the aid of a red filter, it was observed that the diplopia kept increasing as the examination continued.

The patient was allowed to rest and then the diplopia field was reëxamined. The same phenomenon was again observed; namely, increasing separation of images as the testing was prolonged. It was not possible to elicit diplopia in the field of any other ocular muscle even after fatigue.

Slight lid lag was present bilaterally. There was no convergence weakness. Exophthalmometric readings with the Hertl exophthalmometer set at 96 was 12 mm., O.U.

Visual acuity was: R.E., 20/200; L.E., 20/400. A marked degree of compound hyperopic astigmatism was present and the

vision was correctible to 20/25, O.U.

Except for a small corneal scar the anterior segments of the globes were normal. The pupils were round and equal and reacted to light and accommodation.

Examination of the ocular media and fundi revealed no pathologic changes; there were a few opaque nerve fibers on the right nervehead. There were no constrictions or scotomas in the visual field. The intraocular pressure was 22 mm. Hg (Schiøtz), O.U.

General physical examination revealed an obese woman, weighing 230 pounds. There was no abnormal facial expression; she was able to laugh, frown, and wrinkle her forehead with ease. There was no evident impairment of speech, chewing, or swallowing. Gait and station were normal. The deep reflexes were equal and active, and there were no pathologic reflexes. The muscle power was good. There were no abnormalities of superficial or deep sensation.

There was a left mastoid scar. The gums were slightly spongy and the teeth were in need of repair. There was no thyroid enlargement. The lungs were clear. No evidence of enlarged thymus was present. The breasts were large and contained several glandular nodularities. The heart was not enlarged; the sounds were of good quality. A_2 was greater than P_2. The rhythm was regular. Blood pressure was 130/90 mm. Hg.

There was a scar in the right upper quadrant, but there were no abdominal masses or tenderness. On vaginal examination, the fundus was found to be slightly enlarged; there were no adnexal masses. The lower extremities contained many varices but there was no pitting edema.

On fluoroscopy, the lungs were clear and the heart was not enlarged. The basal-metabolism rate was −5 percent. The urine had a specific gravity of 1.024, with a very faint trace of albumin and no glucose; there was an occasional W.B.C. The hemoglobin content was 85 percent (Sahli).

Course. The only positive finding was diplopia due to paresis of the left superior oblique muscle. Diplopia increasing with fatigue was indicative of a myasthenic reaction and prostigmin methylsulfate (1.5 mg.) combined with atropine sulfate (0.6 mg.) was administered subcutaneously.

The diplopia disappeared within five minutes and could no longer be elicited with the aid of fatigue and a red filter. The patient had a sense of strength and well being that had not previously been present. Except for spasm of both masseter muscles, there were no ill effects from the injection.

The patient was placed on an oral maintenance dose of three tablets of prostigmin bromide (15 mg.) daily. There was no diplopia throughout the day and the sense of well being persisted. The effect of one tablet lasted about four hours and then diplopia would appear. The patient was able to regulate the medication herself, depending on the appearance of diplopia.

CASE 2

History. J. C., a 42-year-old Negro, was first observed on May 28, 1947, complaining of double vision. The diplopia had been present since February, 1947. At that time he was employed as a laborer and he attributed his difficulties to exposure to a welder's arc light.

Difficulty in elevating the left upper lid appeared soon after the diplopia and increased rapidly. There had been no difficulties in speech, mastication, or swallowing. No history of weakness or fatigue could be elicited. There was no cough and no respiratory difficulties.

In 1945, a mild craniocerebral trauma was sustained with no postconcussion symptoms. About 10 years ago he had received intravenous and intramuscular injections for "the blood." The Klein reaction was negative in 1946.

Ocular examination. Almost complete ptosis was present in both eyes with only a 3-mm. palpebral fissure present, O.U. (fig. 1). The ptosis increased on successive attempts at looking up. Compensatory wrin-

kling of the brow was marked and the patient walked around with his head thrown back. The power of the orbicularis oculi was extremely poor and diminished rapidly on forced closure of the lids.

All movements of both eyes were considerably diminished and the eyeballs could not be rotated beyond 15 degrees from fixation. There was almost complete paralysis of

Fig. 1 (Lisman). *Case 2.* After repeated attempts at elevating the lids, almost complete ptosis was present.

every extraocular muscle, as well as inability to rotate the eyes conjugately. The oculocephalic reflex (Bielschowsky phenomenon) produced no increase in motility. Complete paralysis of convergence was present. Diplopia was present in all cardinal fields of gaze and could not be mapped because of the extreme variability.

Visual acuity was: 20/200, O.U., correctible to only 20/40. There were no abnormalities of the conjunctiva or corneas. The pupils were small, equal, and regular and reacted very sluggishly to light and for near.

Study of the ocular media and fundi revealed the presence of a recent retinal exudate just nasal to the optic disc in the right eye. The intraocular pressure was 22 mm. Hg (Schiøtz), O.U. The visual fields were tubular and constricted to 15 degrees with various sizes of test objects.

General physical examination. Examination revealed a well-developed, adequately nourished adult Negro. The head was sym-

metrical and ausculation was negative. There were no difficulties in speech, mastication, or swallowing. The jaw opened in the midline. Air conduction was equal bilaterally and the Weber test was properly lateralized. The uvula elevated in the midline and the tongue was without tremor or deviation. The tonsils were markedly enlarged.

Grips were good and equal bilaterally. There was no drift or tremor of the extended hands. The finger-to-nose test was well performed.

The abdominal reflexes were equally active in all quadrants. The reflexes of the upper and lower extremities were present and equal bilaterally. There was no Babinski reaction. Vibratory stimulus was appreciated and there was no disturbance in position sense.

Gait and station were normal. A complete left hemisensory syndrome was present with loss of superficial and deep sensibilities sharply delineated by the midline.

The chest was clear. There was no cardiac enlargement, the sounds were of good quality. Blood pressure was 120/70 mm. Hg. The urine examination revealed a specific gravity of 1.014 without cells or albumin. Skull X-ray examination revealed no abnormal findings. The blood Wassermann reaction was negative. The spinal fluid was clear under normal pressure, and there were no cells or increased protein.

Course. The patient was given an intramuscular injection of 1.5 mg. of prostigmin methylsulfate and 0.6 mg. of atropine sulphate. Within 10 minutes there was marked improvement in the ptosis, increased power of the orbicularis oculi and enormous increase in ocular motility.

The ocular excursions were improved but not normal and diplopia still persisted in all fields. The patient stated that he felt much stronger and full of vigor.

The tubular visual fields and the hemisensory syndrome were considered manifestations of hysterical superimposition. The patient was a shiftless, unreliable individual who disappeared from observation before

maintenance doses of prostigmin could be determined.

COMMENT

The subjective and objective manifestations of muscular weakness in these two cases were limited to the eyes alone. The response to prostigmin was diagnostic of myasthenia gravis.

If the first episode of diplopia is accepted as the first symptom in Case 1, the disease had probably been present for at least 14 years. During all this time no other evidence of muscular weakness had appeared. The disease was mild and the remission complete.

In Case 2, the manifestations of muscular weakness were likewise localized strictly to the eyes. The disease was rapidly progressive and there was a remarkable resemblance to complete external ophthalmoplegia of supranuclear origin. Indeed, the picture was puzzling until the diagnostic injection of prostigmin.

This is the type of case that responds poorly to prostigmin. The ptosis is invariably improved but it is almost impossible to induce a complete remission of the diplopia and the possibility of permanent muscular changes must be considered. There was no response to doses of prostigmin less than 1.5 mg.

These two cases illustrate the marked improvement in muscle tone and general well being after prostigmin is administered to patients who previously had no complaints and manifested no evidence of fatigue.

The ocular manifestations of myasthenia may herald the onset of the disease which rapidly spreads to involve the muscles of the trunk and extremities. On the other hand the disease may be mild as in Case 1, with a remission lasting for many years and then becoming manifest by paresis of only one of the extraocular muscles.

It is interesting to speculate as to how many cases of "functional" diplopia, transient convergence weakness, and mild transitory ptosis are really early cases of myasthenia gravis.

SUMMARY

1. Two cases of myasthenia gravis are presented.

2. The diagnosis was not apparent until after the injection of prostigmin.

3. The signs are localized to the eyes alone.

4. The muscular weakness was confined to only one of the extraocular muscles in Case 1. In Case 2, the appearance was that of a complete external ophthalmoplegia.

654 Madison Avenue (19).

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NOTES, CASES, INSTRUMENTS

DIGITOXIN INTOXICATION

RESULTING IN RETROBULBAR OPTIC NEURITIS

PETER SYKOWSKI, M.D.
Schenectady, New York

Digitalis intoxication, as an etiologic factor in the production of retrobulbar optic neuritis, has been reported by Wagener and others.[1] Theirs was the first case to be published in ophthalmic literature. Another instance of retrobulbar optic neuritis, resulting, however, from digitoxin therapy, is being presented.

REPORT OF CASE

History. An optometrist referred a 47-year-old white man in no acute distress but with the presenting complaint of blurriness of vision in both eyes. Four weeks previously, severe right- and left-sided cardiac decompensation had occurred. For this, therapy with digitoxin (0.2 mg.) was initiated, the frequency of dosage administered being one tablet, three times daily for one week; thereafter, one tablet, twice daily.

During the first two weeks of therapy, there were no complaints. With the onset of the third week, fogginess of vision and inability to read suddenly came on, the diminished visual acuity being pronounced during the day but, in contrast, becoming slightly improved with the approach of dusk.

At no time were there present any general toxic symptoms. The earliest effects of digitalis overdosage—anorexia, nausea, and vomiting—were absent. There was no headache, fatigue, malaise, drowsiness, or delirium. Alterations in cardiac rate and rhythm did not occur. Neither was there any diarrhea, abdominal discomfort, nor pain. Significantly, chromatopsia was absent.

Eye examination. At the time of the ocular examination, a total of 5.4 mg. of digitoxin had been used. Uncorrected visual acuity in the right eye was 20/200, and in the left eye, 20/200—1. Corrected vision was: R.E., 20/100—2; L.E., 20/100—1. Externally, there was present in both eyes 4.5-mm. mydriasis with very sluggish reaction to light and with the contraction not being maintained in continued bright light. Biomicroscopic and ophthalmoscopic examinations were essentially normal.

Under reduced illumination the central visual fields at a distance of one meter revealed the following: (1) Slight enlargement of the cecal areas; (2) pericentral scotomas with a 1-mm. white test object—5 degrees in the right eye and 10 degrees in the left eye; (3) denser pericentral scotomas within each scotoma with a 2-mm. white test object—3 degrees in the right eye and 5 degrees in the left eye.

Treatment and course. Thiamine chloride (20 mg., 3 times daily) was immediately prescribed. The seriousness of the patient's cardiac condition did not warrant discontinuance of digitoxin therapy. After 10 more days of the same dosage, digitoxin was reduced to one tablet per day. On the 4th day of reduced digitoxin therapy the vision was observed to improve subjectively.

On the 7th day of reduced dosage, the uncorrected vision was: R.E., 20/60—1; L.E., 20/80—1. The right eye had a 4-mm., sluggishly reacting pupil; the left eye a 3.5-mm., promptly reacting pupil. The central fields showed reduction in the size of the pericentral scotomas—in both eyes a 5-degree scotoma with a 1-mm. white test object, and a 2-degree denser scotoma with a 2-mm. white test object.

After four weeks of reduced therapy, uncorrected vision in the right eye was 20/50—1; in the left eye, 20/70. The pupils of both eyes were normal. Further reduction in the pericentral scotomas occurred—with a 1-mm. white test object: R.E., 3 degrees, L.E., 4 degrees; with a 2-mm. white test object: R.E., 0.5 degree, L.E., 1 degree.

At this time, the patient volunteered the observation that, upon arising in the morning, vision was clear, but that, after taking the 0.2 mg. digitoxin tablet, some smokiness of vision would recur and would persist throughout the day.

On the 6th and 7th weeks of reduced dosage, the 2-mm. and 1-mm. white test object pericentral scotomas remained approximately the same in circumference. Corrected vision was: O.U., 20/30.

During the 9th week, when digitoxin was not used for a 3-day period, there was complete absence of "smokiness." Corrected vision was 20/25 in both eyes, and the pericentral scotomas were the same in size.

DISCUSSION AND COMMENT

This case presents the problem of digitoxin in ophthalmic toxicology. Hermann and others[2] reported that digitalis poisoning had been more frequent in recent years. This was ascribed to the more generally active and stable commercial preparations and the confusion concerning the activity of the highly potent glucoside preparations now available. Of the glucosides, digitoxin seems to remain active the longest and hence is the most likely to be concerned in cumulative poisoning.

A comparison between digitoxin and digitalis should be of interest to an ophthalmologist. According to Gold and others,[3, 4] digitoxin possesses the action and uses of digitalis with the advantages of complete and more rapid absorption from the gastrointestinal tract, almost complete lack of gastric irritation, and the uniformity of potency characteristic of a pure or almost pure crystalline substance.

Its complete and rapid absorption from the tract and the infrequency of gastric irritation enables the physician to give the full digitalizing dose (about 1.2 mg.) at one time orally and to produce the full digitalis effect in 6 to 8 hours after its ingestion.

Digitalis powder or tincture has, in contrast, incomplete, slow, and variable absorption, local gastric irritation preventing the administration of the full amount in a single dose, a potency 1,000 times less than digitoxin, and the ability to produce full digitalization in 24 to 48 hours. The cumulation and elimination of digitoxin is similar to that of digitalis powder. It is likely, therefore, that the old type digitalis powder and tincture preparations, being less potent, have not figured prominently in ophthalmic toxicology in the past.

Digitoxin has a selective affinity not only for the vagi, the sino-auricular, and auriculoventricular conduction systems, but also, as noted by Wagener, the papillomacular bundle. Through this selective papillomacular bundle affinity, it causes a bilateral central or centrocecal scotoma. (I have had one case in which a centrocecal scotoma was present.) The possibility of direct damage to the optic nerves secondary to generalized systemic intoxication was postulated by Wagener. The mode of action is problematical, however, and may be either neurotoxic or vasotoxic. If vasotoxic, vasoconstriction and thereby secondary neurogenic degeneration through nutritional deficiency may explain the nerve damage. The experiments of Danielopolu[5] suggest a possible mechanism of action in the accumulation of acetylcholine through the inactivating action of digitalis on cholinesterase.

SUMMARY

A case of retrobulbar optic neuritis resulting from digitoxin intoxication is presented. The case is unusual because the only presenting symptom of digitoxin intoxication was that of blurriness of vision.

Since digitoxin is almost completely absorbed and produces almost no gastric irritation, nausea is rare. It is likely, therefore, that a central scotoma may be the early sign of digitoxin poisoning. That thiamine chloride may be of value in the therapy of digitoxin retrobulbar optic neuritis is suggested by the progress of the case presented.

1330 Union Street.

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CYSTICERCUS OF THE VITREOUS

WILBER F. SWETT, M.D.
San Francisco, California

A Mexican man, aged 21 years, working as a section laborer, arrived at the hospital with a diagnosis of traumatic retinal detachment of the right eye.

REPORT OF AN UNUSUAL CASE

History. On April 18, 1945, while the patient was working with a pick on a track section he struck a large rock and a piece flew up and struck his right eye causing severe pain and immediate loss of vision. He was taken to a local physician who found only a small superficial abrasion and limited ecchymosis of the right upper lid. He was told that there was no foreign body in his lid or eye and that he could return to duty, but he found the eye too painful to continue work and returned for further examination and treatment. He was sent to a local ophthalmologist who sent him to San Francisco with a diagnosis of traumatic retinal detachment.

Eye examination. He was first seen in the eye clinic on April 23, 1945, five days after his alleged injury. The vision at this time was: R.E., light perception; L.E., 20/20+.

The right upper lid showed evidence of a slight abrasion with some edema and a little discoloration. The pupil had been dilated with atropine and an examination showed a dark-gray floating detachment which hung down so far that the disc could just be seen.

The peripheral fundus below appeared normal. This confirmed the entrance examination of traumatic retinal detachment. However, no tear could be seen which made us suspicious that it might be a neoplasm or cyst. Transillumination was completely negative in several succeeding examinations. No tear could be located.

The patient's eyes were bandaged and he was kept flat in bed with limited fluid intake and sedatives in an effort to reduce the size of the detachment and find a retinal hole.

Physical examination. The blood showed a normal red count with 100-percent hemoglobin; a white count with 7,000 leukocytes, 62-percent neutrophiles, 22-percent lymphocytes, 8-percent monocytes, and 8-percent eosinophiles. The urine examination and Kolmer and Kahn tests were negative. A stool examination showed Endamoeba coli, Iodamoeba buetschlii, and blastocytes. No ova or segments were seen.

Course. On May 1st and 2nd, during the time he was flat in bed to reduce the detachment, the patient developed a severe headache over the right eye with nausea and vomiting. Examination of the eye showed no change, the detachment seemed to be smaller, the tension normal, but no tear could be located.

Unfortunately, the first material vomited was not examined, but gross examination of the succeeding attacks showed no segments or section of worm or anything to arouse our suspicions as to the presence of a cestode.

There were no further headaches or nausea after May 2nd. Since the retinal condition remained unchanged and no disinsertion or tear could be located, it was decided

to operate on May 27th. Further transillumi-nations disclosed no shadow to indicate a neoplasm and the detachment was floating freely.

Ocular cysticercosis. On May 26th, much to our astonishment, the retina had parted and in place of the detachment was an 'iridescent cysticercus in the vitreous. The following day the bladderlike worm was very active and its movements were most interesting.

It provided us with a clear picture of the true movements and activity of the head and suckers. We discovered that each sucker contained an extensible tubule not mentioned in any descriptions in the textbooks. These tubules were extended and retracted periodi-cally in addition to circular searching move-ments.

The scolex was hard to locate because the ring of hooklets on the rostellum could not be seen at this stage. This led us to believe it was some species of unarmed Taenia. The hooklets were only discovered by micro-

Fig. 2 (Swett). The rostellum. The spaces are due to folding in the neck.

scopic examination following enucleation. The movements were so active that, although several attempts were made to photograph the Taenia, it could not be kept in proper focus.

On June 1st, the distantly seen scolex was directed down and backward into the vitre-ous, but on June 2nd infiltration of the cyst was beginning and the inactive Taenia inside the bladder was only indistinctly seen. By June 4th, the scolex was again down in the vitreous and very active. The base of the Taenia was infiltrated and not well seen, and we still could not differentiate the or-ganism.

The increasing infiltration made it pro-gressively harder to see any details, but the aqueous, lens, and cornea were still clear on June 6th. On June 8th, the scolex extended down into the vitreous and was well seen and moving actively.

The continued study of the suckers showed the interesting phenomenon not re-ported in the literature. The scolex was quad-

Fig. 1 (Swett). The entire cyst. The pseudo-podlike structures are due to shrinkage and loss of fluid from the cyst.

rate in shape with four cupped suctorial pockets. The rostellum appeared dome shaped, but the double row of hooklets could not be seen when viewed with an ophthalmoscope.

The four suckers were moderately protuberant and from each, while active, extended a very fine, transparent, 6- or 8-segmented, truncated tubule. As each tubule was extended it acted like a hollow, tubular

tration of the vitreous surrounding the cysticercus, no further details could be seen. The eye was enucleated.

The microphotographs show sections through the scolex demonstrating the double row of hooklets which were at no time visible during our interesting observations and finally proved the cysticercus to be Taenia solium.

Microscopic study. A study of the sections
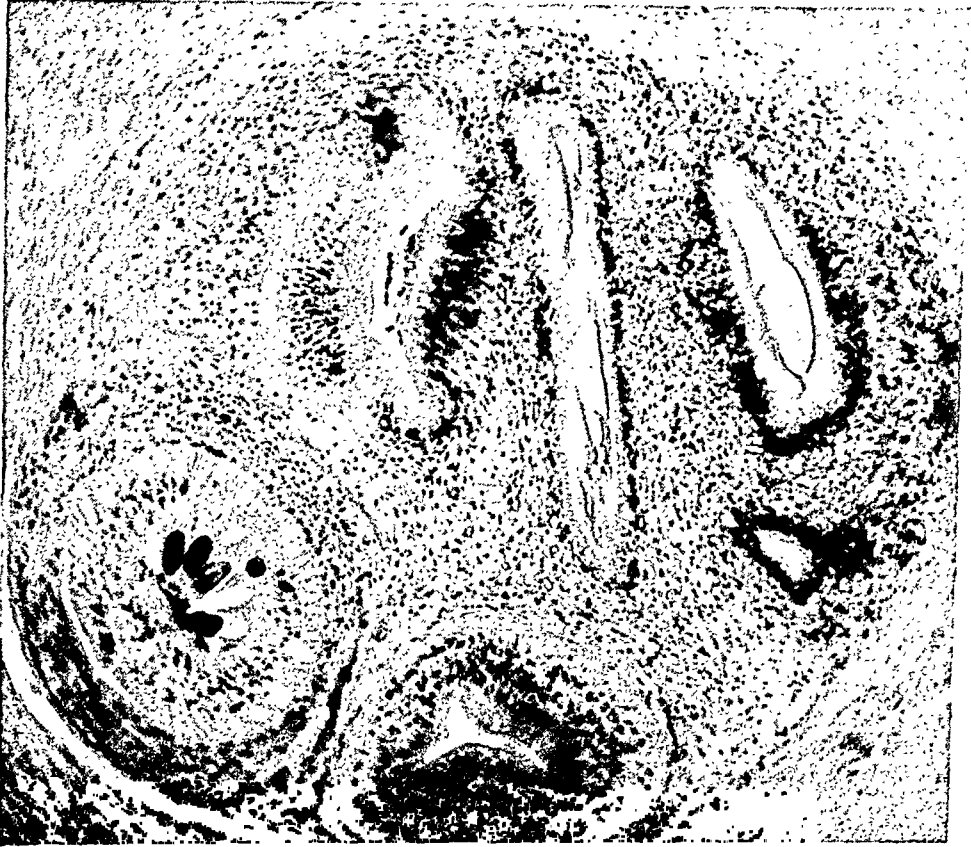
Fig. 3 (Swett). Rostellum with hooklets and two suckers. The other spaces are due to folding in the neck.

feeler, moving slightly this way or that, as the scolex moved to and from searching for something to grasp. One or two suckers would seem to thrust out these hollow, segmented open cones, but all four were not observed at any one time. After seeing this phenomenon, however, it is easy to imagine that, with the scolex anchored by the ring of hooklets, all four suckers could be used simultaneously for feeding.

On June 10th the eye was tender and, due to increasing edema of the adnexa and infil-

showed that there was slight vascularization near the edge of Bowman's membrane. The trabeculum contained large pigment-filled phagocytes, but Schlemm's canal appeared to be normal. The anterior chamber was of normal depth and the angle was free. The iris and ciliary body appeared to be normal. The choroid showed surprisingly little change except for several localized areas of chorioretinitis with adhesions firmly uniting the choroid and retina.

The retina was separated by a serofibrin-

Fig. 4 (Swett). Rostellum with double row of hooklets.

ous, fluid that contained many phagocytic cells. The stroma exhibited a diffuse chronic inflammatory process with marked perivascular round-cell infiltration. The stroma showed considerable degeneration throughout, with disintegration of many nuclei and cystic formation in the fiber layers.

The optic nerve showed signs of atrophy with glial replacement of the nerve bundles.

The vitreous at the upper equator near the inner retinal surface showed a cyst of a typical Cysticerus cellulosae. It was enclosed in a space between the vitreous and the retina. Connective-tissue strands were proliferating along the inner vitreous stroma to wall off this space. Sections through the head (scolex) showed four suckers and a rostellum containing a double row of hooklets, large and small.

The cysticercus walls showed no signs of inflammation.

Diagnosis. The diagnosis was Cysticercus cellulosae in the vitreous and chorioretinitis secondary to cysticercus.

COMMENTS

Several visiting doctors from Mexico stated that this condition was fairly common in certain districts in their country and that the loss of an eye was a fairly common complication of Cysticerus cellulosae in the districts where the people indulged in the eating of raw or insufficiently cooked pork.

This patient entered the United States on September 26, 1944, and developed ocular cysticercosis eight months later. As these worms usually develop in about three months, he evidently contracted it in this country, possibly from some infected countryman working in the same section crew.

490 Post Street (2).

SOCIETY PROCEEDINGS

Edited by Donald J. Lyle, M.D.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

April 5, 1948

Dr. Daniel Kravitz, *president*

This meeting, the annual round-table conference, was devoted to the discussion of "Nonsurgical therapy in ophthalmology." Questions were submitted before the meeting and were divided among the following ophthalmologists, who comprised the panel of experts: Dr. Irving H. Leopold, Dr. Parker Heath, Dr. Ludwig von Sallmann, and Dr. Derrick Vail. Dr. Daniel Kravitz acted as moderator.

Most desirable properties of an ophthalmic drug

Dr. Parker Heath replied that of first importance is effective concentration of the medicament at the suitable point of action. Certain specific characteristics favor the ideal of the proper concentration at the proper point. Some of these characteristics are: the pH range, which should be between 7.0 and 7.6 to avoid dilution of the drug and some stinging and pain sensation from its use. Some drugs actually work better when there is some irritation accompanied by vasodilation, but, in general, any irritation may cause tearing and dilution.

The isotonicity should be within the range of 1.0- to 1.4-percent sodium-chloride solution, the higher percentage being equivalent to the isotonicity of tears, namely 1.32 to 1.427. The isotonicity is usually determined by the freezing point.

The optimum gravity for ophthalmic solutions lies between 1.004 to 1.005. While it is not clearly understood just what part this factor plays, and the range is quite wide, experience has shown the above to be true.

The penetration of some ophthalmic solutions is dependent upon their containing wetting agents. If the substance is to attack the anterior-chamber zone, the medicament should be capable of penetrating the cornea, and this may be aided by a wetting agent, although the medicament must be compatible to the wetting agent.

Another factor besides stability of some significance in ophthalmic drugs is the vehicle used, whether it should be aqueous solution, oily solution, emulsion, ointment, stick, disc, or powder. Another consideration to be had is that of accompanying drugs, such as local anesthesia plus a decongestive; local anesthesia plus an antibiotic, such as penicillin; or other multiple functioning substances or vehicles used with the major desired therapeutic agent.

In aqueous solutions, because of their liability of winking out or passage through the tear channels, multiple dosage is usually employed, or one may put the medicine in an ointment, or, better still, an emulsion which drags it over the cornea with winking. Also, these two vehicles do block the drainage canal and keep the medicament in contact with the cornea longer.

Most of the effective absorption pertaining to the eye is through the cornea, epithelium, and stroma, although there may be considerable absorption through the conjunctiva carried away from the eye by the blood. To avoid further multiple dosage one may use a disc of gelatin or similar substance containing a higher concentration than that obtained in an aqueous solution.

Another principle involved is the use of drugs as teams, which is known as synergism. An example of this would be dilatation of the pupil realized from homatropine plus cocaine. So, the ideal result to be obtained may require multiple medicaments.

Another approach to the use of medicaments is to presensitize the eye by means of heat or by drugs which scuff up the surface of the cornea, such as cocaine, to permit

further penetration through the epithelial barrier. There must also be a balance in the polarity so that the epithelium and the stroma will not prevent the ingress of the substance.

Some substances are effective in mild dosage and destructive or irritative in heavy concentration. The knowledge of the concentration is to be had from experimental studies and samples of the tissue and the aqueous, and noting the effect of the chemical used.

An ideal vehicle for ophthalmic drugs is one which is self-sterilizing to overcome the inevitable contamination from frequent use. This requires a substance, usually one of the benzoic esters, in weak enough concentrations to have no effect on the medicament or produce undue irritation. Another method of avoiding contamination is by the use of individual pipettes for each dose used.

CRITERIA FOR THE USE OF D.F.P.

DR. IRVING LEOPOLD said the interest in the fluorophosphates was stimulated in World War II by information obtained from war prisoners indicating that Germany had prepared quantities of an alkyl derivative of fluorophosphoric acid for possible use as a war gas. It was probably the nerve poison about which rumors were current at the time. Earlier, dimethyl and di-ethyl fluorophosphate had been prepared by Lange and Von Krueger in Germany.

Investigation of the fluorophosphates was initiated in England. A series of alkyl derivatives was prepared and their toxicity to various species of animals studied. A striking feature of their action was an intense, long-lasting constriction of the pupil, and this suggested an action similar to that of physostigmine or cholinesterase. Studies by Mackworth showed this to be the case. Not only was the cholinesterase more sensitive to di-isopropyl fluorophosphate than to physostigmine but the action was more prolonged; indeed it was impossible to obtain any evidence of reversal by the methods effective for physostigmine.

Following the British work, detailed studies were undertaken and carried out in this country through the chemical warfare service, and it is now accepted that the only definite pharmacologic effects of D.F.P. are those related to its inhibitory action on cholinesterase. Thus, the pharmacologic effects of D.F.P. closely resemble those of physostigmine, but the D.F.P. esterase combination is an irreversible one.

Because of these properties of D.F.P., but chiefly because of its great length of action, studies were attempted to evaluate its therapeutic effect in glaucoma. The initial studies, reported in 1946, in glaucoma revealed that this drug could lower intraocular pressure and that its length of action was greater than any previously employed miotic. In addition, these early studies suggested that D.F.P. could be effective in some glaucomatous eyes where other miotics in usually recommended concentrations had failed. The initial report dealt with 56 patients or 78 eyes.

Since the initial report, many ophthalmologists have tried D.F.P. but only a few have reported to date. McDonald confirmed the initial findings in a series of 122 glaucomatous eyes. Lebensohn has also reported favorably. Mare obtained the poorest results, finding that only 1 out of every 6 glaucomatous eyes that could not be controlled with other miotics could be held by D.F.P. four months or longer. Dunphy reported at the College of Physicians in Philadelphia last month that D.F.P. was successful in approximately 1 out of every 3 eyes that failed to respond to other miotics. To date our initial series has been enlarged to over 250 eyes and the period of observation now extends over three years.

Several interesting facts have emerged from this study. D.F.P. does cause some untoward and undesirable effects. The drug produces considerable ciliary spasm, false myopia, and associated ocular pain and brow ache in some patients. A few individuals develop cutaneous sensitivity to the peanut oil vehicle and one patient in this series developed cutaneous sensitivity to D.F.P.

Some eyes show an increase in tension after instillation of D.F.P. This has been observed in narrow-angle glaucoma and in glaucoma secondary to uveitis. One case of retinal detachment in a high myope has been ascribed to this drug but it has not been observed in our series nor has Dr. Dunphy encountered it in his group.

Certain recommendations for the use of D.F.P. can be made from this study. It is effective in mild, early chronic simple glaucoma in concentrations as low as 0.01 percent but best results are obtained with concentrations of 0.025 to 0.1 percent in peanut oil. Mineral oil can be used successfully as a vehicle for eyes sensitized to peanut oil. However, it often allows the D.F.P. to come out of solution and must be watched.

In this study, D.F.P. has been reserved for use in those cases of chronic simple glaucoma which do not respond to pilocarpine in 1- to 6-percent concentrations; to 2-percent pilocarpine combined with 0.5-percent eserine; to 20-percent mecholyl and neostigmine; or to 5-percent or 10-percent furmethide. However, it can be safely employed in mild cases of chronic simple glaucoma that respond to other miotics. Fewer instillations of D.F.P. will be required than with other miotics and the diurnal fluctuations in tension will be reduced because of D.F.P.'s greater length factors.

In narrow-angle glaucoma, it will control tension, but no patient with this type is ever given D.F.P. without observing the initial tension response for at least two hours after instillation. If no rise has occurred, D.F.P. may be continued and the frequency of instillation regulated by daily tension curves. It is usually safe to start with 0.05-percent D.F.P. and, if this lowers the tension but ciliary spasm is very bothersome, it is advisable to drop to 0.025-percent D.F.P. which usually produces less spasm. If 0.05-percent D.F.P. is unsuccessful but has not resulted in rise in tension, 0.1-percent D.F.P. may be tried.

Since the tension rise may be due to the vasodilation produced by D.F.P., it may be advisable to use a vasoconstrictor such as neosynephrin solution or epinephrine bitartrate (2-percent ointment) along with D.F.P., as suggested by the clinical studies of Sugar and the experimental work of von Sallmann.

At present, there is no known reason why, on rare occasions, a case of narrow-angle glaucoma shows a rise in tension and in other eyes with narrow angles, the tension is controlled. So far it has not been correlated with the extent of the synechias.

A number of patients with chronic simple glaucoma have been carried on D.F.P. for 2 to 2½ years, but some have developed a tolerance to D.F.P. after being successfully controlled for many months.

In aphakic glaucoma, D.F.P. in 0.05-percent concentration is the drug of choice provided the aphakic glaucoma is not due to vitreous block, as described by Chandler. Again, the initial treatment should be with 0.05-percent D.F.P. going to higher concentrations if the first proves unsuccessful but does not elevate the tension. It is interesting to note that few aphakic patients are bothered by ciliary spasm. Dr. Leopold said that in his first study he suggested that perhaps intact zonular fibers were required for the production of discomfort. Dunphy recently confirmed the observation and suggested that this might be due to the high concentration of cholinesterase of the exposed vitreous body.

Repeated instillations of 0.1-percent D.F.P. can overcome atropine effects on the pupil. In uveitis, D.F.P. is only used as a last resort. D.F.P. has proved of no value in secondary glaucoma after venous thrombosis. It can be successful in acute glaucoma. D.F.P. should be used prior to eserine but not in the reverse order. Eserine blocks the action of D.F.P., but when eserine is preceded by D.F.P., the resultant effect is greater than either alone.

VALUE OF THE INTRAVITREAL ADMINISTRATION OF PENICILLIN

DR. LUDWIG VON SALLMANN said that

there are two postulates for penicillin therapy which are now generally acknowledged; that is, to start the treatment as early as possible and to obtain at this time a sufficiently high concentration of the antibiotic at the place of the lesion, keeping it there for a sufficient length of time.

It is difficult to observe these rules in infections of the posterior segment of the eye. It takes usually more than 12 hours after an experimental intravitreal infection with pyogenic organisms before alarming signs of the inflammation develop. This is also the case in vitreous infections of man. The phase of logarithmic multiplication of the microörganism in the test tube extends to about 10 hours and, at this time, penicillin is most effective.

Corresponding to the in vitro observation is that of experimental intravitreal infections; they cannot be controlled by any chemotherapy when more than 12 hours have elapsed between infection and treatment. Fortunately, this interval can be extended in human infections of the posterior segment to 24 hours or even longer, as clinical experience shows. The smaller inoculum and the early activation of the cellular defense mechanism are probably the cause of this difference.

The second stumbling block for successful penicillin therapy in such infections is the poor accessibility of the focus in the vitreous. It is true that in rabbits an effective penicillin concentration might be obtained by the subconjunctival administration of the drug in a huge dose or, as Leopold has shown, by combining the retrobulbar injection with subsequent iontophoresis placing the proper pole on the eye. However, the difference in the penetrability of the outer coats of the human eye and those of the rabbit's eye creates a factor of great uncertainty, when this experimental technique is applied to clinical infections.

It is impossible to foretell whether the minimal effective drug level will reach in time the infective focus in an individual case and last sufficiently long, and whether the infective organisms have the high susceptibility to penicillin which would, perhaps, justify this method as a logical approach. In view of these unknowns there remains only one way of handling such infections, and this is the direct injection of crystalline penicillin into the vitreous.

The recommendations of such a treatment depends on the fulfillment of two premises: (1) That the trauma of the injection does not imperil the value of the treatment, and (2) that the preparation has no toxic properties which could endanger the retina, optic nerve, or other structures.

The use of a very fine needle of 27 to 30 gauge and the selection of an area close to the ora serrata for the insertion of the needle reduces the danger of trauma to a minimum. The second prerequisite, that is, lack of toxic action was extensively investigated in the Knapp Laboratory for several brands of commercial penicillin and for the four species of penicillin.

It can be concluded from the table that damage to the retina was absent or minimal when a commercial crystalline penicillin was introduced up to the extremely high dose of 5,000 Oxford units. The pure penicillins, J, F, and X, were also well tolerated, except for small circumscribed lesions, when higher concentrations were used.

On the other hand, penicillin K caused extensive edema and hemorrhages in broad sectors of the retina followed by destruction of the retina. Since penicillin K is undesirable in general, the commercial penicillin now available contains only traces of this species.

A great number of eyes were examined after various time intervals and every globe was sectioned serially and studied thoroughly. On the basis of these data it seems a safe procedure to inject intravitreally one or two thousand units of commercial crystalline penicillin in acute infections of this part of the eye.

This may seem an unnecessarily high dose but the experiments confirm the widely accepted opinion that the minimal threshold

dose is close to the optimal dose and that the latter is not less beneficial than much higher concentrations. That is, in experiments with pneumococci and staphylococci, 10 units were as effective as 500 units. Nevertheless, since a higher dose is not injurious it should be preferred, considering the possibility of a low penicillin sensitivity of the infective organism.

TREATMENT OF HERPES ZOSTER OPHTHALMICUS WITH OCULAR COMPLICATIONS

DR. DERRICK VAIL said that the patient with herpes zoster is a very ill individual, suffering severe pain. Bedrest and sedation, therefore, are necessary. Treatment is both general and local. Whole blood (250 to 450 cc.) should be transfused, from a patient who has had herpes zoster within 6 to 18 months.

While there is some dispute as to the value of iodide, Dr. Vail felt that it could do no harm and he also felt that 100 mg. of thiamine chloride intravenously is also valuable. Obstetrical pituitrin (0.5 cc.) repeated within 48 hours, is useful in some cases for the control of pain. Care must be taken, however, not to use this treatment on patients with any cardiac complication.

If the patient is seen early in the disease, X-ray treatment directed at the gasserian ganglion on the affected side is reported to be very beneficial, particularly in so far as pain is concerned. Robert advises 75r., 2 or 3 applications within 2 weeks.

The use of smallpox vaccine and autoserum is of doubtful value in these cases. Perhaps the most valuable single treatment, from a general viewpoint, is the use of convalescent blood as advocated by Gundersen. Fever therapy is not advised.

As far as local treatment is concerned, during the vesicular stage, the lids can be treated with a solution of 0.5-percent aluminum subacetate in the form of continuous compresses. In the pustular stage, constant application of zinc-oxide ointment or the application of calamine carbolic lotion is helpful.

All patients with corneal involvement will show iritis, frequently accompanied by secondary glaucoma. The latter must be looked for in every case. The iritis is treated with atropine, hot compresses, and so on and, if glaucoma ensues, paracentesis of the anterior chamber should be performed, and repeated if necessary. Neosynephrin solution (10 percent) is very useful in this circumstance, and atropine must be continued right along.

If corneal lesions are present, they should be treated with cocainization, sterilization with strong iodine solution which is neutralized with more cocaine. It may be necessary to perform a delimiting keratotomy. For severe ocular pain, retrobulbar injections of 0.5 cc. of novocaine, followed immediately with the injections of 0.5 to 1 cc. of 40-percent ethyl alcohol, is exceedingly efficacious.

USES OF NEOSYNEPHRIN IN OPHTHALMOLOGY

DR. PARKER HEATH said that clinically it is used as a decongestive, as in mild conjunctivitis, ⅛ of 1-percent solution, or in connection with other drugs ⅛ to 1 percent. To produce a substantial decongestion one may use a 10-percent emulsion or solution.

It may be used as a mydriatic for the purpose of examining the fundus (2.5-percent); freeing adhesions of the iris to the cornea (10-percent); in refraction, especially in presbyopia and myopia in order to obtain objective measurements.

It may be used as an aid to cycloplegia when the iris does not dilate by ordinary means. It may be used to overcome severe myosis in glaucoma where it is used with miotics in concentrations of ⅛ percent on upwards. It may be used to dilate the pupil prior to intraocular surgery. In this it is valuable since it permits early and easy reduction postoperatively by use of a miotic. This drug may be used as a provocative test for glaucoma for determining angle block. It also may be used to supplement a mydriatic when there is sensitivity to the mydriatic used.

A very valuable use of neosynephrin

is in infiltration anesthesia, both for major and minor surgery. Here it has a decongestive, prolonged-action effect, causes slower absorption and is antispasmodic, and, best of all, there are few or no side reactions. The best preparation for this is 1-percent solution, sterile, used in proportion of from 2 to 3 drops to 2 cc. of the anesthesia, in concentrations of 1:3,333 or 1:2,000. Neosynpehrin has also been used in connection with allergy, with cold packs. It has also been of value as a hemodynamic, where it is used in shock dosage, 5 to 10 mg. subcutaneously, or 3 mg. intravenously.

INDICATIONS FOR THE USE AND MODES OF ADMINISTRATION OF STREPTOMYCIN

Dr. IRVING LEOPOLD said that in order for streptomycin to be successful, the infectious agent must be susceptible to streptomycin; the drug must reach the infected area in adequate concentration; and the tissue must tolerate the streptomycin.

The common organisms for which streptomycin definitely should be considered are: B. coli, Hemophilus influenza, B. tularensis, B. proteus, B. pyocyaneus, anthrax, and Friedländer's bacillus. The tubercle bacillus may also respond to streptomycin therapy. Of course, many Gram-positive organisms and the gonococcus are responsive to this drug but they also respond to penicillin and for these penicillin should be the first choice. Streptomycin can be used for penicillin-sensitive infections that have not responded to penicillin or in eyes that have developed a sensitivity to penicillin.

Organisms develop resistance to streptomycin quickly. Therefore, it is essential to attack the infection with adequate concentrations early.

Wherever possible the local route of administration of streptomycin should be used in preference to systemic administration. In this way, many of the toxic reactions of streptomycin can be avoided. The most important and commonest toxic reaction encountered with streptomycin therapy has been interference with vestibular function.

This is probably due to damage to the central nervous system nuclei of the eighth cranial nerve. The auditory branch of the eighth cranial nerve also may be affected, although this occurs less frequently. Neutropenia or agranulocytosis, renal dysfunction, and generalized skin eruptions can develop from systemic streptomycin. The chief dangers of local administration are local tissue reactions and local allergic dermatitis.

According to experimental penetration studies, streptomycin does not penetrate the normal cornea when applied in drop or ointment form. However, adequate corneal levels can be obtained by corneal baths, iontophoresis, cotton packs, and by use of wetting agents. The concentrations obtained in the cornea are much higher when the corneal surface is ulcerated or the cornea itself inflamed.

Solutions of streptomycin hydrochloride or calcium chloride containing 10,000 to 20,000 micrograms per cc. of distilled water are satisfactory for conjunctival infections. This concentration does not inhibit corneal epithelial regeneration. A schedule of instillation every 30 minutes for 3 hours, then hourly until bedtime, can be employed. The treatment interval at night can be lengthened to every 4 hours, and a 2-hour schedule adopted the next day. An ointment containing 10,000 micrograms per unit of base can be used at night. Treatment should be continued for 48 hours after all signs of infection have cleared. Be on the watch for local cutaneous sensitivity; if it appears, stop the treatment.

Corneal ulcers due to streptomycin sensitive organisms can be treated with cotton packs three times daily containing 20,000 micrograms/cc. at 8-hour intervals, corneal baths with the same strength solution, 3 times daily, or by iontophoresis with 5,000 micrograms/cc.

Iontophoresis should be repeated daily. Drops and/or ointment should be used between treatments. Iontophoresis may employ 2 ma. for 2 minutes with the *negative* pole on the neck and the positive pole in

the eye electrode. Occasionally, temporary corneal edema may result from such treatment. The same procedures can be used for anterior-segment infections and, in addition, subconjunctival injection of 50,000 micrograms per 0.1 cc. can be made twice daily using upper and lower halves of globe alternately. Direct anterior-chamber injections have been safely made with 50,000 micrograms per 0.1 cc.

When dealing with intraocular infections, it may be advisable to reënforce local therapy with systemic streptomycin. Systemic dosage should be large initially in an effort to obtain intraocular tissue concentrations. Evidence exists that suggests better therapeutic results with antibiotics when high concentrations are obtained for a short time rather than lower levels for a long time. Four grams daily divided into 4 doses at 6-hour intervals may be tried for 4 days then dropping to 2 gm. daily. If no improvement is noted after 14 days of such therapy, it would seem safer to discontinue systemic treatment. The earliest indication of vestibular or auditory disturbances should be sufficient reason for immediate cessation of systemic treatment.

Dr. Leopold said that he had not seen a case of nonspecific anterior uveitis or of anterior uveitis of so-called tuberculous or brucella origin respond to streptomycin therapy by local or systemic administration.

The work of Grignolo in Italy would indicate some beneficial effect of systemic streptomycin on posterior uveitis due to tuberculosis. He used 2 gm. daily intramuscularly in divided doses every 6 hours but, in addition, also employed promin every 3 hours. Experimentally, he was able to inhibit but not prevent the development of tuberculosis of the anterior segment with systemic streptomycin.

Vitreous infections may be treated with direct intravitreal injections of streptomycin hydrochloride for best results. Five hundred micrograms/cc. can be injected safely into the vitreous. Care must be exercised not to touch the lens. Diathermy puncture may be made about the needle puncture. If the ophthalmologist hesitates about using intravitreal streptomycin, he can try therapy with 50,000 to 100,000 micrograms/cc, anterior-chamber injections of streptomycin or he can inject streptomycin retrobulbarly, applying anterior-segment iontophoresis with the negative pole on the eye electrode. One hundred thousand micrograms in 0.22 cc. to 0.5 cc. can be injected retrobulbarly.

ADVANTAGES AND LIMITATIONS OF IONTOPHORESIS WITH ANTIBIOTICS

DR. LUDWIG VON SALLMANN said that the conservative method of iontophoresis is of interest as a means for obtaining relatively high concentrations of the antibiotics in various eye tissues. Corneal iontophoresis serves the purpose well as far as the anterior segment of the eye is concerned. This has been shown convincingly by several investigators. For example, 40 mg. percent of sulfadiazine and 20 units per cc. of penicillin and, according to Leopold, 70 units of streptomycin were measured in the aqueous humor of rabbits after iontophoretic introduction.

It may be mentioned here that the claims of Hamilton-Paterson, frequently cited in the English literature, that penicillin is a poor conductor and not suited for iontophoresis have been completely disproved by several investigators. The drug level persists high for several hours although the peak of the concentration is reached in about one hour and is followed by a moderately steep disappearance curve. The hypothesis that any method which produces high penicillin levels in the aqueous for this length of time is of definite advantage, is strongly supported by results of in vitro experiments with penicillin. It is shown that a drug concentration of 10 units per cc. is bactericidal on 18-hour staphylococci cultures when the latter is exposed to this concentration of the antibiotic for 4 hours; subcultures of the centrifuged sediment were negative; whereas, lower concentrations of penicillin

did not prevent full growth of such sub-cultures.

The good penetration of penicillin, streptomycin, or sulfonamides into the eye under influence of an electric field with the corneal technique, is almost entirely limited to the anterior chamber, as is the case with other electrolytes. This can be well illustrated by the use of radioactive isotopes (Na 24 and I 131) when one applies a new technique of autoradiography. This method utilizes the photographic action of the radiations emitted from the tracer elements. The autoradiogram depicts the actual distribution of the artificial radio elements in frozen slices of the eye. Sodium is obviously accumulated only in the anterior chamber. It is interesting to see that iodine introduced under the action of an impressed potential is bound predominantly to the structures of the cornea and iris. In aphakic eyes the Na 24 diffuses from the anterior chamber into the vitreous space and here has its beneficial effect.

In a few instances, it was possible to achieve an intense darkening of the film in the area corresponding to the vitreous space of rabbits' eyes with the lens in place. A ring zone between limbus and ora serrata was selected as portal of entry of the current on the eye. However, in other experiments with the same technique the penetration of Na 24 into the vitreous was negligible. Further studies are necessary, therefore, before this technique of iontophoresis can be considered for clinical use.

Another type of iontophoresis (lid iontophoresis) in which the electrode is placed on the closed lid was rather disappointing in numerous experiments. Extracts of the layers of the lids, of conjunctiva, of cornea, and of the aqueous humor of these eyes did not contain much more penicillin or sulfadiazine with the use of the electrical current than with the simple application of wet dressings.

MEDICAL TREATMENT OF CHRONIC SIMPLE GLAUCOMA

DR. DERRICK VAIL said that it is necessary before undertaking medical treatment to classify the case into shallow-chamber or deep-chamber glaucoma. In addition, other factors must be considered. For example, the economic status of the patient, that is to say, whether he is in a position to afford frequent visits for observation of the efficacy of the treatment; whether the distance is too great for frequent trips; whether the patient is intelligent enough to carry out your directions, particularly regarding the technique of instilling the medication; or whether he is likely to prove uncoöperative.

Having decided that a case is suitable for medical treatment, we have at our hand a number of suitable drugs (miotics), the action of each one of which is a little different from the other. It is important to understand these differences in order intelligently to make the best use of the available preparations.

Pilocarpine, for example, acts directly on the iris sphincter fibers, and also has a constricting effect on the iris blood vessels. It, therefore, produces no congestion of the ciliary body, particularly, or of the iris. This is very important, because in the narrow-angle glaucoma, congestion of the ciliary body may increase the shallowness of the angle and make matters worse. D.F.P. has been known to do just this, and a few cases of acute glaucoma have been precipitated by the use of D.F.P.; carcholin (doryl), mecholyl, furmethide, eserine, prostigmine, and D.F.P. all act by destroying the cholinesterase.

As you know, the sphincter of the iris and the ciliary muscle contract by the action of acetylcholine, which is liberated in the ganglion cells and at the myoneural junction of the parasympathetic nerve endings. Acetycholine is constantly being destroyed by cholinesterase (tissue ferment). The formation of too much cholinesterase prevents the normally formed acetylcholine from stimulating the sphincter muscle.

Dr. Leopold has discussed the pharmacology in the action of D.F.P. Dr. Vail said that, in his experience, this drug has been

disappointing. Combining in the same solution, or at the same time, pilocarpine and eserine gives a synergistic action to these drugs, and the effect is enhanced thereby. Similarly, one can combine prostigmine, or D.F.P., with carcholin; 0.75 to 1.5-percent solution of carcholin put into a 1:5,000 zephiran solution is an exceedingly useful drug. A 10-percent solution of mecholyl has been advocated, but it does not, at the moment, seem to be in much favor. A 10-percent solution of furmethide in distilled water is one of the more recent drugs, but it does not seem to be fulfilling our expectations. Furthermore, there is considerable doubt as to its availability.

The weakest solution, or combination of solutions, that will control tension is of great importance. Furthermore, it must not be forgotten that one can use efficiently pilocarpine in solutions that are stronger than 2 percent, even up to 8 percent, without particular injury. Naturally, should the conjunctival sac become sensitive to any of these drugs, it is necessary to switch to another preparation.

Evaluation of the patient as a whole is essential to the treatment of chronic simple glaucoma. It is well known that mental states of imbalance, perturbation, anxiety, grief, fear, rage, irascibility, and so on play a big part in the elevation of intraocular pressure, and attention should be paid to these factors by the physician. The patient's errors of refraction must be corrected and the use of stimulants, such as coffee and tea, should be avoided.

HEAT AND COLD IN OPHTHALMIC DISEASES

DR. PARKER HEATH said that the use of heat is considerably overdone, and the benefits of cold are not usually appreciated. In the use of heat, either by compresses or any other of the usual methods, the pleasing sensations that go with it prolong its use unduly and its frequency of application. It is valuable as a means of treatment and an adjunct to drugs, producing vasodilation, if used for a limited time, not over a week, 3 times a day for 10 minutes each time.

The continued and indiscriminate uses of heat causes the skin to soften and the conjunctiva to become edematous. Sometimes the cornea becomes edematous. The whole globe may acquire a chronic congestion from chronic use of heat.

The methods of applying heat are of some consequence so far as its effectiveness is concerned. Hot, moist heat is the conventional method. Infra-ray heat may be used; deep diathermy; pasteurizing with heated metals; and high-frequency heat. All have their special places, special benefits, and particular usage. Just as with the actual cautery, the thermophore and other methods of applying heat should be used as nearly as possible with precision.

Cold, commonly neglected, is very valuable, particularly postsurgically to reduce tension on the sutures by keeping down the edema, to prevent slippage, to reduce pain, and the use of CO_2 snow is very valuable in certain angiomatous lesions of the lid and may be the method of choice. As a decongestive, cold is still very valuable. It may be applied from an ice cake, using moist compresses; it may be applied by a stream of cold air, or by a CO_2 snow pencil.

PRESENT STATUS OF THE ANTIHISTAMINIC DRUGS IN OPHTHALMOLOGY

DR. IRVING LEOPOLD said that for antihistaminic drugs to be effective in allergic ocular disease, histamine should be released by the allergic condition. This is often a difficult point to prove. Consider the ocular condition of uveitis. This is generally believed to be a manifestation of hypersensitivity. There are anaphylactic and bacterial infections and types of hypersensitivity.

The anaphylactic type is that which results when foreign protein is reintroduced into sensitized tissue. The reaction is characterized by a quick onset after the reintroduction of the foreign protein, by spasmodic contraction of smooth muscle, and by an increase in capillary permeability. This type of

sensitivity can be transferred and is usually accompanied by the presence of specific precipitins in the body fluids.

The bacterial type of hypersensitivity is not characterized by the presence of precipitins in the blood stream and it cannot be passively transferred. It is produced by not only the bacterial bodies but also by soluble bacterial proteins. Bacterial infection type of hypersensitivity is thought to be responsible for the bulk of uveitis. However, the only really suggestive evidence for histamine release is found in the anaphylactic type of reaction. The evidence for the role of histamine in the bacterial type of hypersensitivity is at present very unconvincing. Therefore, if the antihistaminic drugs should have value in uveitis, one would expect to find it in the anaphylactic type of uveitis.

This type of uveitis can be produced experimentally by injecting horse serum into the vitreous and following, 10 days later, with a second injection of horse serum intravenously. A series of rabbits were injected in this manner by Dr. Dean, Dr. Blazar, and Dr. Leopold at the University of Pennsylvania.

One group received intramuscular Pyribenzamine prior to the intoxicating dose of horse serum; another group received Pyribenzamine intramuscularly simultaneously with the intoxicating dose of horse serum; another group received Pyribenzamine 24 hours after the intoxicating dose of horse serum. Subconjunctival injections of a Pyribenzamine solution were made in three groups of rabbits, prior, simultaneously, and after the intravenous dose of horse serum.

The only eyes that were definitely benefited by Pyribenzamine were those that received the drug intramuscularly prior to the intoxicating dose of horse serum. Even repeated intramuscular injections of Pyribenzamine had no significant effect once the uveitis was established.

These preliminary studies indicate that the anaphylactic type of ocular hypersensitivity reaction can be prevented by antihistaminic drugs but cannot be successfully treated once the ophthalmic reaction has been established.

These observations are not very encouraging for uveitis from the therapeutic viewpoint. They possibly may be of some value in suggesting a method of alleviating endophthalmitis phaco-anaphylactica and sympathetic ophthalmia. In both of these instances antihistaminic drugs can be administered prior to the possible onset of the ocular reaction. It may be advisable to give antihistaminic drugs pre- and postoperatively to all cataract extractions, particularly where extracapsular extraction may occur. In ocular injuries, particularly when uveal tract and the lens are injured, it may prove helpful to administer antihistaminic drugs.

IN WHAT CONDITIONS IS BACITRACIN EFFECTIVE?

DR. LUDWIG VON SALLMANN said that information on the usefulness of this compound in ocular infections is scarce. Dr. Bellows has reported briefly on the benefits of local bacitracin therapy in superficial infections of the eye. Dr. Braley used bacitracin therapy in 37 cases of conjunctivitis from which mannitol-positive staphylococci could be cultivated. Frequent instillations of a solution, containing 500 units per cc., extended over 24 hours resulted in negative cultures for a limited period of time. Many of the patients seemed to have benefited from the treatment but no conclusive results were obtained.

The comprehensive data on irritation, penetration, and therapeutic effect in experimental intraocular infections are contained in a study by Dr. Locke of the Eye Institute. He found that concentrations of 5,000 units per cc. produced severe inflammatory response of the lids and conjunctiva and of corneal abrasions when instilled frequently or introduced by the galvanic current. Solutions of 1,000 units per cc. were well tolerated.

Miss B. Johnson, the discoverer of bacitracin, measured 10 units per cc. in the aqueous one hour after iontophoresis of a

solution containing 1,000 units per cc. Despite this high drug level in the aqueous, local bacitracin therapy failed to check experimental infections of the anterior segment of the eye produced by several strains of mannitol-positive staphylococci which had exhibited in vitro an average sensitivity to the drug. This is in clear contrast to results obtained with penicillin or streptomycin.

Systemic use has not been studied in eye diseases, nor were investigations carried out on the transfer of the drug from blood to ocular fluids. To be more specific in predictions concerning the value of this antibiotic on the eye, one has to resort to the clinical results in pyogenic infections of the skin and of surgical wounds and also in syphilitic lesions.

Experience of the Departments of Dermatology and Surgery of the Presbyterian Hospital is excellent in clearing up pyogenic skin infections with bacitracin ointment. Similarly good are the results in surgical infections. The data reported by Dr. Eagle on bacitracin treatment of experimental and clinical syphilis are also promising. It remains to be seen whether there exists a true synergism between penicillin and bacitracin on the bacteria which this author suspects are active in spirochetal infections.

Altogether it seems that infections of the lids, of the conjunctiva, and of the cornea could be controlled by bacitracin possibly as effectively as with penicillin or even better when penicillin-resistant strains are involved. Therefore, bacitracin would permit, in such cases, economy in the use of penicillin, or would supplement it. This is no small advantage if one remembers the continuous increase of the number of penicillin-resistant strains and the frequency of allergic reactions to penicillin or streptomycin.

PROPER HANDLING OF OCULAR TUBERCULOSIS

DR. DERRICK VAIL said that once you have determined that you are dealing with ocular tuberculosis in a given case, the type of lesion present will determine the treatment given. The discussion will, therefore, be limited to cases of uveitis and choroiditis suspected of being tuberculous. In the very acute stage, fever therapy offers our best hope. Typhoid vaccine is the favorite agent, but milk-shots and Coley's serum should not be forgotten. The treatment of tuberculous uveitis is exactly similar to that due to any other etiologic agent; atropine, compresses, paracentesis, and so forth are necessary.

Secondary glaucoma is very frequently present, and must be treated adequately. Autohemic therapy has been advised by a number of authors. However, the plan of replacing the aqueous with blood freshly drawn from the patient is a dangerous and futile step.

Ophthalmologists are the only medical practitioners who are still using tuberculin treatment, and the wisdom of this is not too sure except in cases of sclerosing keratitis, where the response of the lesion to the treatment is sometimes very dramatic. Various forms of tuberculin have been used, but the trend now is to use old tuberculin, and to give the treatment according to the methods described in the various books of ocular therapeutics, beginning, of course, with an exceedingly small dose on patients who show marked skin sensitivity.

It is questionable whether the Mantoux test gives much information that will help in deciding whether a case is tuberculous or not, since it is the experience of most that pathologically proved cases of ocular tuberculosis can be demonstrated in patients who have a negative Mantoux test.

If tuberculin treatment is used, it should be given for a sufficient length of time, often as long as two years, in order to desensitize the patient's skin to the tuberculin. The use of the ultraviolet light treatment locally is no longer advocated, and general treatment with ultraviolet is grossly overrated. Streptomycin and promozol, currently being studied by Dr. Alan C. Woods and the Wilmer Institute group in the treatment of

experimental tuberculosis, offer much more hope for the treatment of human cases.

MEDICAL MANAGEMENT OF CORNEAL DYSTROPHIES

DR. PARKER HEATH said that if one means by corneal dystrophy a local alteration in the metabolism or a local effect from alteration in the metabolism of the body in general, the treatment is apt to be quite different from that for a degenerative process. The so-called corneal degenerations are often not degenerations at all, but active inflammatory lesions, sometimes with minor incidental degenerative changes.

An example of this is lipid interstitial keratitis, which is a storage infiltration disease; a storage of lipids sometimes actively mobilized by cells or by the blood stream or both. The corneal leukomas may follow an overproliferation and repair from a minor primary lesion.

Those lesions requiring purely medical treatment, apart from surgical or mechanical, are certain epithelial and endothelial dystrophies; some forms of band keratitis, wherein the calcium metabolism may be an important factor in the cause; the groups of interstitial keratitis; certain dystrophies associated with the aging process; the so-called neurotrophic group; lesions associated with deficiencies in diet, particularly vitamin A; and the hereditary dystrophies.

For the most part, the best treatment is preventive. It may be palliative, especially if the initial lesion is apparently minor, as a herpes simplex or an abrasion from a cilia or a minute foreign body. In the first instance, the treatment is to eliminate the herpes by pasteurization with heat. In the second instance, the treatment is to remove the foreign body or the lash.

From some minor lesions in a patient who is predisposed there spread across the cornea marked alterations in nutrition with a deposit of foreign material such as fat, calcium, and a proliferation of unwanted fibroblasts. The treatment for the overstorage of fat, by histiocytes or local depots of fat in the cornea, is to put the eye in a state of rest. If uveitis is active, treatment should include the use of atropine or scopolamine, a program of moderate, daily, and sustained exercise, sweats, and thyroid if at all indicated because of low metabolic levels. The use of iodides is indicated from the standpoint of history in therapeutics, and in some cases there is apparently an improvement following their use.

Those dystrophies of endothelium, which produce islands of altered epithelium and some desquamation and staining areas and give the cornea a greasy look in a maplike pattern, ordinarily have a poor prognosis. But the endothelium under certain circumstances, given sufficient time, does regenerate or repair and the bullae subside.

The best local treatment for the bullae is a series of multiple punctures with the actual cautery pushed partly into the stroma, provided it is not in the pupillary zone, and the use of an iodine ointment. Pad the eye to decrease the mechanical irritation and the destructive effect of the upper lid and use a cycloplegic or miotic as indicated.

Scrubbing the epithelium off and applying iodine in these cases may be done once, but often it does not help. The treatment as outlined is much more effective if one has the patience to stay with it.

The nutrition of the cornea is seriously affected, in some instances, by the overgrowth or the ingrowth of blood vessels. When these blood vessels can be reached without too much destruction, it is advisable to scarify or cauterize them.

Those endothelial diseases which produce the aforementioned epithelial changes require treatment over a period of months, sometimes up to two years. Such patients may, with proper treatment, be able to keep their eyes and have a modicum of vision or light perception.

In passing one might mention that some corneal lesions in the dystrophy group, especially with secondary implantation of cal-

cium and fibrous scarring, are best treated by lamellar implants, or through-and-through implant, or simply by partial keratectomy.

USE OF FURMETHIDE IN GLAUCOMA

DR. IRVING LEOPOLD said that clinical investigations with furmethide found it to be more effective in the late stages of acute glaucoma but less effective in the early stages than mecholyl (20 percent) and neostigmine (5 percent). In secondary glaucoma furmethide was found to be about as effective as mecholyl prostigmine. Furmethide has no influence on glaucoma secondary to venous thrombosis. In chronic simple glaucoma, 10-percent furmethide was slightly superior to a 2-percent pilocarpine solution when instilled 3 to 6 times daily.

Furmethide is apparently nonirritating and no cases of sensitivity have been reported. However, it may produce hyperemia of the conjunctival vessels and also narrowing of the anterior chamber. Cases have been reported of moderate perspiration, salivation, and lacrimation after 1 or 2 instillations of the drug. It is certainly an effective miotic. The chief usefulness would seem to be as a substitute for pilocarpine when the individual eye becomes sensitive to pilocarpine.

It can be tried in acute glaucoma in eyes that are sensitive to mecholyl and neostigmine or in which these drugs have not been successful. In chronic simple glaucoma, the drug must be instilled frequently at least 3 to 6 times daily in most cases.

Many patients complain about its taste and, on one occasion, it produced profuse sweating, diarrhea, and almost collapse in a 170-pound man when applied 6 times in 2 hours in an eye with acute glaucoma.

In 20 eyes that have failed to respond to 3-percent pilocarpine, only one showed benefit on subsequent use of furmethide (10 percent) and this was only temporary.

Pilocarpine will continue to be the miotic of choice for most cases of simple glaucoma. It produces few untoward symptoms

such as ciliary spasm, false myopia, or brow ache. It is successful in many cases and has stood the test of time. If low concentrations fail, higher ones can be tried.

Many ophthalmologists feel that any case of chronic simple glaucoma that loses field under pilocarpine therapy should be operated. If stronger drugs are tried with greater effect on the sphincter and ciliary muscles and on the ocular vessels, the patient may suffer undesirable symptoms. But all patients vary in their tolerance to drugs and one cannot always predict which patient will be bothered. Very little will be lost by a short trial period on more potent miotics.

Also, there are cases of patients with one eye in whom the first eye was lost through surgery, patients who refuse surgery, patients in whom operative procedures are inadvisable because of health and age, patients in whom previous surgery has failed, and patients whose tension must be maintained until surgery can be performed.

Even the most ardent supporters of early surgery in glaucoma will, at times, try the stronger miotics. In such cases the newer miotics may prove helpful.

SULFONAMIDES AS THE DRUG OF CHOICE

DR. LUDWIG VON SALLMANN said that from an ophthalmic point of view Bacillus pyocyaneus is the most important member of the group resistant to penicillin but often susceptible to sulfonamides. Its sensitivity to the latter, as well as to streptomycin and bacitracin, varies from strain to strain, which would explain the contradictory reports in the literature. A similar situation may also be encountered in virulent infections belonging to the psittacosis-lymphogranuloma group. The work of Thygeson, Braley, Lindner, and the majority of other investigators provided evidence for the usefulness of sulfonamide therapy in trachoma and inclusion conjunctivitis. To date it has not been proved that penicillin or any other antibiotic surpasses the effect of sulfonamides in trachoma.

Attention must be paid to the properties of the lesion in the treatment of infections for which several suitable drugs are at our disposal. It was recognized at the beginning of sulfonamide therapy that accumulation of products of protein degradation and heavy infections with a paramount number of microörganisms in the lesion either inhibit or influence adversely the action of sulfonamides. However, startling results of sulfonamide therapy were obtained even in purulent intraocular infections with injury of the lens.

On the other hand, there is overwhelming proof that penicillin and also streptomycin therapy is by far more effective in experimental acute intraocular infections induced by the common pyogenic cocci. On the basis of such conclusive experimental data, penicillin or a mixture of penicillin and streptomycin should be selected as the most promising therapeutic weapon.

In chronic and subacute staphylococcic infections of the lid border, conjunctiva, and cornea, Thygeson, Braley, and others describe satisfactory results with sulfonamides. Here in prolonged use, penicillin and streptomycin, although potentially effective, may sensitize the patient to mold products, may elicit allergic reactions, or may render certain bacterial strains drug resistant for many years to come. These disadvantages outweigh a possibly immediate beneficial result. The same criteria applied to sulfonamides lose their sting because the latter are bound to play a less decisive part in emergency therapy of severe infections.

The compatibility of simultaneous systemic or local therapy with some sulfonamides and penicillin or streptomycin has been established for years. Recently Locke found that bacitracin is compatible with some sulfonamides. All this opens a wide field for the use of antibiotic mixtures containing sulfonamides but the question of true synergism between members of the different groups has not yet been settled. Experimental and clinical experience has failed so far to show any preëminence of such combined treatment in infections of the eye.

VASODILATORS IN THE TREATMENT OF RETRO-BULBAR NEURITIS

Dr. Derrick Vail said that there is reason to believe that vasospasm plays considerable part in the eventual injury to the optic-nerve fibers in this mysterious condition. Therefore, any measures that can be taken to dilate the vessels and improve the nutrition seems to be a logical way of beginning to solve the problem. The use of vasodilators has hastened the recovery of useful vision in many patients with retrobulbar neuritis.

There are a number of agents available. Nitroglycerine (1/100 gr.), nicotinic acid (50 mg., 3 times daily), sodium nitrite (1 gr., daily), 10-percent sodium nitrite intravenously (1 cc.), papaverine (1 gr., twice daily), erythrol tetranitrate (¼ to ½ gr., 3 times daily), and typhoid vaccine intravenously are the vasodilators most commonly used.

Of these, typhoid vaccine, as a fever-inducing agent, seems to be the most valuable. Ophthalmologists would be handicapped in the treatment of many inflammatory conditions of the eye and optic nerve without the benefit of typhoid vaccine.

While dicumarol cannot be classified as a vasodilator, its recent use in the treatment of multiple sclerosis by Putman offers new hope in the treatment of that disease, particularly. If 300 mg. of this drug is given daily, it is necessary to check the prothrombin time frequently and, therefore, the treatment had best be carried out in the hospital.

The startling improvement in the vision of a patient suffering from acute retrobulbar optic neuritis that so often follows the opening of the sinuses, particularly the sphenoid, is convincing proof of the value of vasodilators in the treatment of retrobulbar optic neuritis.

Bernard Kronenberg,
Recording Secretary.

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THE MOTOR VEHICLE DRIVER

A driver's license is now mandatory throughout the Union, although Kansas, Missouri, and South Dakota require no examination, visual or otherwise. The latest survey of state requirements for motor vehicle operators—annually published by the American Optical Company—still shows a lamentable diversity in almost every item, although voluntary uniformity is gaining ground as already evidenced by the increasing similarity in signals, signs, and road markers. The eligible age for acquiring a driver's license varies from 18 years in New York, Pennsylvania, and Vermont to 14 years in North Dakota, New Mexico, and South Carolina.

The requirement for corrected visual acuity is 20/20 in South Carolina; 20/60 in Illinois, Nevada, and West Virginia; and 20/70 in Massachusetts and Maryland. The one-eyed driver is accepted everywhere if his seeing eye has a full field and a corrected acuity of 20/20 (Texas, Alabama) to 20/70 (Massachusetts). No state yet tests for night vision or glare resistance. In several states drivers are restricted to daylight hours if their deficient acuity is not adequately cor-

rectible, but the discriminatory level varies from 20/100 in Maryland to 20/70 in Oregon and 20/50 in Pennsylvania.

The total of drivers now licensed in the United States reaches 50 million. Six million are examined annually. Reëxamination for renewal is required only in Colorado, Iowa, and North Carolina. Visual screening tests that will gain official approval must be performed rapidly, with relatively simple and inexpensive apparatus, by lay personnel of limited training. In some states (Minnesota, Florida, and California) the applicant who fails is given a record blank and referred for further investigation to a "visual specialist" (ophthalmologist or optometrist) of his own choice. In Florida, where 20/50 acuity is passing, 15,000 of the 200,000 applicants for driver's license in 1947 were referred for visual examination. Eventually the visual tests for drivers should be as significant for the adult population as the screeening tests in schools are for children.

The Driving Research Laboratory of Iowa State College states that 60 percent of the general adult population require glasses, but only 30 percent are using them, and, of the glasses worn, 30 percent were no longer correct at the time of examination. Uncorrectible poor vision is present in 5 percent. Of 889 truck drivers checked by the U.S. Public Health Service in 1941, only 45 percent had 20/20 acuity in each eye, but just 8 percent were wearing glasses.

The American Association of Motor Vehicle Administrators recommends that the driver's license of those requiring glasses be stamped: "Must wear *corrective* glasses while driving." The word "corrective" is stressed because, otherwise, plain or sunglasses would technically meet the requirement.

Education should emphasize the trifling disadvantages of glasses compared to the signal importance of reading signs and markers easily and quickly. The average stopping distance on dry pavement for a car at 60 miles per hour is about 200 feet, and the average traffic sign can be read at 225 feet if the visual acuity is 20/20. With lesser acuity this distance is, however, reduced proportionately. The reading of signs stimulates both the attention and the visual outlook. A driver is able to perceive an unexpected obstacle only half as far away as he can see an expected one. The National Safety Council would require that glasses be worn, if binocular vision is less than 20/40; but in monocular vision 20/30 is the suggested minimum.

In the past two years America has had the lowest annual mileage death rate in its history but motor vehicle accidents still rate tenth among the leading causes of death. In 1947, the total of traffic deaths in the nation was 32,000, averaging 8.6 deaths per 100 million miles of travel, being about twice as heavy in the rural areas as in the cities. One fifth of the road accidents involved children, being highest in the age group of 5 to 6 years. The lowest mileage death rates— 4.3 and 4.7 per 100 million miles, respectively— were reported in Connecticut and Rhode Island. In both states the minimum acceptable acuity is 20/40.

More important for traffic safety than skillful driving and adequate visual capacity is a sense of social responsibility. Greater pride should be taken in being a safe driver than a fast one. The 16-to-20-years age group is involved in five times as many accidents as those aged between 45 and 50 years. Although it is known that 15 percent of the drivers are responsible for 90 percent of accidents, the factors responsible for accident proneness still require critical evaluation. Deficiencies in dark adaptation, field of vision, eye-hand and eye-foot coördination are all more significant than central visual acuity. The macular vision of accident-prone drivers does not differ from that of the average driver. Many drivers with only 20/200 vision have had no accidents in 20 years of driving. Since most hazards are very large, the perception of contrast is probably of more value than simple acuity.

The American Association of Motor Vehicle Administrators feels that most drivers with substandard vision can be allowed the privilege of doing the kind of driving they are able to do in reasonable safety; and hence, they should be restricted to daylight hours, limited speed, or a certain class of roads.

Rarely is a person so color blind that he cannot distinguish between red and green traffic lights. Besides the brightness difference, the standard position from above down of red, yellow, and green is an additional clue that allows most drivers to overcome their color deficiency. The "red and green" traffic lights are usually yellow-red and blue-green and these yellow and blue components also aid differentiation. In fact the color blind are less confused by the red and green lights than by the red and amber.

To the ophthalmic specialty belongs the task of determining the amount and quality of vision needed to be a safe driver and to improve, simplify, and standardize the screening tests required. For the rating of visual acuity, standardized illumination should be provided, and an unlearnable letter chart, as has been used in the U. S. Navy, is probably more suitable and effective than the Snellen refraction chart now in vogue. Visual field tests may be restricted for the sake of time to the horizontal meridian since that is the angle most important in driving. Simplified tests for night vision and glare resistance are urgently needed.

James E. Lebensohn.

A RUMANIAN EYE JOURNAL

Apart from Norway and Sweden, the European countries bordering on Russia occupy at present a somewhat uncertain position in relation to the civilization of western Europe. The results of the two great world wars have, on the one hand, given them great changes in area and population, and, on the other hand, have made more manifest than ever their natural commercial and cultural ties with Russia, whose communistic ideologies are playing an enormous part in organization and development of these border areas. Yet the latter display strong nationalistic tendencies in which it seems inevitable that western civilization will ultimately have a powerful influence.

Rumania is an especially interesting illustration of these competing influences, with a language distinctly Roman in structure although extensively Slavic in vocabulary, and a people whose originally Slavic dominance was early modified by Roman military colonization. The religion of its people is mainly Greek orthodoxy; its most widely used channel of linguistic contact with the outside world is still the French tongue. In that idiom the reports of Rumanian medical gatherings are most likely to reach the scientific reader of other countries.

Prominent in ophthalmology for very many years has been Nicholas Blatt, active in moves toward improved clinical resources and for the control of blindness. From time to time Blatt's contributions to the literature of ophthalmology reach the United States. Now comes a further example of his enterprise in the form of the first Rumanian journal entirely devoted to ophthalmology, the *Revista de Oftalmologie*.

On the editorial board of the new journal, the name of Blatt (Nicolae Blatt in Rumanian), as director, is associated with Filatof (Russia), Bailliart and Jeandelize (France), Bietti (Italy), Busacca (Brazil), Cosmettatos (Greece), Franceschetti (Switzerland), Igersheimer (U. S. A.), Pascheff (Bulgaria), Duke-Elder (Great Britain), and Weve (Holland). The editorial secretaries are Virgil Popovici, Nicolae Zolog, and Ion Moisescu.

Issue number one of the new journal, dated July to September, 1948, carries 172 pages of original articles, including six papers in French, four in Rumanian, and two in English. The Revista is the official

organ of the Rumanian Ophthalmological Society.

W. H. Crisp.

OBITUARIES
JOHN ELMER WEEKS
(1853-1949)

After a short illness, Dr. John Elmer Weeks died on February 2nd at La Jolla, California, where he was spending the winter. Thus ended a long and illustrious career for he was born on August 9, 1853, in Painesville, Ohio. He was the son of Seth R. and Deborah Ann (Blyenburgh) Weeks. In 1881, he received his medical degree from the University of Michigan. He then came to New York for an internship in the Alms House and Workhouse Hospital on Welfare Island.

Learning of his capabilities, Dr. Herman Knapp invited him to become associated with the Ophthalmic and Aural Institute. He first served it as a clinical assistant in 1882, but, in 1884, he interrupted his studies there to take a year of postgraduate work at the University of Berlin. He returned to the Institute in 1885 as resident physician and in 1887 became an assistant surgeon. He labored long and hard under the tutelage of Dr. Knapp whose stimulating influence sparked the natural ambitions of his apt pupil.

Dr. Weeks' great desire for knowledge and intense interest in research led him to investigate the bacteriology of acute epidemic conjunctivitis. In 1886, out of these studies came his epoch-making report identifying the organism which bears the name of Koch-Weeks bacillus as the causative agent. While this discovery was acclaimed far and wide, he accepted the honors with characteristic modesty and merely went on his way.

He served as chief of clinic, Vanderbilt Clinic, College of Physicians and Surgeons,

in 1888, and continued his association with Dr. Knapp until 1890, when he resigned to accept a surgeonship at the New York Eye and Ear Infirmary—a position he continued to hold until his retirement in 1920. At that time he was made a consulting surgeon. This institution soon became his absorbing interest and he devoted much time to its clinics and its pathologic laboratory. Here he found ample opportunity to develop his natural surgical ability to that degree of perfection he attained. Not only was he a most adept surgeon, but also a diagnostician of great ability.

Coupling these achievements with a sound knowledge of bacteriology and pathology it is no wonder that he held many responsible positions and achieved great fame. Among his teaching assignments were:

Lecturer in ophthalmology, Bellevue Hospital Medical College, 1890-92

Professor ophthalmology and otology, Woman's Infirmary Medical College, 1892-99

Professor of ophthalmology, University and Bellevue Medical College, (which became New York University in 1921), 1892-1921

Emeritus professor since 1921

Honorary professor of ophthalmology, University of Oregon Medical School, since 1940

During his active professional life his entire efforts were devoted to ophthalmology. He worked assiduously on the many problems in his specialty. He was one of the founders and early members of the American Board of Ophthalmology.

However, he did not allow his large private practice to usurp all his energies for he travelled much—always in search of new methods and new ideas. He attended medical meetings both at home and abroad, giving as well as receiving instruction. His presentations were largely of a practical nature with a natural emphasis on the surgical aspect. His method of reconstructing an orbital socket, which he presented in 1904 before

the International Congress of Ophthalmology, won him wide acclaim. His writings on the surgical treatment of such conditions as cataract and glaucoma did much to earn for him his well-deserved reputation as an outstanding ophthalmic surgeon. His manual dexterity along with his gentle handling of

JOHN ELMER WEEKS

tissues caused many ophthalmologists to be eager to observe the master at work. One of his favorite surgical procedures was the Lagrange operation, at which he was at his best.

As an author, he produced, in addition to his many articles on all phases of ophthalmology, two textbooks. His first was published in 1892, *Diseases of the Eye, Ear, Nose and Throat, A Manual for Students and Practitioners*, and then, in 1910, his *Diseases of the Eye*. This latter volume added greatly to his reputation for it was widely read and remained for many years one of the standard textbooks in ophthalmology.

Naturally, along with such achievements

came many honors. He was chairman of the Section on Ophthalmology of the American Medical Association in 1902, at the same time holding the chairmanship of the Section of Ophthalmology at the New York Academy of Medicine. In 1910, he was president of the New York County Medical Society; he was president of the American Ophthalmological Society in 1921, and the recipient of the Ophthalmic Research Medal given by the Section of Ophthalmology of the American Medical Association in 1929. He held honorary degrees from three institutions. In 1912 the University of Michigan, his alma mater, awarded him the degree of Doctor of Science; in 1923, the New York University recognized his achievements with the degree of Doctor of Laws; and, in 1940, the University of Oregon honored him with a Doctor of Science degree.

In addition to the societies already mentioned, Dr. Weeks was a member of the Hospital Graduates Club of New York, the New York Ophthalmological Society (president, in 1912), Pacific Coast Oto-ophthalmological Society, Association for Research in Ophthalmology, Ophthalmological Society of the United Kingdom, American College of Surgeons, and the Canadian Medical Association. He also held honorary membership in the Medical Society of Budapest, the Royal Hungarian Medical Society, the Chicago Ophthalmological Society, and the Portland Oregon Academy of Medicine.

On April 29, 1890, he was married to Jennie Post Parker, a union of which there was one daughter, Eveline Weeks Mount; both wife and daughter survive him. In his wife, Dr. Weeks found an ideal work mate. She accompanied him on most of his journeys and her gracious charm did much to make them a most sought-after couple. Her efforts were untiring and she devoted all her energies to love and care of him. His interests were hers and to her belongs no little share of his preëminence. Her implicit faith in his ability undoubtedly did much to bring out the best that was in this modest, retiring man.

Upon his retirement from active practice in 1924, he moved to Portland, Oregon, to be near his daughter and grandchildren. Here he rapidly assumed an important place in the medical life of that city. For several years he devoted one morning a week to consultations and surgery, but a great part of his time was spent at the University of Oregon Medical School. Recognizing their need of an adequate library he donated the funds for such a building. He counselled the department of ophthalmology and supported much of their research program. His interest in the progress of ophthalmology never waned for, even in the last few years of his life, he was a regular attendant at all lectures sponsored by that department. His presence and sage advice were a great stimulus and help to Dr. Kenneth Swan in the rebuilding of the department of ophthalmology at the University of Oregon.

In spite of the fullness of his professional life, Dr. Weeks found time to pursue his favorite recreations—golfing and fishing. His ability as a fisherman was only matched by that of his wife for the two rarely returned from such an expedition without having established some new records—either for size or for number of fish caught. He loved travel for travel's sake and fortunately lived to enjoy these pleasures he had so justly earned.

In manner, Dr. Weeks was shy, modest, and retiring, at times even appearing cold to the new acquaintance, but underneath this veneer, to those who knew him well, he was a man of sterling character. He was straightforward, honest, and unpretentious. His ideas were of the highest and his heart of the warmest so his passing has created a void in the hearts of his many friends. To American ophthalmology his death means the loss of one of its most illustrious sons. His life will serve as an inspiration and guide to future generations, for what more can one mortal do than to exemplify so completely the value of diligent application, honesty, and modesty. Success and fame were rightly his but the heritage of our specialty has been greatly enriched by the acts and deeds of this noble man.

John H. Dunnington.

HUNTER HOLMES McGUIRE
(1873-1949)

To most it is given to know intimately not more than half a dozen of his fellow men and fortunate is he who can choose these wisely. These few friends may color one's life as much as anything in that life. To those who were fortunate enough to be able to include Hunter McGuire among their intimates, a great richness was added. Quiet, unassuming, he was a physician almost by heredity as he followed in the footsteps of a father and a grandfather. Not to belittle his nobility and professional stature in the least, his outstanding characteristics seemed to be gentleness and kindliness. He radiated culture and hospitality, as might have been expected of a Virginian, scion of such a distinguished family.

His grandfather, Dr. Hugh Holmes McGuire, was a general surgeon who is said to have performed the first cataract operation in Virginia. He founded the first medical school in that state, in 1829, the Winchester Medical College. Another notable relative was an uncle who was medical director of the Army of Northern Virginia and physician to Gen. Stonewall Jackson.

Dr. Hunter McGuire was born in Winchester, March 30, 1873, and died in his sleep at his home in that city of a coronary occlusion on January 22, 1949. He was badly crippled by an attack of poliomyelitis at the age of two years and throughout his life was handicapped in getting about, but this never affected his disposition or his career. On the contrary, it must have developed a compensation in his understanding and sympathizing with the troubles of others. Never did it occasion self-pity, but enhanced a great courage.

It has been said that to learn to know a man one must turn to his writings. Dr.

McGuire has told something of himself in an address entitled "Forty-eight Years' Experience in Ophthalmology." We learn that, as premedical training after graduation from the University College of Medicine, Richmond, Virginia, in 1897, he spent a year in a local drugstore learning the practical side

HUNTER HOLMES McGUIRE

of drug dispensing and that there he discovered the evil of unrestricted sales of narcotics to the many addicts who were unprotected by the Harrison Anti-Narcotic Law enacted later.

In those days the medical course was only of three years' duration and, after completion of this, he went to Johns Hopkins for the study of eye diseases under Dr. Samuel Theobald, who was then professor and head of the Department of Ophthalmology at The Johns Hopkins Medical School, and Dr. Russell Murdock. He worked in the then small clinics at Johns Hopkins and the Baltimore Eye, Ear and Throat Hospital.

After one year in Baltimore, he returned to Winchester to start practicing. It was customary in those days in Virginia, and in the South in general, to combine the practice of ophthalmology and otolaryngology. And this Dr. McGuire did, although he never cared for the latter specialty and after many years confined his practice to the former.

Dr. McGuire's account of the early days of his practice recalls the days of the "Horse and Buggy" doctor. Operations were usually in the home of the patient and with inadequate anesthesia and assistants. Safety measures, now almost universally practiced, had not yet been discovered so it is a mystery how results were good enough to encourage the surgeon to persist.

As Dr. McGuire states, he had not been long in practice before he realized that his training had not been sufficient to satisfy him. So, he made a decision that undoubtedly was responsible to no small degree for making him the outstanding ophthalmologist that he became. This was to spend a considerable time each year in the ophthalmological centers of America. He studied for three autumns in New York City at the old New York Eye and Ear Infirmary. Immediately thereafter, the Winchester Memorial Hospital was founded by him and others. He was appointed the first president where his duties included being director, bookkeeper, manager, collector of accounts receivable, and distributor of funds. When these ran low, it was his task to solicit more. For 15 years he had to close his office at one o'clock in the afternoon and spend the remainder of the day in hospital duties.

It was only after these years that he was able to go regularly to Philadelphia where he was fortunate enough to attract the interest of Dr. George de Schweinitz, perhaps America's foremost ophthalmologist. Dr. McGuire was captivated by the charm of de Schweinitz and greatly impressed by his learning and ability to teach and to stimulate young men to think. With two others, Thomas Holloway and Emory Hill, a foursome began that was to remain in close

association until death claimed one after the other.

Hunter McGuire was married twice, the first time to Charlotte Claybrook of Westmoreland County, Virginia, and of this marriage there are three children surviving, William P. McGuire, who is carrying on the ophthalmic tradition, Mrs. Julian Broster Lindsey of Alexandria, and Mrs. Thomas Macaulay Booth of London, England. He is also survived by his second wife who was the former Miss Jane Love of Waynesville, North Carolina.

Of Dr. McGuire's many honors, there are a few that must be mentioned. He was a member of the American Ophthalmological Society from 1918 until his death. He was in the council from 1927 to 1931 and president in 1943. He served as first vice-president of the American Academy of Ophthalmology and Otolaryngology in 1924, was co-founder and first president of the Virginia Society of Ophthalmology and Otolaryngology, member of the Southern Medical Association, the College of Physicians of Philadelphia, the American Association for Research in Ophthalmology, the Ophthalmological Society of the United Kingdom, the Pan-American Association for Ophthalmology, and a Fellow of the American College of Surgeons. He was certified by the American Board of Ophthalmology in 1920.

On the skeleton of the bare facts of a man's life, his writings, his photograph, how poorly we do depict the man. Most of these are soon forgotten; even the memory of the dear face grows dim, but what never fades is the warmth, the spirit, the affection the man has imparted and this was kindled in large measure in all who knew Hunter McGuire. A man's physical accomplishments in his brief three score years and ten are few indeed. His most important contribution is his effect on the people whom he contacts during his lifetime. The influences that he has for good or evil are incalculable. As a stone dropped into a calm pool sends ripples to the far shores, so does a man spread his personality. But the simile fails in that the ripples are soon lost; whereas, the good influence lives on and on in the lives of others, and so it is with Hunter McGuire. Those who knew him are better and happier because of this and will, through the years, pass on to others something of his spirit.

Lawrence T. Post.

CORRESPONDENCE

REFRACTIVE TREATMENT OF ASTHENOPIA
Editor,
American Journal of Ophthalmology:

I would like to comment that Dr. Paul W. Miles's article, "Refractive treatment of asthenopia," contained many important pointers on treatment. He states that "correction of phoria by use of horizontal prisms is not very successful." I have had several patients who were treated by other physicians, with horizontal prisms, and little benefit. On phoria testing, I found that there was a vertical component which had not been appreciated. Correction of the vertical phoria by prisms in these cases was usually sufficient for symptomatic relief.

The use of the lensometer for the measurement of the pupillary decentration of old glasses is a very important part of any examination. It will usually explain difficulties and asthenopias that seem baffling.

In going over my records for the past two years, I have 57 cases of vertical prism prescriptions, which were successfully used in correction of asthenopia. Four of these cases had previously required base-out prisms in their correction. Of these, three were satisfied by use of vertical prisms, up to one prism diopter. Up to six prism diopters of vertical prism correction was prescribed with easy acceptance. These were particularly useful in correction of "headaches," "blurring of vision," "head tilting," and "burning." These symptoms occurred in hyperopes, myopes, and cases with astigmatism. In myopes with anisometropia, a vertical prism component was found in

asthenopia, and other ocular symptoms. Davson, as an academic physiologist, has lacked this awareness, but on the other hand has been more fascinated than dismayed by the nebulous implications of theoretical research.

Perhaps it is not surprising to find, even in a book of this quality, some errors. Davson postulates that the trigeminal pupillary reflex is mediated through a connection with the constrictor center, although Adler clearly pointed out that it is purely a vascular reflex. Rochat (Arch. f. Ophth., 118: 260, 1927) found that the dilated pupil that resulted after resection of the sympathetic and oculomotor nerves was insensitive to light or body irritation. Stimulation of the fifth nerve, however, anterior or posterior to the ganglion, produced a pupillary contraction that was affected by adrenalin, but not by atropine.

The chapter on optics is a lucid condensation of the subject and characteristically introduces new material including a review of the X-ray determinations of the length of the eye and the size of the image in the living subject.

Although this volume does not replace the older texts on ocular physiology, it is an invaluable supplement.

James E. Lebensohn.

DOCTORS OF INFAMY: The Story of the Nazi Medical Crimes. By Alexander Mitschlerlich and Fred Mielké. New York, Henry Schuman, 1949. 172 pages. Price, $3.00.

By this time the world is somewhat familiar with the Nazi atrocities perpetrated in World War II, proved and documented beyond question. Among these beastly activities, the criminal experiments performed on living human beings by Nazi physicians stand out in unbelievable horror.

The experiments they performed "for the interest of science" and "for the good of the services" involved thousands of helpless people, few of whom survived their superhuman sufferings. The torture and the suffering they endured were all in vain, for nothing of scientific value to mankind was learned by these frightful experiments. Nothing that could not have been found out with more humane methods and the use of experimental animals was added to our knowledge. What a sadistic mockery this is.

The German medical profession shares as a body in the guilt of these experiments, some of which reached their knowledge through scientific journals, others were described at medical meetings by the cruel investigators themselves, without one word of protest, apparently, coming from the audience.

Dr. Mitschlerlich was the head of the German Medical Commission to Military Tribunal No. 1, Nuremberg. The co-author is likewise German. They were as far away from actual participation in the medical crimes of their colleagues as was possible for any German doctor to be. Yet, they feel the collective guilt of their people, and try to atone or at least explain. One of the defendants, Karl Brandt, spoke of "preëminent government interest" to which the physicians must submit.

The authors say "Here again the bonds that tie the physician to society—that is, to human beings who appeal to his aid in their need—are confounded with obedience to absolute state society. . . . Physicians, treating patients under national health insurance, are obliged to communicate their diagnosis to the government officials there employed.

". . . All the gruff commands, all the unconditional obedience, all the chilly ways of bureaucracy—where have they led us but to the very death of brotherly love? And where charity lies entombed, small wonder that millions share its grave, that our very history as a people has become expunged."

This small book contains the protocols of frightfulness and the records of the damned. The reading and rereading of it will make you weep for the victims and the perpetrators. It will make you ask this question, "Is this the end of the road of state medicine?"

Derrick Vail.

ABSTRACT DEPARTMENT

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

11

RETINA AND VITREOUS

Turtz, C. A. Solar burns of the fundi. New York State J. Med. 48:2489-2490, Nov. 15, 1948.

Three cases of solar burn of the retina due to exposure to sunlight and two cases due to exposure to sun lamps are described. All patients complain of early lacrimation and blurred vision. The pain is caused by the action of light upon the cornea, iris, and ciliary body. Early ophthalmoscopic examination showed gray punctate spots in one case. Four patients had relative central scotomata and one had an absolute central scotoma for green.

The intense heat probably causes a localized vasospasm of the retinal vessels and a compensatory dilatation causes increased capillary permeability. This may lead to severe edema, necrosis of the retina and even to a hole at the macula. The author recommends widespread warning of the dangers from prolonged exposure to sunlight or sun lamps.

H. C. Weinberg.

Urrets Zavalia, A., Jr. Experimental study on transplantation and replacement of the vitreous. Ophth. ibero am. 10:1-20 (Spanish), 21-37 (English), 1948.

For experiments on rabbits, it is recommended to cauterize the part of the sclera where the incision is to be made. After placing a U-shaped scleral stitch, the author incises the sclera with a cataract knife held perpendicularly. He inserts a blunt canula 25 mm. long and 1 mm. in diameter to which he attaches first an empty syringe and then one full of the material to be injected. Although the rabbit eye tolerates replacement of almost the entire vitreous, in man it is not desirable to replace more than 2 cc. The best replacement material is 0.85-percent solution of sodium chloride. The differences between the composition of this fluid and that of the vitreous do not damage the delicate structures with which the fluid comes into contact and the same fact applies to the human eye.

W. H. Crisp.

12

OPTIC NERVE AND CHIASM

Fischer, Frantz. The appearance of the optic disc in acute retrobulbar neuritis. Klin. Monatsbl. f. Augenh. 110:578-580, 1945.

In 56 of 78 cases of acute retrobulbar neuritis an edema of the disc was found, sometimes with a swelling of one or two diopters. They were not different in any other way from the cases with normal discs except that both eyes were usually involved.   Gertrude S. Hausmann.

Horton, B. T., and Wagener, H. P. Retrobulbar neuritis; treatment with histamine. J. Lab. and Cl. Med. 33:1611-1612, Dec., 1948.

Histamine, used as a vasodilator to increase the blood supply to the optic nerve in retrobulbar neuritis, is administered as an intravenous drip of 24 to 48 drops per minute for 90 minutes daily or on alternate days for periods of one week to 3½ years. Of 61 patients treated, 24 regained normal vision, and ten regained from 50 to 75 percent of their vision. Typhoid vaccine had been given intravenously to 18 before the histamine therapy. Five of these patients regained normal vision, five were distinctly improved and eight did not change.   H. C. Weinberg.

Larsson, Sven. The macula and its reflexes in optic atrophy due to retrobulbar neuritis. Acta Psychiat. et Neurol, suppl. 46, pp. 187-193, 1947.

The writer agrees with Haab and Vogt that the observation of the macular reflexes is valuable because changes may be indicative of retinal atrophy in retrobulbar neuritis. This is especially true in unilateral affections where a comparison can be made between the healthy and the diseased eye. No decisive significance can, however, be attributed to them. Disappearance or breaking down of the reflexes must indicate an elimination of the differences of level within the macular area as a result of atrophy, but atrophy can evidently exist even where the structural levels and the reflexes are normal.
          Donald T. Hughson.

Marin-Amat, M. Phantom tumors of the optic nerve. Ann. d'ocul. 181:621-626, Oct., 1948.

A 20-year-old woman with exophthalmus of 10 mm. on the left side apparently had a vascular tumor of the optic nerve located near the sclera. A Kroenlein operation was performed; the tumor mass was isolated and removed, and the patient made an uneventful recovery. The tumor which measured 20 mm. by 12 mm. consisted of chronic inflammatory tissue surrounding the nerve. In a similar case, X-ray therapy was successfully employed without operation.   Chas. A. Bahn.

Schibdler, H. Report on a new successful treatment of methyl alcohol poisoning with optic atrophy. Klin. Monatsbl. f. Augenh. 110:584-589, 1945.

Four new and three old cases of methyl alcohol poisoning were treated with retrobulbar injections of atropine sulfate. The lasting action of the atropine in retrobulbar application seems to be the most important factor in the treatment. The visual field and the central vision showed marked improvement.
          Gertrude S. Hausmann.

13

NEURO-OPHTHALMOLOGY

Ali, Vittorio. A peculiar reaction of galvanic nystagmus observed during deep insulin coma. Riv. oto-neuro-oftal. 23:51-56, Jan.-Feb., 1948.

A woman, 27 years old, showed a peculiar galvanic vestibular reaction during a state of hypoglycemic coma, characterized by monocular abduction toward the positive pole which the writer ascribed to a disturbance of the association between the vestibular and the oculomotor centers.   Melchiore Lombardo.

Brain, W. R. Some observations on visual hallucinations and cerebral meta-

morphopsia. Acta Psychiat. et Neurol. suppl. 46, pp. 28-40, 1947.

The object of this paper is to report two patients who experienced visual hallucinations and other visuopsychic disturbances, which in one were a symptom of hypertensive encephalopathy and in the other were caused by alcoholism, and to point out that these diverse causes produced hallucinations which not only resembled each other but also possessed features in common with the hallucinations induced by mescaline. The author discusses the location of lesions that cause visual hallucinations and the relation of hallucinations to hemianopia.

Donald T. Hughson.

Mata López, Pedro. **The role of neurovegetative dystonia in asthenopia.** Arch. Soc. oftal. hispano-am. 8:907-917, Sept., 1948.

The following conclusions emerge from a review of the literature on the disturbances of the autonomic nervous system, and the author's ophthalmologic experience. 1. The existence of a nervous or retinal asthenopia, alone or associated with refractive errors or disturbances of binocular balance, is a clinical entity, caused by a lability or dystonia of the neurovegetative system on a psychosomatic basis. 2. There are two types of asthenopia: the parasympathetic type, caused by a lesion of the frontal portion of the cranial parasympathetic, which is in intimate relation with the oculomotor nuclei, and the sympathetic parasympathetic type, which is a pure psychosomatic dystonia. 3. The exciting factors in the dystonias and the associated asthenopia may be excessive, poorly remunerative work, burdensome responsibilities, improper diet, infections, particularly of the paranasal sinuses, and psychic and hormonal disturbances, especially of the pituitary. 4. There is an endogenous predisposition,

influenced by the mode of life and environment of the individual. 5. There is a common type of vegetative asthenopia, rooted in the conflict between the required task, the psychic impetus to carry it out, and the functional capacity for work. 6. The classical pharmacologic tests are no longer regarded important in the diagnosis of neurovegetative disturbances; it is made on clinical symptoms. 7. To avoid confusion in the diagnosis of neurovegetative dystonia, one should seek to establish the etiology, the pathogenesis, the seat and extent of the disturbance, both functional and psychic. 8. In the treatment, rest and diet are important and the drugs which are useful are the depressors of the diencephalic centers, and stabilizing tonics of the vegetative system, such as arsenic, calcium, and phosphorus. Elimination of focal infection, correction of menstrual irregularities, regulation of the diet, prohibition of toxins such as coffee and nocotine, and avoidance of excessive work are parts of the therapeutic pattern. By these means asthenopia which does not respond to correction of refractive errors may be relieved.

Ray K. Daily.

Milletti, M. **The clinical syndrome of the aneurysms of the opticochiasmatic region.** Riv. oto-neuro-oftal. 23:1-22, Jan.-Feb., 1948.

Cerebral arteriography can determine the nature and the special localization of aneurysms in the anterior cerebral artery, the anterior communicating artery or the endodural internal carotid. Sooner or later, however, they produce identical symptoms according to the size attained or the directions taken in their development and one cannot be differentiated clinically from the other. The writer proposes to group them as a "syndrome of the aneurysms of the opticochiasmatic region." To illustrate he reports in detail

four cases. To differentiate these aneurysms from those of the region of the cavernous sinus he points out that the nerves that control eye movements and the sensory brach of the fifth nerve are affected in the latter. Aneurysms of the region immediately posterior, that of the pes pedunculi, are characterized by isolated paralysis of the third nerve. (9 figures, bibliography.)

Melchiore Lombardo.

Morano, Massimo. **Ocular paralyses in the course of ophthalmic herpes zoster.** Riv. oto-neuro-oftal. 23:37-50, Jan.-Feb., 1948.

Two women, 60 and 70 years old, had recently had herpes zoster of the ophthalmic branch of the trigeminal nerve of one side. Both patients had anesthesia of the affected areas and paralysis of the third cranial nerve and in one patient the fourth nerve was also paralyzed. After the zoster symptoms subside the virus may remain latent for a time and may become virulent again and affect other segments of the ectoderm. To avoid this the writer suggests a treatment with vitamin B_1, methylene blue, X rays and sulfonamides before the virus injures other areas. (1 figure.)

Melchiore Lombardo.

Morone, G. **Pupillographic investigations in myotonic dystrophy.** Boll. d'ocul. 27:481-506, Aug., 1948.

Ten patients were studied by means of pupillography; six of them were suffering from dystrophia myotonica. Two were of the same family as the six others and had some myotonic signs themselves but no dystrophy and the other two were related but were without any pathologic manifestations. In those with frank myotonic dystrophy an atypical pupillotonia was frequently encountered. According to Adie's classification, it may be considered

to be an incomplete absolute rigidity. (8 pupillograms; references.)

K. W. Ascher.

Mylius, K. **Meningioma of the ala minor of the sphenoid bone.** Klin. Monatsbl. f. Augenh. 113:105-110, 1948.

The meningiomas of the smaller wing of the sphenoid bone are flat tumors originating from prongs of the arachnoidea. They may penetrate the bone and appear under the skin of the temple. A slowly developing exophthalmos in middle aged persons, facial asymmetry and thickening of the sphenopalatine bone, especially around the optic foramen and the superior orbital fissure are the clinical findings. The author stresses the necessity of special X-ray investigation of this region to avoid the mistaken diagnosis of intraorbital tumor. Involvement of the optic nerve as well as of the nerves passing through the supraorbital fissure may develop in advanced cases. Metastatic carcinoma and aneurysm of the carotid must be excluded. Two patients who had this type of meningioma are described.   Max Hirschfelder.

Pau, H. **Supranuclear ophthalmoplegia with bilateral homonym hemianopia due to vascular spasms.** Klin. Monatsbl. f. Augenh. 113:110-113, 1948.

A case of total ophthalmoplegia with homonymous hemianopia and a myocardial infarct is reported. A left-sided hemiplegia and facial paresis accompanied the condition. Symptoms subsided within a month after treatment with strophanthin. Spasms in the region of both medial cerebral arteries were the likely cause of the condition. (References.)   Max Hirschfelder.

Piper, H. F. **Ophthalmoplegia after birth trauma.** Klin. Monatsbl. f. Augenh. 113:113-116, 1948.

In a young boy with a supranuclear ophthalmoplegia the voluntary movements were almost lacking in both eyes. Targets could be followed in only a most limited manner. Fixation could not be held when the head was turned slowly but the eyes made rapid reflex movements when the head was turned rapidly. He had convergent strabismus and one eye was amblyopic. A birth trauma was known to have occurred. The author discusses the possible cerebral lesion. He believes that damage to the corticopontine pathways in early childhood was responsible for the lack of spontaneous eye movements. This damage may have been small, but was significant, because it occurred during an important stage of development. (References.)

Max Hirschfelder.

Rubino, A. **Ocular signs and symptoms in the meningocranioses.** *Riv. oto-neuro-oftal.* 23:23-36, Jan.-Feb., 1948.

The writer discusses the signs and symptoms which may be found in arachnitis and in endocraniosis (chronic frontobasilar inflammations of Lunadei). Particular attention is given in the discussion to the ophthalmoscopic and perimetric data which frequently reveal a circulatory, neuroretinal, and endocranial disturbance and a lesion of the lower crossed optic fibers at the level of the chiasm (chiasmatic sign of Rubino). (5 figures.) Melchiore Lombardo.

Sjörgren, Torsten. **Hereditary congenital spinocerebellar ataxia combined with congenital cataract and oligophrenia.** *Acta Psychiat. et Neurol.* suppl. 46, pp. 286-289, 1947.

This rare and peculiar disease has only been described in the literature once before by Marinesco, Draganesco and Vasiliu. The author reports two additional families in which it occurred.

Donald T. Hughson.

Tönnis, W. **The significance of angiographic diagnosis for the treatment of brain tumors.** Klin. Monatsbl. f. Augenh. 113:97-105, 1948.

Forty percent of brain tumors cannot be exactly diagnosed by means of history, clinical findings and simple X-ray studies. These diagnostically more difficult tumors need further investigation by ventriculography and angiography, two methods which supplement each other. Angiographic X-ray demonstration of aneurysms and angioblastic tumors determines their character, spread and operability. Malignant gliomas often exhibit characteristic vascularization and in 60 percent arteriovenous aneurysms can be discovered by this method. Surgery of meningiomas can be made easier by preoperative study of their blood supply. Dislocation of the blood vessels is helpful for localization, especially in cases of olfactory meningioma. The differential diagnosis between glioblastoma, abscess and subdural hematoma is frequently made easier by angiography. The future of the method lies in the possibility of its use for functional tests of the intracranial circulation. Max Hirschfelder.

Vetter, Joachim. **Eye symptoms in juvenile tabes dorsalis.** Klin. Monatbl. f. Augenh. 110:581-583, 1945.

It is characteristic for juvenile tabes that the eye symptoms precede the general neurological symptoms, sometimes by several years. The only symptoms an 11-year-old girl showed were loss of vision, optic atrophy and rigid pupils. She was treated with malaria.

Gertrude S. Hausmann.

14

EYEBALL, ORBIT, SINUSES

Espildora-Luque, C., Villaseca, A., Mehech, M., and Ossandon, M. **Two cases of inflammatory pseudotumor of the**

orbit. Arch. Soc. oftal. hispano-am. 8:879-890, Sept., 1948.

The literature on these bizarre lesions is reviewed and two cases reported. The first case was seen in a girl, 16 years old, who developed left exophthalmos, restricted ocular motility, and ptosis of the left lid. After various therapeutic agents proved ineffective, a diagnosis of a possible malignant tumor was made and a hard mass of tissue was removed from the orbit surgically. A histologic diagnosis of chronic inflammatory process was made. Ten days after the operation a similar mass appeared in the right orbit. Except for a positive Pirquet test the general examination was negative. The etiology of this inflammatory process was therefore assumed to be tuberculosis, but tuberculin therapy was without effect.

The second case occurred in a woman, 38 years old. She had bilateral exophthalmos, associated with severe pain, vertigo and transitory diplopia. The left eyeball had a circumscribed focus of diffuse episcleritis. There were periods of acute inflammatory symptoms and both eyes had retinal detachments which were attributed to the inflammatory process. Treatment was ineffective. Antiluetic therapy with neosalvarsan and bismuth brought some relief from pain but had no effect on the objective manifestations. The patient was lost from observation for two years, when she returned, stating that she was treated during this time with various tonics. The left eye had recovered sufficiently for her to resume work. The exophthalmos receded, motility was restored, there was no sign of episcleritis, and the retina was reattached. There were several foci of pigmented choroiditis, which involved the macula; vision was corrected to 5/15. The right eye remained proptosed, immobile, with high tension, and seclusion of the pupil. It was totally blind and extremely painful. It was enucleated with difficulty, because of the dense cicatricial tissue which bound it within the orbit. The pathologic process involved chiefly the posterior portion of the eyeball; it was characterized by a granulation tissue with a marked tendency to cicatrization which consisted of blood vessels and an abundance of various types of cells, predominantly fibroblasts, lymphocytes, and plasma cells. The infiltration was in part diffuse, and in places had a tendency to form lymphoid nodules. The process extended into the extraocular muscles. The histology gave no clue to the etiology. While the patient was in the hospital she developed an acute exacerbation of the inflammatory process in the right eye, which subsided with antiluetic therapy within 21 days. The authors suggest that antiluetic therapy may be of value in cases of obscure etiology in spite of negative serologic data. (6 figures)

Ray K. Daily.

Goldberg, J. **A Case of spontaneous exophthalmos during delivery.** Brit. J. Ophth. 32:914-915, Dec., 1948.

A case of sudden, severe, unilateral exophthalmos which occurred during delivery is presented. It slowly and spontaneously subsided, only to recur twelve days after delivery. The diagnosis was orbital hemorrhage. The final result was optic nerve atrophy, and degenerative changes in the macula.

Orvyn H. Ellis.

Klar, R. **Plastic polyviol implants after enucleation.** Klin. Monatsbl. f. Augenh. 113:145-146, 1948.

The author refers to his former paper on plastic implants and states that he had favorable results when such implants were indicated. He warns against too large an implant, especially for late implants. Iced compresses reduced the postoperative reaction. Max Hirschfelder.

Marin Amat., M., and Gonzales-Novelles, M. B. **Hydatid cyst of the orbit.** Arch. Soc. oftal. hispano-am. 8:939-945, Sept., 1948.

Poor hygienic conditions, crowded living conditions and poverty led to an increased frequency of hydatid cysts in Spain. The author's case occurred in a five-year-old boy who suffered from recurrent attacks of pain in the left eye associated with edema of the lids. Examination revealed an exophthalmos, limitation of ocular movements, edema of the lids, and descending optic atrophy. A diagnosis of hydatid cyst was made because of a positive reaction to hydatid antigen. The cyst was removed by a Krönlein operation. The symptoms and differential diagnosis are discussed in detail.

Ray K. Daily.

15

EYELIDS, LACRIMAL APPARATUS

Alcalá López, Antonio. **An unexpected finding during a dacryocystorhinostomy.** Arch. Soc. oftal. hispano-am. 8:1046-1054, Oct., 1948.

In the course of a dacryocystorhinostomy, for chronic dacryocystitis with fistula, the author encountered a dermoid cyst overlying the lacrimal sac. The cyst contained a tooth, and was the source of the fistula. The dacryocystitis is attributed to the compression of the lacrimal sac by the cyst. The pathogenesis of dermoid cysts in this region is discussed, the literature referred to briefly, and the evolution of the lacrimal sulcus is illustrated. (6 figures.)   Ray K. Daily.

Allen, J. H. **Diagnosis and treatment of blepharo-conjunctivitis.** J. Iowa M. Soc. 39:5-8, Jan., 1949.

Blepharo-conjunctivitis may be a generalized inflammation of the lids or a localized lesion. The common forms described may be of either type. Seborrheic blepharitis is usually secondary to seborrheic dermatitis of the scalp. It is usually bilateral with dull dirty gray loose scales on a slightly red lid margin. Yeast cells are found in lid scrapings. Treatment for dandruff and the application of 3-percent ammoniated mercury to the lids three times a day is advised. Staphylococcic blepharitis produces a squamous or ulcerated lesion. The scales are tenacious. Hordeola occur frequently. Treatment with vaccine and toxoid is recommended if local applications of 1/5000 aqueous solution of zephiran chloride with massage and cleansing of the lids are inadequate. Mixed seborrheic and staphylococcic lesions also occur. Morax-Axenfeld blepharitis is characterized by maceration usually at the outer canthi. Treatment with 5-percent sulfathiazole ointment four times a day for four weeks is recommended. Allergic blepharitis may appear as a slight itching or as severe vesiculation and excoriation of the skin. The skin appears thin, wrinkled and often shows eczematoid changes. The treatment is to use the anti-allergic drugs and remove the cause if found.

H. C. Weinberg.

Amyot, Roma. **Hereditary, familial and acquired ptosis late in onset.** Canad. M.A.J. 59:434-438, Nov., 1948.

Nine cases of bilateral, familial, hereditary ocular ptosis are reported. All appeared after 50 years of age. There was some limitation of upward gaze in three cases. Ptosis is due to a myopathy of the levator. Difficulty in swallowing was present in six patients.

Irwin E. Gaynon.

Arriaga Cantullera, José. **A contribution to dacryocystorhinostomy.** Arch. Soc. oftal. hispano-am. 8:1031-1036, Oct., 1948.

The modification proposed by Arriaga applies to the closure of the wound, which

is done by a suture similar to the Blascovics suture for strabismus. A number 0 silk suture passes successively through the skin, the periosteum, the anterior flap of the nasal mucous membrane, the anterior wall of the sac, and the skin on the opposite side of the incision. The anterior face of the anastomotic cavity is thus fixed to the skin, and there are no buried sutures. The edges of the skin incision are then co-apted with fine silk. (6 figures.)   Ray K. Daily.

Aznarez García, José. A rapid dacryocystorhinostomy with a continuous suture. Arch. Soc. oftal. hispano-am. 8: 1037-1045, Oct., 1948.

The suture described can be understood much better from the illustrations than from a description. It is similar in principle to the Blasckovics suture for myectomy, in which three needles are used on one suture, with the difference that instead of ending in two knots, this one ends in three. The knots are tied over rubber or gauze. The osseous opening is made with a Citelli forceps, rather than a burr. (5 figures.)   Ray K. Daily.

Bitran, David. Accidental ocular vaccination. Arch. chilenos de oft. 4:465-470, 1947.

The first patient was a boy of nine years, whose sister had been vaccinated against smallpox two weeks previously. There were three vesicles in the swollen lower lid, and the lymphatic glands of the preauricular and mastoid regions were enlarged. The second patient was a girl of five years whose left lid margins had multiple infection and who had been vaccinated in the right arm a week earlier. The treatment in each case was merely prophylactic, with penicillin, against secondary infection, and no permanent disability resulted. (4 figures.)
                    W. H. Crisp.

Castresana y Guinea, Angel. Palpebral edema caused by an intranasal foreign body. Arch. Soc. oftal. hispano-am. 8: 1114-1120, Nov., 1948.

A 15-year-old patient had intense palpebral edema of the left eye for about 12 days, which at first was attributed to an insect bite. In the course of a rhinological examination a piece of eraser rubber was found in the left middle nasal meatus. Four years previously the boy accidentally pushed a piece of rubber into his nose, but having no symptoms he had forgotten about it. The pathogenesis of palpebral edema caused by intranasal foreign bodies is discussed, and it is believed that in this case the nasal obstruction interfered with the airation of the paranasal sinuses, which is frequently accompanied by edema of the lids. The possibility of intranasal foreign bodies must be kept in mind in noninflammatory palpebral edema.   Ray K. Daily.

Glüh, B. Suggestions for covering a lid defect according to Kreibig. Klin. Monatsbl. f. Augenh. 113:143-145, 1948.

This operation serves to restore a total defect of the upper and lower lid, if the inner canthus is intact and the region surrounding the lids is not destroyed. During a first operation one half of a skin flap is prepared from the skin of the forehead, and its back is covered with mucous membrane from the mouth. The rest of the flap is prepared two weeks later and is put into place in the defect. Restoration of an upper and lower lid necessitates a somewhat broader flap, which finally is split during a third operation a month later. Skin containing hair follicles is taken from behind the ear to restore the eye lashes. (3 figures.)
                    Max Hirschfelder.

Hartmann, Karl. Extirpation of a chalazion in a true bleeder with application

of Vivocoll and chalazion suture. Klin. Monatsbl. f. Augenh. 110:397-399, May-June, 1944.

The almost fatal bleeding was stopped eventually by injection and surface application of Vivocoll and chalazion sutures. Vivocoll is made from blood of cattle and coagulates rapidly when injected into the bleeding tissue, or is applied to its surface. Two double-armed sutures through the whole thickness of the lid and tied on the skin stop even a severe hemorrhage after chalazion extirpation. George Brown.

MacMillan, J. A. Diseases of the lacrimal gland and ocular complications. J.A.M.A. 138:801-805, Nov. 13, 1948.

The anatomy and histology of the lacrimal gland is reviewed. MacMillan stresses the fact that the aponeurosis of the levator muscles divides the gland into two parts. The cells of the acini are columnar and resemble the serous cells of the salivary gland. The gland is supplied by fibers from the fifth, seventh, and sympathetic nerves. The secretory parasympathetic fibers for the gland are derived from the superior nucleus salivatorius of the seventh nerve in the medulla and through the greater superficial petrosal nerve reach the gland through the zygomatic or lacrimal nerves. The role of the sympathetic nerve in lacrimation is obscure. It conveys vasodilator and vasoconstrictor fibers to the gland, and motor fibers to the basket cells of the acini and tubules. Diminished secretion of tears is found in keratoconjunctivitis sicca (Sjögren's syndrome). Often this is associated with swelling of the parotid gland and arthritis. Neuroparalytic keratitis also occurs with symptoms of drying of the cornea due to postoperative diminution in secretion of tears after surgery or alcohol injection for the relief of fifth-nerve neuralgia. The orbital and palpebral lobes of the lacrimal gland may be removed with safety when Krause's glands are not affected. The protein content of the lacrimal secretion nourishes the anterior layers of the cornea.

Hypersecretion of tears should be treated by removal of the inferior lobe of the lacrimal gland. This should also be done when there is tearing after the lacrimal sac has been excised. Three cases of tumor of the lacrimal gland are described. H. C. Weinberg.

Moreu, Angel. Recent advances in hemostasis. Arch. Soc. oftal. hispano-am. 8:1024-1030, Oct., 1948.

Moreu investigated the effectiveness of jel-foam and thrombin in preventing secondary hemorrhages after dacryocystorhinostomies. Its use in 53 cases convinced him of the value of this hemostatic agent. He uses it as follows: after trephining the osseous opening into the nose, and before incising the nasal mucosa, he places a piece of jel-foam against the mucosa, and holds it there by a piece of gauze saturated in thrombin; while the hemostatics are taking effect on the nasal mucosa the lacrimal sac is opened and prepared for the anastomosis; the nasal mucosa is then incised without hemorrhage; after the anastomosis between the sac and the nasal mucosa is completed, a piece of jel-foam is introduced into the cavity, and compressed against the osseous opening, and another piece placed on the anterior surface of the anastomosed flaps. Ray K. Daily.

Mosquera, Sanchez. Penicillin and malignant pustule. Arch. Soc. oftal. hispano-am. 8:949, Sept. 1948.

Mosquera reports a case of malignant pustule of the lid which was cured within a few days by intramuscular injections of penicillin. The diagnosis was confirmed bacteriologically. Ray K. Daily.

Németh, L. Surgical treatment of ectropion caused by blepharoadenitis. Ophthalmologica 116:162-166, Sept., 1948.

Besides the cicatricial and the paralytic forms of ectropion there is, in the author's opinion, a form due to chronic inflammatory processes at the border as well as in the substance of the lid. This leads to atrophy of the ciliary portion of the orbicularis and to loosening of the lid borders. For its correction the author recommends an operation consisting of: elevation of the skin by means of an intermarginal incision along the entire lid border, carried beyond the proximal edge of the tarsus and extended beyond and upward of the outer canthus where a crescent-shaped piece of skin is excised (similar to the Szymanowski procedure), a canthotomy, and elevation of the tarsus by means of a suture placed in the lower fornix and brought out through the skin of the lower lid.   Peter C. Kronfeld.

Pajtaš, J. **Blepharoconjunctivitis due to diocaine.** Ophthalmologica 116:144-148, Sept., 1948.

The report concerns an elderly woman who first used diocaine topically in 0.2 percent concentration for the relief of intense itching of her eyes. After several weeks of this treatment the itching ceased and the instillations of diocaine were discontinued. Several months later the treatment was resumed and promptly caused acute blepharoconjunctivitis which subsided within five days of abstinence from all drugs. Several months later diagnostic instillation tests revealed marked hypersensitivity to diocaine. The author succeeded in desensitizing the patient by a seven months' course of intramuscular injection of increasing amounts of diocaine.   Peter C. Kronfeld.

Tóth, Z. **Functional tests for the lacrimal pathways above the sac.** Klin. Monatsbl. f. Augenh. 113:158-167, 1948.

Irrigation of the lacrimal sac yields only information about free passage of tears within the sac and lacrimal duct. It does not investigate the more important functions of the punctum lacrimale and the lacrimal canal. The author describes three different procedures to test the function of these parts. In the first a drop of 3-percent collargol is instilled. Collection of brown fluid between lid margin and bulbus indicates stasis. Observation of the punctum when the lid is pulled down slightly enables the observer to study its function and movements. Regurgitation occurs in stenosis of the sac. The play of the punctum is lacking when this part of the lacrimal pathways is involved. A second procedure is the introduction of a small canula into the punctum. A quick passage of the staining media through such a canula is proof that the tear point was the cause of the stasis. The third test consists of transillumination of the lacrimal canal after instillation of collargol into the conjunctival sac. The brown column of fluid can be observed during its passage from the tearpoint to the lacrimal sac. (11 figures, references.)   Max Hirschfelder.

16

TUMORS

Bernoulli, R. **Lid carcinoma in a dog.** Ophthalmologica 116:101-106, Aug., 1948.

A melano-carcinoma in a bitch could be traced back histologically to the Malpighian stratum of a papilloma and to the basal epithelium of an adjacent tarsal gland.   Peter C. Kronfeld.

Focosi, M. **An unusual case of trichoepithelioma of the eyebrow.** Boll. d'ocul. 27:417-423, July, 1948.

A single lobulated tumor, which had developed during two years, was removed from the eyebrow of a 52-year-old man. Histologic examination revealed that the tumor originated from the outer layers of the hair follicles, that there was

no involvement of any sudiferous or sebaceous glands and that small cysts contained an acidophile fluid. Usually these tumors occur in young people, begin as multiple tumors, and are familial. (4 photomicrographs, references.)

K. W. Ascher.

Lowe, R. F. **Intra-ocular phakomata—a report of three cases.** Brit. J. Ophth. 32:847-853, Nov., 1948.

The author reports three cases of phakoma, two of the Bourneville type (tuberous sclerosis) and one of von Recklinghausen (neurofibromatosis). All three patients were low grade idiots, all had cutaneous and retinal spots and all probably had intracranial lesions. All three had secondary optic atrophy and markedly diminished vision.   Morris Kaplan.

MacDonald, A. E. **Lindau's Disease—progression in affected family.** Brit. J. Ophth. 32:575-580, Sept., 1948.

The familial condition in which multiple capillary hemangioendothelioma occurs in the cerebellum, cerebrum, retina, spinal chord, kidneys, pancreas, epididymis, liver and bone should be termed Lindau's disease. A family is described in which three of four siblings had definite and proved Lindau's disease, and the mother most probably had it. One of the sisters died after three removals for recurrent tumors in the brain and two are apparently well after a single removal of one brain tumor. They have demonstrable tumors in one eye which has been held in check by radium therapy.

Morris Kaplan.

Marin Amat, M., and Marin Enciso, M. **Epibulbar epithelioma cured by diathermy coagulation.** Arch. Soc. oftal. hispano-am. 8:1142-1144, Nov., 1948.

A 55-year-old woman had an epibulbar carcinoma at the limbus which had been excised twice, and had rapidly recurred each time. The neoplasm was destroyed by diathermy, and the coagulated area was covered with conjunctiva. At the end of four months there was no recurrence. The authors believe that diathermy coagulation should be used rather than the more destructive processes such as X-ray or radium therapy. (1 figure.)

Ray K. Daily.

Scuderi, G.. **The neurinoma of the orbit.** Boll. d'ocul. 27:507-530, Aug., 1948.

The 61-year-old patient noticed four years ago that his left external canthus itched and was continually sore. Only a few months later, his left eye started to protrude and a tumor developed under his left lower lid. When first seen, he had 8.5 mm. difference on the Hertel exophthalmometer and was otherwise normal. Fundus aand vision were normal. A smooth tumor measuring 3.5 by 2.8 cm., histologically a neurinoma type A (Antoni's classification), was removed from the temporal side of the orbit by external orbitotomy. Some areas showed neurofibromatous changes. The tumor most probably originated from one of the posterior ciliary nerves. The pathogenesis of the neurinomas is discussed. (6 figures, 50 references.)   K. W. Ascher.

Stallard, H. B. **Radiotherapy of malignant intraocular neoplasms.** Brit. J. Ophth. 32:618-639, Sept., 1948.

The tissues of glioma retinae are very radiosensitive and when a quadrant or less of the retina has been affected by the growth, treatment by means of radon seeds has caused the tumor to disappear. In a series of patients treated at St. Bartholomew's Hospital there has been no recurrence in nearly 20 years. The treatment of malignant melanoma is less successful but metastatic carcinoma of the choroid is very radiosensitive and often its treatment is justified. The dose

must be carefully chosen. It must be large, be strong enough to affect the tumor and yet cause minimal damage to the eye. The source of irradiation must be as close to the tumor as possible and in this series the radon needles were sutured to the sclera in apposition to the mass. Tentatively the dose has been set at 3.5 r to destroy glioma occupying one quadrant of the interior of the eye; the seeds are left in place four to eight days.

The technique of application in 15 cases is described in great detail. Complications included irradiation cataract, retinal exudation and hemorrhage, and retinal detachment.   Morris Kaplan.

17

INJURIES

Marin Amat, M. An intraocular BB shot localized and easily extracted under radiographic control. Arch. Soc. oftal. hispano-am. 8:1090-1096, Nov., 1948.

A man, 39 years old, was shot in the left eye and a BB shot penetrated the eyeball. Hemorrhage into the vitreous made ophthalmoscopic examination impossible. The shot was localized by X-ray study with the Comberg contact lens. The operative area was coagulated by diathermy, and on the operating table an Arruga localizing pin was introduced into the sclera at the area where the shot was localized. Another roentgenograph taken on the operating table demonstrated that the pin was in contact with the shot. On withdrawal of the pin the shot appeared in the wound and was withdrawn with a Daviel spoon. The patient made an uneventful recovery, with a final visual acuity of 1/10. (4 figures.)   Ray K. Daily.

Michaelson, J. C. Traversing intraocular foreign bodies with retinal detachment. Tr. Ophth. Soc. U. Kingdom 66: 193-210, 1946.

The author describes six cases of intraocular foreign body from battle injuries. The foreign bodies frequently traverse the globe, leave the eye posteriorly, and lodge in the orbital tissues because of the high velocity. They may also pass the vitreous tangentially and cause a retinochoroidal lesion in which a massive proliferative choroiditis is the outstanding feature. The mechanism of the detachment in the "tangential" group appears to be traction on the retina caused by contraction of scars in the choroid several months after injury. The trajectory of the foreign body through the vitreous may be marked by a cone of vitreous opacity between the wounds of entrance and exit. Retinal detachment may be remote from the site of reaction in the choroidal wound with its vitreous bands, but no dialysis is found.

If a dialysis is present in an eye with a tangential trajectory, a barrage should be applied to the area of the cicatrizing choroiditis but not too close to the area of proliferative choroiditis, and the subretinal fluid should be evacuated. The treatment of the retinal detachment in the transvitreous injuries is similar to that of retinal detachment in general.
Beulah Cushman.

Senna, S. Extraction of intraocular foreign bodies under stereoscopic radioscopy. Arch. Soc. oftal. hispano-am. 8: 1097-1107, Nov., 1948.

Senna advocates removal of intraocular nonmagnetic foreign bodies under stereoscopic fluoroscopy. The principles involved in stereoscopic fluoroscopy are explained in detail and it is pointed out that the removal of intraocular foreign bodies is a cooperative effort between an ophthalmologist and the author. The ophthalmologist prepares the operative field, and makes the scleral incision in the area determined by accurate localization and coagulated by diathermy; a forceps introduced into the incision is taken over by

the roentgenologist, who removes the foreign body under direct observation. In the method devised by the author the screen is placed vertically at the side of the operating table, and not horizontally above the patient. The dark box for stereoscopic fluoroscopy is adequate for tridimensional perception. The removal of intraocular foreign bodies becomes a simple procedure, aand the results depend on the extent of trauma inflicted by the injury rather than by the surgery. (4 figures.) Ray K. Daily.

18

SYSTEMIC DISEASE AND PARASITES

Borioni, D. **Eye affections observed during breast feeding.** Boll. d'ocul. 27: 471-473, July, 1948.

Three cases of neuritis of the optic nerves, all unilateral and in regression towards atrophy when first seen, and one of spasm of the accommodation, all attributed to lactation are briefly reported. Other causes were ruled out by careful general physical examination.

K. W. Ascher.

Galindez Iglesias, Fermin. **Some aspects of endocrine exophthalmos.** Arch. Soc. oftal. hispano-am. 8:1121-1141, Nov., 1948.

The author reviews the literature and reports his investigation of 25 hyperthyroid patients with high metabolic rates. None had fundus lesions. Seven patients had bitemporal contractions of the visual fields of 15 to 30 degrees. The degree of exophthalmos as measured by the Hertel exophthalmometer did not exceed 20 mm. and was below 15 mm. in three cases, in three it was equal in both eyes, and in 22 it was unequal. The author regards normal visual fields indicative of a primary disturbance of the thyroid, and bitemporal retraction suggestive of a

thyroid involvement secondary to a pituitary disturbance. Ray K. Daily.

Givner, Isadore. **Some associated eye and skin manifestations of systemic disease.** New York State J. Med. 48:2700-2705, Dec. 15, 1948.

A brief discussion of diseases which manifest skin and eye lesions is given. The phakomatoses are reviewed. A case of Bourneville's disease is illustrated. A case of Recklinghausen's disease with pulsating exophthalmos is described. Sturge-Weber's disease, in which studies with fluorescein indicate increased capillary permeability, is described. Patients with amino acid deficiencies in which a deficiency of valine was found to cause a corneal dystrophy also showed a loss of total proteins, especially in the albumin fraction. Acute disseminated lupus erythematosus should be considered in patients showing exudates in a fundus with no other vessel changes. It is said to be accompanied by fever and skin lesions which are aggravated by sunlight and sulfonamides. Boeck's sarcoid and its relationship to tuberculosis is discussed. Recurrent aphthous uveitis with mucocutaneous lesions resembles Steven-Johnson's disease and bacteriological studies are reported. Two cases of Vogt-Koyanagi disease, and skin and eye lesions of brucellosis and monocytic leukemia are described. (2 figures.)

H. C. Weinberg.

Lama San Martin, L. C. **Associated ophthalmic and nasal myiasis.** Arch. chilenos de oft. 4:471-484, 1947.

In this case the offending mosco was Cochliomyia hominivorax. The patient was a man of 66 years who had had his right eye enucleated after an injury 30 years previously. He did not use an orbital prothesis. Four months previously, while working on construction, he had

fallen on a pile of rubble, losing consciousness for a short time. The facial injury was trifling. A developing discomfort in the eye socket received no attention because the man was afraid of losing his job. Three days before the eye examination he had come to the clinic on account of abundant hemorrhage from the mouth, nose, and orbit. He was sent to the eye department because "worms" had been found in the orbital cavity. There was an overwhelmingly fetid odor, and the man had an accelerated pulse rate and elevated temperature. The orbit was completely packed with hundreds of larvae in incessant movement, and similar larvae were promptly encountered in the right nasal cavity. In the course of treatment, and after an X-ray picture had been taken, a little water-pipe cap was extracted from the depth of the right nasal cavity, and a piece of slag from the depth of the orbit. (9 figures.)

W. H. Crisp.

Lindsay-Rea, R. **Ocular disturbances associated with malnutrition.** Tr. Ophth. Soc. U. Kingdom 66:109-111, 1946.

The author discusses three patients in whom ocular symptoms were associated with malnutrition. A woman, after a reducing program, showed symptoms of Sjögren's syndrome and improved rapidly with 500 mg. vitamin C given intravenously daily for six days, then orally for one month, when the keratitis had disappeared. A man, aged 28 years, had been a prisoner in Siam for four years. His myopia had increased 2 diopters in the right eye and 0.5 diopters in the left. The third patient, a man, aged 25 years, had been in an internement camp in Hong Kong for three years and developed bilateral central blindness with an absolute central scotoma of 5 to 10°. He neither smoked nor drank but his mother had had a disseminated sclerosis

with lateral pallor of the disks.

Beulah Cushman.

Lowther, A. H. **Ocular disturbances associated with malnutrition.** Tr. Ophth. Soc. U. Kingdom 66:104-107, 1946.

The author had charge of 145 patients with malnutritional amblyopia during three and one-half years as a prisoner of the Japanese in Singapore. The onset was usually gradual and the age distribution resembled that of tobacco amblyopia. The visual acuity ranged from 6/60 to 6/5. There was a paracentral scotoma in 64 patients, a pericentral one in 42, and there were small islet defects around the fixation point in some. The blind spot was enlarged in three patients. The clearing of the vision in the center and a gradual change in the ring scotoma suggested that the condition was a retrobulbar neuropathy. Ten patients had bilateral and four unilateral papillomacular atrophy. Forty patients had parasthesia and sensory changes in the limbs and 41 had alterations in the tendon reflexes, 22 had a sore and red tongue and nine had dry eczema of the scrotum. Fourteen cases were severe and showed no improvement at the end of internement, in 41 the vision improved to 6/9 and 90 patients recovered full vision. Although the field defects were not typical of tobacco amblyopia all patients were advised to stop smoking because the author feels that the toxins of tobacco may precipitate the ocular disturbance in malnutrition. Beulah Cushman.

Mejer, F. **Fundus findings in streptomycin treatment of tuberculous meningitis and miliary tuberculosis of the lung.** Wien. klin. Wchnschr. 60:842-844, Dec. 31, 1948.

Now that tuberculous meningitis and miliary pulmonary tuberculosis can be successfully treated with streptomycin,

the changes observed in the fundus in these diseases have particular diagnostic significance. In 42 children suffering from these forms of tuberculosis and treated with streptomycin, the fundus was repeatedly examined. Changes in the disc were found in over one-third of the cases. The presence or absence of slight swelling early in the disease has no diagnostic or prognostic significance. Papilledema indicates that the illness will be long and serious. Late changes indicate complications. In over one-third of the cases multiple miliary or solitary tubercles of the choroid were also seen, chiefly in patients with miliary lung tuberculosis. Under treatment with streptomycin these regressed rapidly as the child's general condition improved. Slow regression pointed to complications or other setback. Injury to the optic nerve, sometimes attributed in the literature to streptomycin, is probably due to the disease, not to the drug. However, this needs further study.　　　B. T. Haessler.

Pacheco-Luna, R. Onchocercosis in Guatemala. Ann. d'ocul. 181:463-467, Aug., 1948.

This filarial ocular disease was brought to Guatemala by negro slaves from Africa. Now, however, it is not proportionately more frequent in negroes than in other races. In Guatemala, onchocercosis is limited to a zone between 400 and 1600 meters above sea level. The parasite is ovoviperous; the male measures 30 by 0.2 mm. the female, 300 by 0.5 mm. Infected men are inoculated by several species of flies which live near ponds and in very shady places. Only the female attacks man. The micro-filaria are deposited in the skin. They migrate to the stomach and thoracic muscles, and after ten days larvae form. The ocular tissues involved are principally the lid, conjunctiva, cornea and uveal tract. The tissue

reaction is variable. The subjective symptoms are most frequently photophobia, blepharospasm, and defective vision. The reaction of the tissues is essentially defensive in that the parasites are walled off from the rest of the body by scar tissue. Living organisms do not usually cause as much irritation as do dead filaria. Parasites have been known to live 20 years, and 20 nodules with enclosed filaria have been removed from the head of one patient. The differential diagnosis includes numerous skin tumors and forms of subacute and chronic keratitis and uveitis. Supplementary diagnostic confirmation may be made by biomicroscopy, biopsy of the skin and conjunctival lesion, and blood count. Eosinophilia is present in 50 percent. The ocular condition is usually progressive and frequently causes blindness by cicatrization. Effective treatment is not known. (16 references.) Chas. A. Bahn.

Pasca, G. The value of Mester's reaction in ocular manifestations of possibly rheumatic origin. Boll. d'ocul. 27:439-455, July, 1948.

In 1937, Mester observed a definite relative leukopenia after injecting one cubic centimeter of a 0.1-percent salicylic acid solution under the epidermis of patients suffering from a rheumatic infection. Pasca applied this test to 97 patients of the Sassari Eye Clinic and describes the technique and results in detail. Twelve hours after a meal, five white blood cell counts are taken from an incision in the skin of the finger slightly more than 3 mm. deep. The average of these 5 counts is compared with a similar average obtained 30 to 60 minutes after the intradermal injection of one cubic centimeter of a 0.15 salicylic acid solution, divided into five wheels, each of which contains 0.2 cc. of the solution. Changes up to a 10-percent relative leucopenia were con-

sidered negative; 10 to 15 percent were charted as questionable, and those over 30 percent decrease as strongly positive. Three tables showing age, sex, clinical diagnosis, and additional clinical notes facilitate the comparison of the results of the Mester reactions with those of the Wassermann and tuberculin reactions. Among 50 patients with a possibly rheumatic eye disease 28 had a positive or stronger Mester reaction. Among 10 patients with unquestionably rheumatic disease, the Mester test was positive nine times. Among 27 patients with eye disease other than rheumatic none gave a positive Mester test. In ten subjects suffering from probably tuberculous eye disease the Mester test was always negative. (References.) K. W. Ascher.

Paufique, L., and Guinet, P. **The association of malignant exophthalmus, increased basal metabolism and Parkinsonism with Basedow's disease.** Ann. d'ocul. 181:665-675, Nov., 1948.

A 60-year-old man developed progressive nonreducible exophthalmos with Parkinsonism and greatly increased metabolic rate. After treatment with aminophylline, gardenal, and diethylstilbestrol the exophthalmus subsided and only a slight hypofunction of the right superior rectus persisted. The left eye was lost from exposure keratitis during a similar attack of exophthalmos. In the development of the symptom complex pituitary dysfunction, and not thyroid, seems dominant. Parkinsonism is discussed in some detail in its relation to numerous encephalopathies.

Charles A. Bahn.

Poos, E. E. **Psychosomatic manifestations in ophthalmology.** J. Aviation Med. 19:442-446, Dec., 1948.

Psychosomatic manifestations are in the main produced by stimulation of the sympathetic or parasympathetic systems. Conversion hysteria may manifest itself as hysterical amblyopia, amaurosis, blepharospasm, angioneurotic edema and photophobia. Convergence paresis and headaches following accidents are examples of neurasthenia. An anxiety state may cause a ciliary spasm.

Irwin E. Gaynon.

Satyasray, R. S., **Night-blindness.** Calcutta M. J. 45:272, July-Aug.-Sept., 1948.

The author is aware of the importance of vitamin A in night-blindness and discusses particularly and in detail the vitamin content of foods used in India.

F. H. Haessler.

Schepens, C. L. **Is tobacco amblyopia a deficiency disease?** Tr. Ophth. Soc. U. Kingdom 66:309-331, 1946.

The author reports on the incidence of tobacco amblyopia in Belgium before the war, when it was seldom found, and then on fifty times as many cases in 1942. He questioned whether it was due to the consumption of tobacco of poor quality, associated with the intake of adulterated alcohol or a deficiency of food. The patients who used the war-time home-grown tobacco suffered most severely. Alcohol consumption seemed to have little influence on the tobacco amblyopia. The moderate smoker who developed tobacco amblyopia was generally undernourished. The disease had occurred between the ages of 55 and 65 years but now was seen in subjects near the age of 30 years. It was frequently associated with emotional shock. Fundus alterations were found more frequently in the undernourished patients as were the general symptoms of tobacco intoxication. The form and position of the centrocaecal defect bears a relation to the cilioretinal angioscotomas. It expanded in all directions around the blind spot and tended

to be pericaecal instead of centrocaecal. The author believes that tobacco amblyopia occurs when the intake of toxic substances resulting from tobacco consumption exceeds the capacity of the liver to neutralize these poisons. The clinical picture was altered during the war because of the chronic undernourishment. The poison seems to act on the retina itself and not on the optic nerve. (12 figures.)

Beulah Cushman.

Simpson, Thomas. **Papilloedema in emphysema.** Brit. M. J. pp. 639-641, Oct. 2, 1948.

Three patients are described who had emphysema with bilateral papilloedema and engorgement of the retinal veins. The literature is briefly reviewed and the possible theories as to the causes of the papilloedema are discussed. A rise in general venous pressure does not provide a sufficient explanation and an intracranial factor is postulated. The author believes, from observations on animals and on his patients, that because of a lack of oxygen and an accumulation of CO_2 in the arterial blood of emphysematous patients, there is enough cerebral vasodilatation to raise the cerebrospinal fluid pressure to the level at which papilloedema ensues. The possibility that polycythaemia, which often appears in emphysema, could be a cause of the papilloedema is discarded by the author. His patients did not have a high red blood cell count. (2 tables.)   H. C. Weinberg.

Skinsnes, O. K. **Generalized ochronosis; report of an instance in which it was diagnosed as melanosarcoma with resultant enucleation of an eye.** Arch. Path. 45:552-558, April, 1948.

The remaining eye of a man was removed for pain and a blue-gray discoloration of the sclera. The preoperative ocular diagnosis was melanosarcoma but no neo-

plastic growth was found on a gross examination. The man died from what was interpreted as bronchopneumonia. Autopsy showed, among other findings, a marked dorsal kyphosis, arthritic fusion of the vertebrae, a marked raven-black pigmentation of all cartilages examined, less intense pigmentation of the endocardium and aortic endothelium, and a bluish discoloration of the ears and the fingernail beds. The first eye had previously been removed after trauma.

The eye had been removed because ocular ochronotic pigmentation had been mistaken for melanosarcoma. The triad of pigmentation of the ears and sclera, dark color of the urine, and arthritis is pathognomonic of ochronosis.

Francis M. Crage.

19

CONGENITAL DEFORMITIES, HEREDITY

Stadlin, W. and Klein, D. **Congenital ectopia lentis with spherophakia and brachymorphia accompanied by gaze paresis.** Ann. d'ocul. 181:692-701, Nov., 1948.

The above symptoms are called the syndrome of Marchesani. Four familial cases are presented to illustrate a genetic tree in which the parents were cousins, though not affected. In the patient most affected slight ptosis was accompanied by a defect of ocular elevation, small round lenses displaced upward, and limited movements to the left. The patient also had short small hands and feet and mental retardation. This syndrome is considered to be a dominant hypoplasia of mesodermal tissues. In the Marfan syndrome, in contrast, the principal symtoms are dolicocephaly, long fingers and toes, and ectopia lentis. Chas. A. Bahn.

Vrabec, F. **The pathogenesis of freely movable intraocular cysts.** Ophthalmologica 116:129-140, Sept., 1948.

The author found a small intraocular cyst in one eye of a 10-week-old human embryo. By means of a narrow stalk this cyst was connected with the marginal sinus of von Szily. In the wall of the cyst the very beginning of the differentiation of retinal pigment cells could be observed. Cystic formations which arise from the marginal sinus may, in the mature eye, be located in the anterior chamber or in the viterous cavity. The author favors the theory of origin of all congenital, free, intraocular cysts from the marginal sinus. (See Perera, Archives of Ophthalmology 18:1015, 1936.)

Peter C. Kronfeld.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Chavarría López, F. A. **Comment on ocular hygiene.** Arch. Soc. oftal. hispano-am. 8:985-987, Oct., 1948.

Chavarría points out the danger of ocular contagion from the trying on of sunglasses in optical shops. He suggests that the ophthalmological society work for legislation requiring that sun glasses be kept in tightly closed cases, kept sterile by formalin tablets. Ray K. Daily.

Hartmann, E. **Psychosomatic phenomena in ophthalmology.** Ann. d'ocul. 181:588-603, Oct., 1948.

Every ophthalmic function may be involved in psychosomatic disease. Among angiospastic disfunctions are migraine and numerous retinopathies with or without exudation and hemorrhages. Motor disturbances include blepharospasm, mydriasis, myosis and refractive changes. Sensory changes include photophobia as well as dysthesias; the chief secretory disturbance is lacrimation. The course of numerous structural diseases such as diabetes mellitus, hyperthyroidism, glau-coma and the phorias and tropias is modified by psychosomatic factors. A series of brief case histories illustrates the psychosomatic factor in several of the conditions mentioned as well as the results of understanding psychosomatic treatment. Chas. A. Bahn.

Livingston, P. C. **Visual protection in aerial warfare.** Brit. J. Ophth. 32:689-700, Sept., 1948.

The destruction of sight seemed to be so little feared by aviators that difficulty was experienced in persuading personnel to take reasonable precautions against ocular injury. Some methods of assuring eye protection were the use of bullet proof glass screens and armour plates fitted within the structure of the aircraft, of flight goggles fitted with safety glass, either plain or ground to prescription, or of contact lenses where refractive errors cannot be otherwise adequately treated. Visual training in the best use of the eyes in low illumination is also of considerable help. The record of eye injuries among the R.A.F. in flying operations justified the campaign against the hazard of loss of sight.

Morris Kaplan.

Melanowski, W. H. **The more important pages from the history of Polish ophthalmology.** Tr. Ophth. Soc. U. Kingdom 66:265-290, 1946.

The author outlines Polish ophthalmology from the year 1220 to the present time and describes the original work of many individuals in ophthalmology. In 1903, Galezowski, for example, presented before the French Ophthalmological Society results of his cautery of the tear in retinal detachment similar to those which Gonin described in 1929.

Twenty-seven ophthalmologists, other medical personnel, and university professors were murdered by the intruders

in the last war. Many of their hospitals have been burned down or robbed during the war, but postwar research is going on.

Beulah Cushman.

Redslob, E. The causes of blindness of twenty years ago and today. Ann. d'ocul. 181:535-543, Sept., 1948.

Surveys made in 1928 and 1948 in an institute for the blind, showed a decrease in gonorrheal ophthalmia and phlyctenular disease. Congenital affections, however, had increased. Pigmentary retinal degenerations rose from 3.8 percent in 1928 to 15 percent in 1948. Congenital glaucoma also increased. Several cases of amblyopia are briefly described; no objective symptoms were observed which accounted for visual impairment. Traumatic cases numbered approximately the same in both surveys. Chas. A. Bahn.

Rychener, R. O., and Robinson, A. Reading disabilities and the ophthalmologist. Tr. Am. Acad. Ophth. pp. 107-120, Nov.-Dec., 1948.

Primary reading disability is one of a seven syndrome complex of language developmental disorders as classified by Orton. Etiologically, reading has been shown to be a complex activity requiring the functional integrity and interplay of several brain areas, including the angular gyrus of the dominant hemisphere. Birth injuries and disorders of myelination of cerebral tracts are among the suggested etiologic factors. The problem, although mainly educational, is of interest to the ophthalmologist because it is he who most often sees the patient first, and who must recognize the condition and refer the patient to a reading clinic where proper treatment can be instituted. Diagnosis is based upon a careful history and a brief test in reading and spelling certain words which a poor reader most

often tends to jumble. Transposing such letters as B and D, P and Q, and reversing words, "was" for "saw," and "no" for "on," are common examples. The reading lists are prepared for various age and educational levels. Quantitative determinations of the severity of reading disability are made with the ophthalmograph. Evaluation of reading ability is made through determinations of words read per minute, fixations per hundred words, span of recognition, and comprehension. Two hundred and twenty-five patients with reading disability were investigated. Of these, 35 percent were definitely in need of remedial reading classes, 45 percent needed less rigorous treatment, and 10 percent were not amenable to treatment. In the latter group, the disability was attributable to convergence insufficiency. Correction of reading disability can be brought about through the the use of phonetic and kinesthetic training methods. Morale must be kept at a high level, and the patient's confidence in himself established. A bibliography on reading disability is presented to the patient in order that he may gain some insight into his problem. The patient receives a form letter which outlines the course of treatment. Chas. A. Bahn.

Somerville-Large, L. B. The first Irish ocular pathologist. Arthur Jacob—(1790-1874). Brit. J. Ophth. 32:601-617, Sept., 1948.

The life and ophthalmologic contributions of Arthur Jacob, great Irish oculist of the nineteenth century are presented in some detail. He founded two ophthalmic hospitals, a medical school, a medical journal and served as professor of anatomy and physiology for 41 years. He was the first to describe the nerve layer of the retina (membrana Jacobi) and the rodent ulcer of the lids (Jacob's ulcer). He read his "Account of a membrane in the eye"

before the Royal Society in 1819 in which he described a membrane attached to the retina and also attached to the choroid; apparently he was describing the neural layer only and he was quite widely acclaimed for his observations. In 1827 he published in the Dublin Hospital Reports "Observations respecting an ulcer of peculiar character which attacks the eyelids and other parts of the face." Here he described with much accuracy the condition now known as rodent ulcer and very little has been added to his description.   Morris Kaplan.

Williamson-Noble, F. A. **Adaptation to environment.** Brit. J. Ophth. 32:673-677, Sept., 1948.

The author considers the fitness of men for the task of ophthalmology and also the effect of ophthalmology on the men who practice it. Most men seem to go into medicine in rather a haphazard fashion and it is rather extraordinary that most doctors make good. Are we all worn into the same shape after 15 to 20 years of ophthalmic practice? The author examines the characteristics one may justifiably look for in an ophthalmologist of some years experience.

He became aware that his patients behaved much better than they did 20 years ago. First he ascribed it to improved pre-operative techniques but soon realized that it was he who had changed. His confidence in himself had increased and it was easier to impart this confidence to his patients.   Morris Kaplan.

Wright, W. D. **Colour vision, 1868 and 1948.** Brit. J. Ophth. 32:597-601, Sept., 1948.

A history of the acquisition and organization of our knowledge of color vision in which Sir John Parsons has played so great a part, is presented. In 1924 Sir John published his remarkable book on color vision. Of utmost importance has been the realization that study of color must consider the physical stimulus, the physiological reaction, and the psychological sensation.   Morris Kaplan.

HISTORICAL MINIATURE

Hirschberg (*Graefe-Saemisch Handbuch,* volume 13, pp. 330) points out the striking similarity between the outstanding British ophthalmographer who edited a second edition of a translation of Jacques Guillemeau's *Des Maladies de l'Oeil qui sont en Nombre de Cent Treize aux quelles il est Subject* in 1622 and his German counterpart, George Bartisch, who published his *Augendienst* in 1583. To Bartisch may be assigned almost the same place in German ophthalmology that is given to Hans Sachs in poetry.

Both Banister and Bartisch were characterized, on the one hand, by the narrow mindedness of the guild member, the jealousy of the competing tradesman, and superstition and, on the other, by sincerity, the proficiency of the skillful craftsman, a lively literary style, and a considerable poetic gift.

NEWS ITEMS

ANNOUNCEMENTS

WILLS CLINICAL CONFERENCE

The first annual clinical conference of the Wills Hospital will be held in Philadelphia, May 6 and 7, 1949. Members of the hospital staff and ex-resident physicians will provide the program which will consist of lectures throughout both days and an evening session on May 6. Eye operations will also be scheduled for both days.

Among the papers to be presented are: "Some practical facts regarding retinal surgery: With a report of results in more than 400 unselected and consecutive cases," Dr. James S. Shipman; "The surgical corrections of ptosis, congenital and acquired, when complicated by other oculomotor situations," Dr. Edmund B. Spaeth; "Causes of failure in the surgical treatment of glaucoma," Dr. John S. McGavic; "A followup concerning basket implants," Dr. Wilfred E. Fry; "Study of end results of glaucoma at the Wills Hospital, 1936 to 1948," Dr. Louis Lehrfeld; "Dibutyline sulfite: A comparative study of its cycloplegic effects," Dr. Bernard C. Gettes; "Further studies of the chemical and immunilogical properties of human tears," Dr. Irving H. Leopold; "Ophthalmoplegia·due to secondary malignancy at the orbital apex," Dr. Issac S. Tassman; "Diagnosis of syphilitic primary optic atrophy in the pre-atrophic stage," Dr. Joseph V. Klauder and Dr. George P. Meyer; "The optics of cylinder magnification," Dr. Joseph W. Hallett.

Guest speakers for the occasion will be Dr. Cecil O'Brien of The State University of Iowa, and Dr. Arthur J. Bedell of Albany, New York. At the conclusion of the conference the Wills Hospital Society of ex-Resident Physicians will hold its annual meeting.

ORTHOPTIC INSTRUCTION COURSE

The American Orthoptic Council announces the second annual course of instruction for orthoptic technicians. This course consists of two parts; the first, 9 weeks of lectures, demonstrations, and laboratory work by outstanding ophthalmologists and certified technicians, from June 25 to August 27, 1949, at Nasson College, Maine.

This basic instruction will be followed by the second part which consists of 6 to 12 months of practical work in clinics and offices, throughout the United States, under the supervision of certified orthoptic technicians. Completion of the full course will qualify the student to take the American Orthoptic Council examinations. For further information, write the American Orthoptic Council, 1605 22nd Street, N.W., Washington 8, D.C.

STRABISMUS SYMPOSIUM

A symposium on strabismus is to be held at the University of Iowa May 22 through 28, 1949. In addition to the regular staff of the department of ophthalmology the following guest lecturers will participate: Dr. Walter B. Lancaster, Boston; Dr. Francis H. Adler, Philadelphia; Dr. Harold W. Brown, New York City; Dr. Frank D. Costenbader, Washington, D.C.; Dr. Kenneth C. Swan, Portland, Oregon; Dr. George P. Guibor, Chicago; Dr. Richard G. Scobee, St. Louis; Dr. Walter H. Fink, Minneapolis, and Dr. Hermann W. Burian, Boston.

Further information regarding the details of the course may be obtained from Dr. James H. Allen of the department of ophthalmology, University of Iowa Medical School, Iowa City, Iowa. The registration fee is $150, and the enrollment will be limited to 25 physicians.

WAYNE GRADUATE DEGREE

Through the facilities of the College of Medicine, the Wayne University Graduate School, Detroit, is now offering graduate work leading to the degree of master of science in ophthalmology.

OXFORD OPHTHALMOLOGICAL CONGRESS

The Oxford Ophthalmological Congress will be held on July 7, 8, and 9, 1949, at Oxford, England. The Doyne Memorial Lecture will be given on this occasion by Professor Goldman of Berne, Switzerland. The main topic of discussion before the congress will be "Principles and practice in maintaining asepsis during ophthalmic operations."

ORTHOPTIC EXAMINATIONS

Applications for the examinations to be conducted by the American Orthoptic Council during September and October, 1949, will not be accepted after July 1, 1949. Until that date applications will be received by the office of the secretary, Dr. Frank D. Costenbader, 1605 22nd Street, N.W., Washington 8, D.C., and must be accompanied by the examination fee of $25.

MISCELLANEOUS

CLINIC FOR CORNEAL DISORDERS

A new eye clinic for diagnosis and treatment of corneal disorders has been established at the Manhattan Eye, Ear, and Throat Hospital, 210 East 64th Street, New York, as a coöperative undertaking sponsored by The Eye-Bank for Sight Restoration, Inc., and the hospital.

Under the direction of Dr. R. Townley Paton, the clinic meets at 9:30 A.M. every Wednesday morning when the patients are assembled and examined by Dr. Paton and his staff, including Dr. Herbert M. Katzin, director of the Eye-Bank Laboratory. They are assisted by a nurse, a nurse technician, a secretary, and a social worker.

The patients are referred to this clinic from the other eye services of the Manhattan Eye, Ear, and Throat Hospital, from other physicians, from public health organizations, and from some of the national and state societies for the prevention of blindness.

Complete records, including photographs and progress notes, are maintained. Visiting physicians are welcomed to observe the work of the clinic and to see the cases both before and after operation.

N.S.P.B. PROGRAM

At the 40th anniversary conference of the National Society for the Prevention of Blindness, the following program was presented.

"The battle against blindness," Mr. Mason H. Bigelow, president of the society; and "The next 40 years," Dr. Franklin M. Foote, executive director.

Dr. Conrad Berens, New York, chairman of the panel on "Conserving vision for old age," presented the following speakers: Dr. Edwin B. Dunphy, Boston, "How does middle age affect the eyes?"; Mr. Theodate H. Soule, New York, "Family and social problems of eye patients"; Dr. Henry L. Birge, Hartford, Connecticut, "Psychosomatic eye problems"; Dr. A. L. Chapman, United States Public Health Service, Washington, "What can the public health worker do?" Dr. Brittain F. Payne, New York, was discussant.

The panel, "Better sight for youth," had as its chairman, Dr. Leona Baumgartner, New York, and the speakers were: Dr. George N. Shuster, New York, "Vision in education"; Dr. Albert E. Sloane, Boston, "Sight as it affects the power to learn"; Mr. C. L. Crouch, New York, "Lighting the classroom."

The chairman of the panel on "Teaching the child with defective eyesight," Dr. Frank J. O'Brien, New York, introduced: Dr. Hunter H. Romaine, New York, "Reading and eye trouble"; Dr. Romaine P. Mackie, Washington, D.C., "The partially seeing child in urban and rural areas." Dr. Vivian Ellis, Albany, New York, was the discussant.

The panel, "Vision in industry," had as chairman, Mr. W. J. Niederauer, New York, who presented the following speakers: Mr. R. L. Otten, Baltimore, "What an eye program can do for management"; Dr. Ralph S. McLaughlin, Charleston, West Virginia, "The ophthalmologist's contribution to industry"; Mr. L. M. Endres, Washington, "Using light and color"; Mr. A. G. Bungenstock, Kearny, New Jersey, "Promoting eye safety"; Cmdr. R. Roswell Sullivan, "The Navy eye program."

Dr. Eugene M. Blake, New Haven, Connecticut, was chairman of the panel on "Medical progress in eye health." Speakers on this panel were: Dr. V. Everett Kinsey, Boston, "Retrolental fibroplasia"; Dr. Joseph Warkany, Cincinnati, "Congenital abnormalities of the eye: Some etiologic considerations"; Dr. Frank D. Costenbader, Washington, "Treatment of crossed eyes"; Dr. Alan C.

Woods, Baltimore, "Pigment degeneration of the retina"; Dr. Dorland J. Davis, Bethesda, Maryland, "Epidemic sore eyes in the Rio Grande Valley."

Dr. Willis S. Knighton, New York, was moderator for the panel discussion on "Glaucoma: An increasing public health problem." Dr. Solomon S. Brav, Philadelphia; Miss Margaret Gnade, Pittsburgh; and Miss Helen E. Weaver, New York, discussed "What needs to be done about glaucoma?" Mr. Erik Barnouw, New York; Mr. Willard Van Dyke, New York; and Miss Jane Stafford, Washington; discussed "How can the average citizen be warned about the danger of glaucoma?"

Miss Helen Keller was guest of honor at the conference dinner at which Dr. Marcus D. Kogel, New York, spoke on "The place of the hospital in preventive medicine," and Dr. John Z. Bowers, Washington, spoke on "Atomic energy and eyesight."

ORTHOPTIC CLINIC DEDICATED

On February 4 the Barbara Gregg Ingalls Orthoptic Clinic was dedicated at the Medical College of Alabama in the Thigpen Eye Hospital. It was named in honor of the granddaughter of Mr. Robert I. Ingalls, Sr., industrialist-philanthropist, who has indicated a continuing interest in the clinic. Orthoptic examination and treatment are now offered without charge to the indigent children of Alabama.

WILLS HOSPITAL APPOINTMENTS

Dr. Carroll R. Mullen has been named executive surgeon to the Wills Hospital. This position has not been filled since the death of the late Dr. J. Milton Griscom. Dr. P. Robb McDonald has been appointed attending surgeon to the Wills Hospital succeeding Dr. Frank Parker, who has retired after 49 years of continuous service to this institution. Dr. Warren S. Reese has been elected president of the board of attending surgeons, Dr. James S. Shipman is vice-president, and Dr. Wilfred E. Fry is secretary.

SOCIETIES

MILWAUKEE CLINICAL PRESENTATION

The February 15 meeting of the Milwaukee Oto-Ophthalmic Society was held at the United States Veterans Hospital. Those making clinical presentations of ophthalmic cases were: Dr. George Roncke, Dr. Arvid Holm, Dr. Thomas Burns, Dr. Erwin Grossmann, and Dr. John Hitz.

CENTRAL ILLINOIS MEETING

The next meeting of the Central Illinois Society of Ophthalmology and Otolaryngology will be held at the Pere Marquette Hotel, Peoria, Illinois, on April 22, 23, and 24, 1949.

Dr. Donald J. Lyle, professor of ophthalmology, University of Cincinnati, will give lectures on: "Clinical diagnosis of lesions of the visual system," "Eye involvement resulting from head in-

juries," "Clinical study of vascular affections of brain and eye."

Dr. B. E. Ellis, associate professor of otolaryngology, Indiana University, will lecture on "Congenital cysts of the head and nasal bridge," "Congenital cysts of the neck," "Rhinoplasty procedures in the practice of otolaryngology."

Mrs. Ben Humphrey Gray, executive secretary of the Illinois Society for the Prevention of Blindness, will speak on the school visual screening program in Illinois.

READING MEETING

The 90th meeting of the Reading Eye, Ear, Nose, and Throat Society, held February 16th, was the fifth annual joint meeting of the Diplomates Association of Berks County Physicians and the Reading Eye, Ear, Nose, and Throat Society. The speaker was Dr. Stephen S. Hudack of New York who discussed "Restoration of joints with articular replacement and changing concepts in the mechanism of bone healing."

WILMER RESIDENTS ASSOCIATION

On the program of the eighth clinical meeting of the Wilmer Residents Association, April 6 to 8, at the Wilmer Institute, Baltimore, are:

"Classification and special symptomatology of uveitis," Dr. Alan C. Woods; "Surgical correction of horizontal strabismus: A new concept of the mechanics involved," Dr. Jack S. Guyton; "Some ocular effects of a new anticholinesterase agent, tetraethyl pyrophosphate (T.E.P.P.)," Dr. William G. Marr; "Modern status of antibiotics," Dr. Perrin Long; "A new variety of corneal pigmentation," Dr. Robert C. Laughlin; "Vitamin E studies in relation to retrolental fibroplasia," Dr. William C. Owens and Dr. Ella Uhler Owens; "Polysaccharides in ocular tissue," Dr. Robert Day; "Histochemical localization of choline esterase in ocular tissue," Dr. George B. Koelle.

"Heparin and ocular hypersensitivity," Dr. Malcolm W. Bick and Dr. Ronald Wood; "The etiological diagnosis of uveitis," Dr. Alan C. Woods; "Sympathetic ophthalmia following intraocular surgery," Dr. Howard A. Naquin; "New radon and radium-D applicators," Dr. William F. Hughes, Jr.; "Corneoscleral trephine and intracapsular extraction in one procedure for primary glaucoma combined with cataract," Dr. Angus L. MacLean; "Inhibition of mitosis in the corneal epithelium by ionizing radiation," Dr. Jonas S. Friedenwald; "Cataract section following filtering operations," Dr. Russell T. Snip; "A battery-handle extension for the Bausch and Lomb ophthalmoscope," Dr.

Norman R. Davis; "Surgical management of the iris," Dr. John M. McLean; "The anatomy of neurologic defects in pituitary tumor," Dr. Frank B. Walsh.

"Selection of operation in acute glaucoma," Dr. Herman K. Goldberg; "Treatment of uveitis," Dr. Alan C. Woods; "Surgery of the horizontal recti: Approach through a concealed conjunctival incision," Dr. Jack S. Guyton; "Total color blindness," Dr. Louise L. Sloan and Miss Lorraine Wollach; "Demonstration of new retinal recording methods from the intact eye," Dr. Carlton C. Hunt, Dr. Stephen W. Kuffler, and Dr. Samuel Talbot; "Prognosis for vision in anoxia," Dr. Walter H. Benedict; "Use of radioactive indicators for study of aqueous humor," Dr. Roy O. Scholz; "Changes in intraocular pressure following miotics," Dr. Rufus C. Goodwin; "The effect of retrobulbar alcohol injections on the eyes of experimental animals," Dr. Walter Kornblueth; and "Clinical pathological conference," Dr. Jonas S. Friedenwald and Dr. Howard A. Naquin.

PERSONALS

TULANE UNIVERSITY LECTURER

Dr. F. L. P. Koch discussed "The eye in internal medicine," at the postgraduate course in general medicine conducted recently at the School of Medicine of The Tulane University of Louisiana.

RECEIVES DANA MEDAL

The Leslie Dana Gold Medal for 1948, a national award given annually for outstanding achievement in the prevention of blindness and the conservation of vision, was presented on March 25th at a dinner in St. Louis to Dr. Lawrence T. Post of that city.

Dr. Post was selected for this honor by the St. Louis Society for the Blind, through which the medal is offered by Mr. Leslie Dana of St. Louis. This important award in the field of public health is given upon the recommendation of the Association for Research in Ophthalmology.

ERRATUM

The hormone referred to in the discussion by Dr. P. Robb McDonald on page 281 of the February, 1949, issue of the JOURNAL should have been the melanophore expanding hormone of the pituitary gland instead of Marfan's hormone, as reported.

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CONTENTS

SURGICAL TREATMENT OF TUMORS AND CYSTS OF THE ORBIT*

THE ELEVENTH DE SCHWEINITZ LECTURE

WILLIAM L. BENEDICT, M.D.

Rochester, Minnesota

My participation in the series of lectures sponsored by this society in memory of Dr. de Schweinitz is an honor that I look upon with high regard and with appreciation of the broad interests of the ophthalmologists of Philadelphia. My training in clinical ophthalmology was acquired under the tutelage of Dr. Walter R. Parker at the University Hospital in Michigan. Dr. Parker was a University of Pennsylvania (1891) and a Wills man, and was thoroughly a Philadelphia product. Those of us who served under Dr. Parker as internes and assistants considered ourselves as somehow connected with the Philadelphia school of ophthalmology. We were concerned with the activities of the University of Pennsylvania and of Wills Hospital with an interest that could not have been exceeded if we had been serving there in residence, for our chief, a graduate of both institutions, was as much a part of them as any loyal alumnus could be. We became familiar with the names of the chiefs of the ophthalmic services in all of the Philadelphia medical colleges and hospitals, and we felt a loyalty to these men. A few years after my residency, the University of Michigan conferred the honorary degree, Master of Science, on Dr. de Schweinitz, (1923) and I held a pardonable personal pride on this occasion.

It was during the first World War, when my chief and his close friend, Dr. de Schweinitz, served together in the office of the Surgeon General of the Army, that I met and had my first personal contact with a man whose work as a teacher and as an administrator I had come to admire. When I assumed the duties of head of the Section on Ophthalmology at the Mayo Clinic, in 1917, my first thought was to interview Dr. Parker and Dr. de Schweinitz, and the organization of the work of my section could easily be recognized as a grandchild of the Philadelphia-Michigan system.

May I say now that the invitation to address you on this occasion seems to me like an invitation to attend a family reunion as one of the poor relations, but one who, nevertheless, has his heart in it. To the section, and your committee on selection of speaker for this occasion, I humbly offer my sincere thanks for thinking of me.

The possibilities of improved surgical treatment of tumors of the orbit have intrigued general surgeons as well as ophthalmologists during the period of development of surgical practices for the relief of blindness and other ocular disturbances resulting from abnormal growths about the visual pathways. The anatomic limitations of the orbit are definitely set by its bony walls, and the field of surgical procedures by the ophthalmic surgeon has been thereby limited.

Neurosurgeons, however, have accepted no such limitations to their field of activity. Late comers to the field as they are, never-

theless, their progress has been remarkable in the field of ophthalmology. The general surgeon has abandoned the central nervous system and its disorders to this newly specialized group of surgeons, and now the field of surgery of the head is allocated to the neurosurgeon, the ophthalmologist, and the otorhinologist.

Unfortunately the anatomic barriers of the orbit that have so clearly defined the surgical field of the ophthalmologist have not limited the extent of involvement of pathologic processes that disrupt functions of the brain and especially involve the eye and the orbit. The diagnosis of these processes for the most part has remained within the province of the ophthalmologist and, in collaboration with the neurosurgeon, the newer methods of surgical treatment have brought about most gratifying results in conservation of vision and in the treatment of many of the tumors and cysts that affect the visual pathways.

DIAGNOSIS OF TUMORS OF THE ORBIT

Space-taking lesions within the orbit produce exophthalmos. The amount of proptosis of the globe and direction of its displacement only in general indicate the size and position of the lesion within the orbit. The rigid orbital walls constitute a barrier to expansion of a lesion but do not prevent extension through the bone of such tumors as meningioma and hemangioma.

The onset of proptosis may be an early or a rather late sign of an intraorbital growth. A tumor that grows readily within the orbit forces a change in the position of the eye within a few days or weeks but, in some cases of orbital tumor, it has been observed that, due to its slow development and adjustments within the orbit, proptosis and lateral displacement of the globe occur only after the tumor has reached a size equal to that of the globe or larger. However, in such cases, when proptosis finally occurs, it is usually marked and rapidly progressive.

The extent to which the optic nerve and the extraocular muscles may be pushed aside is quite remarkable in some cases of slow-growing tumors. A minimum of disturbance of visual function is sometimes seen in an orbit which contains a tumor of such size that it seems unbelievable that it could exist without producing more obvious displacement of the globe.

The question of extraorbital extension of a tumor is always present and seldom easily answered before surgical intervention. This is particularly true of tumors situated in the posterior portion of the orbit.

Types of tumors that are common to both the orbit and the cranial cavity, such as endotheliomas, may be present in both places. Hemangiomas and endotheliomas that arise within the orbit are not always limited to the orbit but may extend into the cranial cavity or the paranasal sinuses with little discernible evidence of their having done so. Obviously surgical treatment of such conditions must be planned on a basis broad enough to care for any extension that may be found. Failure to do so has resulted in many surgical tragedies.

As has been pointed out by Spaeth[1] and other writers on orbital surgery, the common factor of all space-taking lesions of the orbit is exophthalmos, so it is quite clear that exophthalmos, particularly when it is bilateral, cannot always be an indication of neoplasm. Inflammatory diseases of the orbit, Mikulicz's disease, and some of the blood dyscrasias also produce exophthalmos.

Metabolic diseases, especially goiter, are usually recognized by general systemic changes in addition to the ocular signs which in most instances are bilateral. Although the exophthalmos is distinctive in some cases of hyperthyroidism and the exophthalmos may be accompanied by lid retraction, chemosis, and disturbance of the function of the extraocular muscles, goiter is not usually considered in the case of a patient who experienced none of the systemic symptoms of the disease. Yet, in a patient whose history is negative for exophthalmic goiter and whose

basal metabolic rate is normal, unilateral exophthalmos due to toxic goiter is not uncommon, as is shown by the changes in the extraocular muscles seen on microscopic examination.

The difficulty of distinguishing between tumor of the orbit and the inflammatory and metabolic causes of exophthalmos cannot always be overcome even with all of the refinements in diagnosis. In such cases, surgical exploration of the orbit may be justified on a presumptive diagnosis of tumor, when there are no important contraindications to operation and when loss of vision or other serious damage seems imminent.

The orbit may be explored by several methods of approach without much risk to life or vision and with little or no resulting deformity. Indeed the involved surgical risk may be a small price to pay for the advantage of a confirmed and accurate diagnosis because, in the treatment of malignant neoplasms anywhere in the body, there is a great advantage in early acquisition of all information by whatever means.

Exophthalmos is not the only indication of space-taking lesions of the orbit. Disturbance of ocular motility and loss of vision, existing either alone or together with exophthalmos, are common to tumors and cysts of the orbit and to cellulitis, pseudotumors, and trauma. Often several confusing and contradictory signs appear that make it impossible at a given moment to make a definite diagnosis. The conditions involved are probably more common in the experience of the ophthalmologist than of the neurosurgeon and the decision on surgical intervention must be left to the ophthalmologist when the significance of the orbital signs are inconclusive and the cause is in doubt.

SURGICAL PROCEDURES

It is incumbent on the ophthalmologist to determine when surgical treatment of orbital disease is indicated and what type of approach can be used to the best advantage.

The latter requires judgment based on experience because of a dual purpose in operating. If the condition suspected is found, the operation serves as means of a cure but, if something else besides the suspected condition is found, the surgeon must be prepared and equipped to proceed to do what is necessary and to complete the operation, if possible, rather than to withdraw from the field after a fruitless entry. The opening of the orbit for biopsy only is poor practice and should be discouraged.

Of the surgical approaches to the orbit, the most direct is through the outlet, the anterior opening.[2] Resection of the lateral wall of the orbit is but a modification that is useful in certain cases. "For the removal of tumors that are definitely confined to the orbit, even in the posterior third, the frontal or the Krönlein operation may be entirely adequate, as has been proved many times. However, one seldom can be certain that a tumor known to be in the apical portion of the orbit does not extend beyond the orbital walls, or where its origin might be."[3]

The orbit, from the standpoint of surgical approach, may be roughly divided into an anterior third, posterior or apical third, and a middle portion. The entire orbit may be explored through a frontal approach, but the removal of a tumor originating in the posterior one third of the orbit or of a tumor of the optic nerve without removal of the eye is extremely difficult. If the transcranial approach is used, the task is less complicated.

Tumors of the anterior third, particularly of the lateral and inferior portions, as well as those that lie along the superior wall, can be most satisfactorily removed by way of the frontal or the frontolateral approach.

Tumors of the posterior third can be reached more directly by a transcranial approach where the operator can work under direct vision. The transcranial route permits full exploration of the orbit after removal of the roof, and it is possible to explore the orbit further anteriorly by direct vision

through the transcranial route than it is to explore the apical portion backward through the orbital outlet. Adequate removal of tumors that arise within the orbit and extend through bone or through the fissures into the cranial cavity can be accomplished only by the transcranial route. By this method, resection of the entire roof and the lateral wall of the orbit and uncovering of the op-
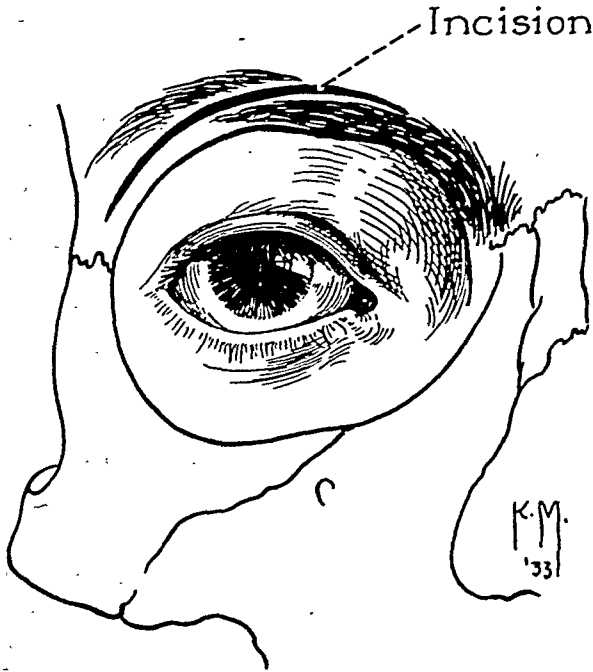
Fig. 1 (Benedict). The incision is made through the skin and periosteum parallel with and 5 mm. above the rim of the orbit on the superior temporal side. (Republished with permission. From Benedict, W. L.: Removal of orbital tumors. Surg., Gynec. & Obst., 58:383-389 [Feb. 15] 1934.)

tic canal is often necessary and can be done without serious damage to the orbital contents.

The attempt to save all ocular function as far as possible makes it necessary to dissect close to the tumor within its capsule and, when the frontal approach is used, much of the dissection must be done by touch rather than sight. The important matter is to remove the tumor with as little trauma as possible and leave the question of the origin of the tumor to be decided after the histopathologic examination. Immediate pathologic examination of frozen sections has proved to be most helpful in determining how extensively the resection of tissue surrounding the tumor should be carried out.

SURGICAL ZONES

Within the orbit the anatomic structure of the soft tissues forms three divisions: the subperiosteal, the intramuscular cone, and the space between the two. Tumors or cysts arising within any one of these divisions tend to expand within fibrous capsules or delimiting membranes, pushing aside surrounding structures without actually infiltrating them and, for the most part, they tend to remain within the zone in which they originate. The chief exception to this rule is the metastatic or invading carcinoma of the mixed basal-cell and squamous-cell type; also, the dermoid and some forms of neurofibroma are exceptions.

It is not my intention to describe the technique of various surgical operations on the orbit, except as it is necessary to the understanding of a surgical procedure recommended for a special purpose.

The size and position of a tumor lying in the anterior third of the orbit will largely determine the method of frontal approach. Such a tumor obviously lies outside the muscle cone. The greater number of tumors in the anterior part of the orbit lie above or temporal to the globe and can be reached by direct frontal approach. A large number of the tumors in this region are encapsulated hemangiomas, low-grade adenocarcinomas, and neurofibromas.

One method of approach is through the conjunctival cul-de-sac along the temporal rim of the orbit after a small canthotomy. Since the tumor lies outside of the muscle cone, it is not necessary to divide the external rectus muscle as illustrated in some texts and motion pictures. The tissues are flexible and the eye can be pushed aside and rotated toward the nose, affording plenty of room for operating.

After exposure of the tumor by sharp dissection, it should be separated from its capsule by blunt dissection and delivered

by gentle pressure from below by the blades of blunt scissors or a hemostat. Adherent tissue, including the capsule, should be trimmed close to the tumor and left in place. Unnecessary damage to the surrounding tissue should be avoided. The incision may be closed without drainage and a pressure dressing applied until danger of bleeding is past. Full recovery without deformity or disfigurement usually follows with a minimum of inflammatory reaction.

Moderately large encapsulated tumors of the lacrimal fossa, those situated in the dome of the roof, and those along the nasal wall may be reached more easily by the frontal approach through a brow incision.[4] I have described the technique of this operation elsewhere and an illustrated description of the method appears in Spaeth's textbook on ophthalmic surgery (page 95—figures 1, 2, and 3). This method is also used for extraperiosteal tumors.

For the removal of any tumor that should be removed by the frontal route, adequate space is made available by depressing the orbital contents. If the tumor is found to be too large or extends too far posteriorly for separation and removal in the available space, the frontal wound should be closed and the transcranial or some other suitable route employed.

Resection of the lateral wall of the orbit (Krönlein's operation) affords a little more room to work than the frontal route through the brow incision. It is most helpful in operating on orbits with small outlets for tumors situated in the posterior third of the orbit.

Tumors of the optic nerve have been successfully removed with preservation of the eyeball by the Krönlein method. Successful removal of tumors of the optic-nerve sheath, with preservation of vision, by the Krönlein method has been reported, but we now know that such tumors can be more easily removed under direct vision by the transcranial operation.

Although it is not possible to know the type of tumor, the size, and its probable situation, and, in some cases, whether it extends beyond the walls of the orbit can be determined with reasonably certainty. Some types of tumors predominate in one of the three anatomic devisions.

In the muscle-cone zone, tumors of the optic nerve and its sheath, endotheliomas, and the extension of retinoblastomas along
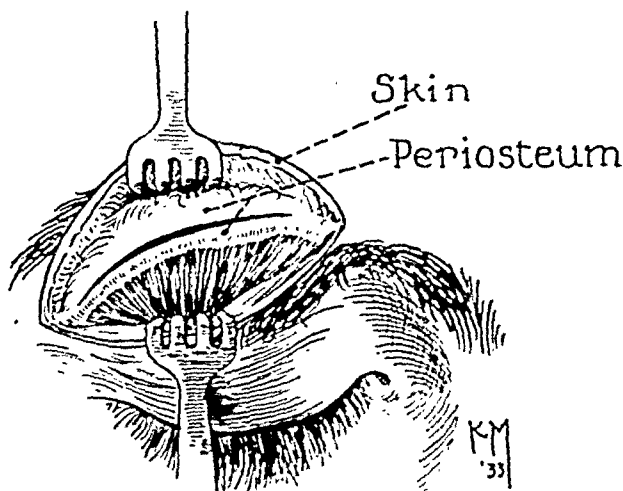
Fig. 2 (Benedict). The periosteum along the orbital rim and its extension, the periorbita, are separated from the bone with a nasal septal elevator. (Republished with permission. From Benedict, W. L.: Removal of orbital tumors. Surg., Gynec. & Obst., 58:383-389 [Feb. 15] 1934.)

the optic nerve predominate.[5] Metastasis of carcinomas to the optic nerve have been reported but are rare. Tumors situated in the muscle cone are characterized by progressive proptosis, early visual loss, and edema of the lids without lateral displacement of the eye. Movements of the eye are not usually impaired to the extent of producing diplopia. We have not encountered bilateral tumors of this type, but bilateral orbital tumors can be removed in one stage by utilization of the coronal or Souttar flap.

In the subperiosteal zone the most common tumors are osteomas, which have their beginning in the paranasal sinuses, and meningiomas that extend into the orbit from the cranial cavity.

The term, "osteoma," should be reserved for the bony tumors of the sinuses which

invade the orbit. They are always rounded and covered by a mucous membrane continuous with the lining of the sinus from which they originate. They are said to expand along the lines of least resistance and are to be found in the cranial cavity or the orbit or both. They are, of course, extraperiosteal and extradural. A large osteoma of the orbit may extend well into the cranial cavity, push the dura-covered cerebrum before it, and erode the frontal bone, and yet produce no signs or symptoms except exophthalmos.

Osteomas are pedunculated on a base in the thin walls of the sinus and are, as a rule, easily removed by dividing the peduncle. Recurrences are rare. Osteomas of the orbit are objectionable only when they become large enough to cause proptosis, or in some manner to interfere with the movements of the eye. They grow very slowly and removal is not an urgent matter.

In our series of orbital tumors there were 38 osteomas of the orbit, 19 of which were operated on and removed by the frontal method with no fatality. One patient had postoperative rhinorrhea and died of meningitis two years afterward.

Hyperostosis of the bones of the orbit when accompanied by thickening of several bones of the skull, especially the facial bones, is not a surgical condition; acromegaly is an example. The roentgenogram shows very clearly the type of bone disturbance in any case of bone tumor but the diagnosis is always clearer in osteoma than in hyperostosis from any cause because of the distinct outlines of the osteoma and the absence of other than local symptoms.

Of the three bony disorders of the extraperiosteal division, only the osteoma can be removed by the frontal route. Hyperostosis and exostosis call for transcranial surgical removal.

The bony roof is sometimes eroded by cranial meningiomas but in 25 percent of cases the bone is infiltrated by the tumor and hyperplasia appears in the roentgeno-gram as hyperostosis. This is an important diagnositic sign of cranial meningioma but not pathognomonic, since vascular tumors may also produce such a hyperostosis.

When hyperostosis of the sphenoidal ridge is present, one cannot say whether the tumor originated within or outside the orbit. Very seldom, however, does a meningioma arising within the orbit produce a hyperostosis of the sphenoidal ridge. Therefore, in patients who do present hyperostosis of the orbital roof, the frontal method of approach is contraindicated.

Prior to the introduction of the trans-cranial method of approach to the orbit, complete exenteration of the orbit was done for orbital tumors even with extensive hyperostosis. The results of the operations were not encouraging, for in no instance could the entire tumor be removed. Bone tumors of the orbit other than hyperostosis can usually be completely removed by the frontal approach through a brow incision as previously mentioned.

The greatest number of primary tumors of the orbit arise in the middle zone, between the periorbita and the muscle cone. It is often impossible to trace the origin of an orbital tumor but, in most cases, one can say that it was situated in one of the three anatomic divisions.

From the records of the Mayo Clinic it has been shown that in the years 1907 to 1947, inclusive, there were 3,190 patients who had tumors of the eye or the adnexa or both, of whom 740 had tumors of the orbit. Thirty-three types of tumors were diagnosed pathologically, while a few were indeterminate. Most of them were primary tumors of the orbit in various stages of development. Operation was performed on a total of 420 by methods best designed to meet the demands of the situation. The transcranial method was employed in 48 cases from November 6, 1933, through December 31, 1947. Analysis of data on orbital tumors removed transcranially showed that in 28 cases the tumor was entirely within the orbit;

whereas, in 17 cases there was intracranial extension. In 3 cases there was extension into adjacent bone or into the frontal sinus and in 1 case even into the nose. There was only 1 death in the series.

A comprehensive report on the menin-

and must be differentiated from intraorbital tumors. They may have extended into the orbit through an enlarged superior orbital fissure or by destruction of the bone and penetration into the orbit.

In 17 cases, primary intraorbital menin-
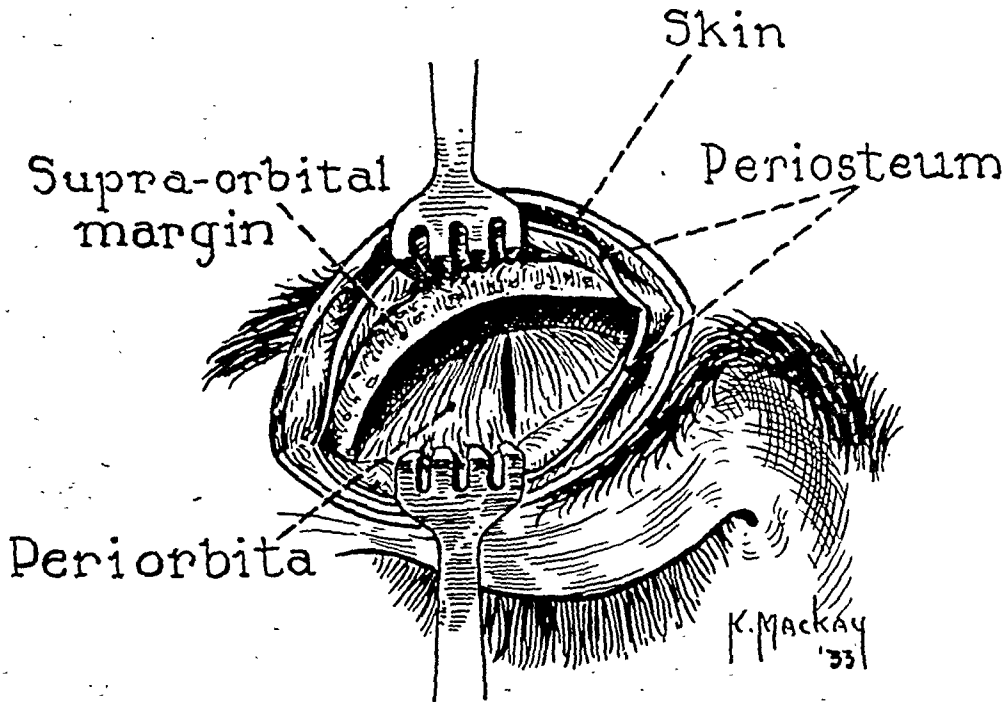
Fig. 3 (Benedict). The periorbita is pulled forward and down so that the contents of the orbit can be palpated and the tumor located. The incision through the periorbita can be made at the most advantageous place. On closure of the wound, the edges of the periorbital incision are reunited with catgut, the periosteum is reattached above the rim of the orbit with fine catgut, and the skin incision is closed with silk. The skin does not come in contact with the bone, and so, deep scarring is avoided. (Republished with permission. From Benedict, W. L.: Removal of orbital tumors. Surg., Gynec. & Obst., 58:383-389 [Feb. 15] 1934.)

giomas of the orbit operated on at the Mayo Clinic shows that the origin of these tumors still is a somewhat controversial subject. Whether they are truly primary growths arising from the coverings of the intra-orbital part of the optic nerve, and possibly from the other structures within the intra-orbital cavity, or whether they merely extend into the orbit from a similar growth within the cranium has been, and still is, a moot point.

As was clearly brought out by Cushing, meningiomas possess a tendency to expand along lines of least resistance and force their way into "all anatomical crannies and pockets." Meningiomas of the sphenoidal ridge may cause unilateral exophthalmos

giomas have been recognized and treated surgically at the clinic. All were verified microscopically and were studied carefully to establish their identity as essential primary intraorbital growths. The presenting clinical signs and symptoms consisted of visual impairment, a measurable proptosis, and headache. Either visual failure or proptosis or both were present in every instance. Visual impairment was present in 14, proptosis in 13, and headache in 5 cases.

In 35 cases, meningiomas were found to have invaded the orbit from an intracranial source. In both groups the lesions were more common in women than in men by a ratio of 4:1.

This series suggests that primary tumors

are likely to be encountered at much the same age as are secondary, or invading, neoplasms, and as are meningiomas elsewhere. The order in which proptosis and visual impairment may appear does not serve as a reliable aid in distinguishing the intraorbital meningiomas from other intraorbital lesions. Roentgen changes about the orbit are usually suggestive of an invading type of intraorbital meningioma. The transcranial route of approach best meets any contingencies which may arise in the attack upon these tumors.

The greater number of orbital tumors of this series of 490 cases were removed by the frontal approach. They were situated mostly in the middle division of the middle and anterior zones and were operated on by whatever method gave promise of the best results.

Of the 420 operations for orbital tumor, 32 were for epithelioma of the face with secondary involvement of the orbit. Some began as epithelioma of the eyelids, others of the caruncle, that extended into the orbit along the periosteum after repeated excisions, cauterization, and irradiation had failed to halt their progress.

Epitheliomas of the squamous-cell type are prone to extend to bone where they become fixed. They not only spread along the periosteum but actually invade the bony walls of the orbit causing marked necrosis. Extensive removal of bone sequestra and cauterization of the soft parts must be carried beyond the limits of tumor invasion. Exenteration of the orbit was required in 7 of the 32 cases. Surgical removal of neoplastic tissue may be followed by irradiation with good effect.

Generalized metastasis from squamous-cell epithelioma is rare, although occurrence of other primary neoplasms of different types is not uncommon. Adenocarcinoma of the breast and neurocytoma of the brain were seen as examples of primary tumors following some years after exenteration of the orbit, in one case for squamous-cell

epithelioma and in another for melano-epithelioma.

The frontal approach was used in 340 cases of orbital tumor. In this group, there were 40 exenterations of the orbit for extensive neoplasm and 10 were by the Krönlein method. These tumors had their origin within the orbit. These included, somewhat in order of their frequency, carcinomas, sarcomas, hemangiomas, dermoid cysts, endotheliomas, and a number of rare tumors encountered only 1 to 5 times in the series.

The most common location of carcinomas was in the superior temporal quadrant. For the most part they were associated with the lacrimal gland or the accessary lacrimal glands and were of two types, mixed tumors and cylindromas.

The adenocarcinomas occurred in a variety of sizes and degrees of malignancy. Many of them were entirely encapsulated, were only loosely attached to the lacrimal gland, and, when removed, showed no tendency to recur. The most malignant type of adenocarcinoma becomes fixed to the bony orbit through the periosteum early in its course and, by the time exophthalmos is produced, the tumor has spread well back along the walls of the orbit and in many cases has invaded the bone as well. Such tumors maintain their glandular activity and, as they progress by direct extension, will form cysts of considerable size.

One patient with adenocarcinoma of the orbit was reoperated on 3 times at 5-year intervals. At the second and third operations, only a small amount of neoplastic tissue was found, but between the skin and the dura much of the frontal bone had sequestrated and in this region cysts containing 1 to 3 ounces (30 to 90 cc.) of fluid were formed.

The adenocarcinomas that arise in the orbit expand by direct invasion of neighboring tissue but seldom give rise to generalized metastasis. The so-called mixed tumor grows more slowly, is less malignant, and is not accompanied by the severe necrosis of bone as seen in other types of carcinoma.

In this series of eye tumors there were 43 metastatic tumors, 19 of which reached the orbit but only 1 of which was removed. Most of the metastatic tumors were carcinomas from the stomach, breast, and intestinal canal. All were highly malignant and were seen late in the course of the disease as a part of general metastasis.

Melano-epitheliomas are common about the lids, conjunctiva, and the uveal tract. They form a very interesting group of tumors that have their origin in and about the eye and invade the orbit by direct extension. Of 333 patients who had melanomas, benign and malignant, 12 percent had tumors of the orbit.

In a few cases the orbit was invaded by direct extension through the sclera from melanomas of the choroid. Others were primary in the caruncle and conjunctiva. A few melanomas were found deep in the orbit and, so far as could be determined, were primary tumors. It is unfortunate that we have no way of determining the degree of malignancy of melanomas. One cannot predict from the microscopic appearance of a melanoma whether it will metastasize or remain dormant.

I have reported elsewhere on a patient with extensive malignant disease of the right orbit with deep melanosis of the conjunctiva, the mucous membrane of the mouth, nares, and nasopharynx of the same side. Exophthalmos was noted when the child was about 8 years of age. By the time he was 14 years of age, and after several years of roentgen therapy, the right orbit was exenterated because of a large melanoma which caused extreme exophthalmos and loss of the cornea. A complete exenteration of the orbit was done but necrotic pigmented tissue remained at the fissures and the apex and could not be removed. Tissue removed was diagnosed as Grade 4 melano-epithelioma. After 20 years, the orbit gradually has filled in and the outlet is practically covered by skin. The melanosis of the mucous membrane of the nose and the mouth remains practically unchanged and there has been no extension, no recurrence, and no metastasis.

In another patient the right eye was removed because of an intraocular neoplasm shown to be malignant melanoma. The sclera was perforated in many places by the neoplasm which, however, did not extend deeply into the orbit. At the time of enucleation, the orbit was clean. Within six months after the enucleation, the conjunctiva of the socket was studded with 8 isolated, deeply pigmented nodules of melanoma that were from 3 to 8 mm. in size. For the past six years there has been no change in the size or appearance of these melanomas. The patient wears an artificial eye but there is no evidence that the pigmented nodules are irritated by rubbing. There are no metastatic lesions anywhere in the body and the patient is, so far as general examination shows, entirely free from evidence of melanoma elsewhere in the body.

These rather extreme examples of arrest of what appeared to be Grade 4 malignant neoplasms are not explained by histopathologic examination of the tissue. The malignancy of the neoplasm bears no relation to the amount of pigment contained. There is ample clinical evidence to show that in some individuals melanomas take on a high degree of malignancy and give rise to extensive metastasis and, in others, the growth of malignant neoplasms becomes halted and their activity is stationary, at least for a number of years. Except for melanomas of the uveal tract which are most commonly limited to the eyeball, there is very little clinical or histopathologic indication for wide surgical removal of melanotic tissue.

The very rapid and extensive metastasis of melanomas in other cases illustrates the reverse of arrested development. This tendency to accelerated extension of melanomas has been known to set in several years after removal of an eye for tumor of the uveal

tract and without activation of any other known primary source.

This wide difference of the tendency of melanomas to remain dormant indefinitely, or to become reactivated after a number of years, and to flare immediately into violent activity by direct expansion and metastasis, opens speculation as to whether there is an immunity present in some persons and not in others, and whether immunity is developed in some cases and lost in others.

The clinical behavior of melano-epitheliomas is peculiar in the field of malignant neoplasms. It would seem that their origin and their true nature have not yet been satisfactorily explained. The key to further understanding of cancer may well be found by research in this type of tumor.

Hemangiomas of the orbit constitute a group of vascular tumors of which there are a number of structural types and histopathologic variations. Usually situated in the middle division of the orbit, they may simulate meningiomas by causing erosion of the orbital walls or hyperostosis.

In the series of 3,190 eye tumors, 205 were diagnosed as angiomas of some type and 64 were located in the orbit. Thirtythree were diagnosed as hemangio-endotheliomas. They were more frequent in the posterior part of the orbit where they were sometimes confused with dural endotheliomas.

These endotheliomas are quite similar in their clinical characteristics as well as in their histopathologic features. They are highly malignant and extend by expansion along anatomic structures into every part of the orbit where nerves and blood vessels run. They are seldom encapsulated, are difficult to remove, and prone to recur, and are particularly resistant to irradiation. In common with other hemangiomas they are more frequent in persons under 25 years of age and often assume sufficient size to warrant surgical removal before the age of puberty. The prognosis in hemangio-endothelioma

is always grave. Complete surgical removal is imperative wherever possible. As they are clinically indistinguishable from other types of endotheliomas and usually occur within the posterior third of the orbit, they come within the field of the neurosurgeon and are removed by the transcranial route.

The greater number of vascular tumors of the orbit are made up of a proliferation of small vessels and a mass of fibrous tissue. Many of them are encapsulated, firm, fibrous, rounded masses that have scant blood supply and grow slowly. They are benign, do not give rise to metastasis, and do not recur after surgical removal. They are frequently found in children, rarely, if ever, arising after middle age. The prognosis in such cases is good.

Another type, however, that is troublesome for the surgeon is the cavernous angioma. This tumor is made up of thinwalled vessels, mostly on the venous side, and may be similar in most respects to a venous aneurysm. Since it occurs most frequently in children, it probably is congenital.

The tumor develops slowly under normal conditions. The cavernous spaces hold considerable blood, almost stagnant, which becomes noticeable only when thrombosis occurs. Under this condition the mass increases to the extent of elasticity of the affected vessels and there constitutes a space-taking lesion, as would any kind of tumor of equal size. Exophthalmos of several millimeters comes on within a few hours. There is edema of the lids and, after a few days, discoloration of the skin of the lids. Chemosis is usually mild.

If unmolested, the venous walls give way, a break occurs, and the contained blood, which has become a thin black fluid, escapes into the surrounding tissues and is absorbed. The exophthalmos subsides and all signs of tumor disappear. However, recurrence is common. In patients who have undergone operation the prognosis must be guarded.

The gross appearance of the tumors in

the surgical field is that of a tangled mass of thin-walled vessels, several millimeters in diameter, and filled with dark blood. The mass is surrounded by a number of thin, fibrous sheaths with septa weaving among the vessels to provide a frail supporting framework.

In trying to dissect such a tumor, nicking or rupture of a vessel wall usually occurs, whereupon the mass collapses, the bloody fluid escapes, and the tumor becomes indistinguishable from its fibrous sheaths. It is hardly ever possible to remove it entirely. Recurrence of the angioma is the rule. The varicosity of the vessels slowly progresses and extends even beyond the orbit's walls.

An angioma of this type, which involved both the orbit and the cranial cavity and clinically resembled a meningioma in its roentgen aspects, was a notable one in this series. It was a clear demonstration of the possibility of hyperostosis of the sphenoidal ridge by a tumor other than meningioma.

The cavernous type of hemangioma is not a malignant neoplastic disease in that it induces necrosis in tissue. However, areas of calcification shown in the roentgenogram speak for pathologic processes that may lead to disturbance of ocular function.

CONCLUSIONS

It is seldom that one can make a diagnosis of any particular type of orbital tumor from clinical evidence alone. In some cases one cannot distinguish between a tumor, a cyst, a venous aneurysm, a pyocele of the paranasal sinuses, toxic goiter, or inflammatory and metabolic disease with orbital involvement.

When all methods of differentiation have been utilized, the surgeon must decide whether exploration of the orbit is necessary and what method or route is best suited. The deciding factors are these: the threat to vision; the probable location and extent of the lesion; the evidence of growth and metastasis; and the age and general condition of the patient.

The threat to vision is probably the most important reason for surgical exploration of the orbit in cases of space-taking lesions. Progressive loss of visual acuity, with or without changes in the visual fields, may be the outstanding sign of orbital tumor, and surgical treatment may be the only means of preventing blindness. There are indeterminate lesions that do not demand immediate surgical intervention because there is no definite threat to vision, and roentgen therapy and medical treatment, under observation, may prove to be satisfactory treatment.

Loss of vision, exophthalmos, disturbance of motility, and impairment of function of the eyelids must be carefully observed for signs of expansion or growth so characteristic of tumors and cysts. The choosing of the optimal time for surgical intervention is often a difficult problem and even the most experienced surgeon will make mistakes.

The one admonition that my experience in dealing with more than 700 surgical cases of ophthalmic tumors and cysts points to is that of preparedness to complete the necessary surgical treatment involved in any attempted operation and to refrain from meddlesome interference to satisfy curiosity in indeterminate cases.

The Mayo Clinic.

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LOCAL USE OF HEPARIN IN THE EYE*

Pellet implantation at an experimental filtering site

Malcolm W. Bick, M.D.
Springfield, Massachusetts
AND
Robert W. Haines, M.D.
Baltimore, Maryland

The desirability of using heparin to prevent postoperative fibrosis after glaucoma surgery was mentioned in a previous paper.[1] Methods of heparinization of the eye were investigated and it was shown that heparin did not enter the primary aqueous. It was concluded that direct local introduction of heparin would be the most efficient and practical means of heparinizing the eye. This study concerns the local use of heparin in the form of pellets and the results obtained from the implantation of such pellets at the site of an experimental filtering operation. Observations on the local absorption of heparin are made.

Preparation of pellets

The preparation of pellets of sodium heparin for local use was undertaken to provide a readily controllable mass of heparin to remain at a local site for a longer period of time than the heparin powder or the heparin solution.

The following technique was employed for the preparation of heparin pellets. Powdered sodium heparin was loaded into one end of a cellophane soda straw for a distance of about 1 cm. The open end was moistened with a few drops of distilled water until the heparin powder melted. A mosquito clamp was placed distal to the heparin mass to prevent it from running down the cellophane tube. The segment of tube containing the wet heparin was placed in a vacuum drying jar for 24 hours. The cellophane was then easily peeled off and the pellet of fused heparin was removed, weighed, and placed in absolute alcohol for storage.

Pellets remaining in absolute alcohol lost no weight in three months. The pellets were cylindrical in shape with tapered ends and were quite brittle. They varied in weight from 60 to 34 mg. each, with an average weight of about 45 mg. Before use, the pellets were air dried on a sterile towel to remove the alcohol.

Absorption of heparin pellets

Two experiments using heparin pellets were undertaken to determine the rate of solution of heparin in the intraocular fluid of the rabbit. An anterior-chamber implant of a 41-mg. pellet dissolved completely in 21 minutes, while 66 mg. of sodium heparin dissolved in 41 minutes. In order to insert a pellet of the latter size, it was necessary to dislocate the lens backward slightly. Subconjunctival implants of 43- and 55-mg. pellets dissolved in an hour and an hour and 15 minutes, respectively. In these experiments, there was no local inflammatory reaction.

In Figure 1, a comparison is made between an intravenous dose of heparin of 25 mg. per kilogram and a similar dose in the form of a subconjunctival pellet implantation. When the heparin is given intravenously, the anticoagulant effect reaches a maximum immediately and is almost dissipated at six hours. In the case of the subconjunctival pellet, six hours are required for the maximal anticoagulant effect.

Heparinization of the blood stream per-
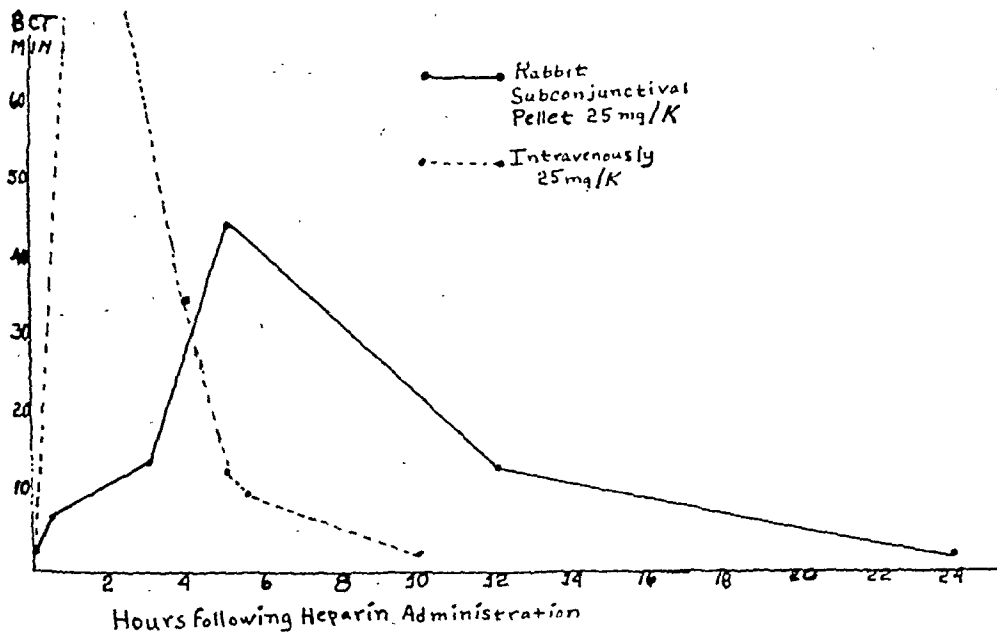
Fig. 1 (Bick and Haines). Anticoagulant effect of intravenous heparin and a subconjunctival heparin pellet implant.

sists for 18 to 24 hours after pellet implantation. If a similar pellet is implanted at the site of a filtering operation (fig. 2), there is a delay in the appearance of heparin in the blood stream and a maximal clotting time is reached in two hours.

The anticoagulant effect of a pellet of 34 mg. (15 mg./kg.) implanted at a filtering site is also plotted in Figure 2. Both curves represent heparin which is released from the local site in excess of the capacity of the tissues to hold heparin. With pellets smaller
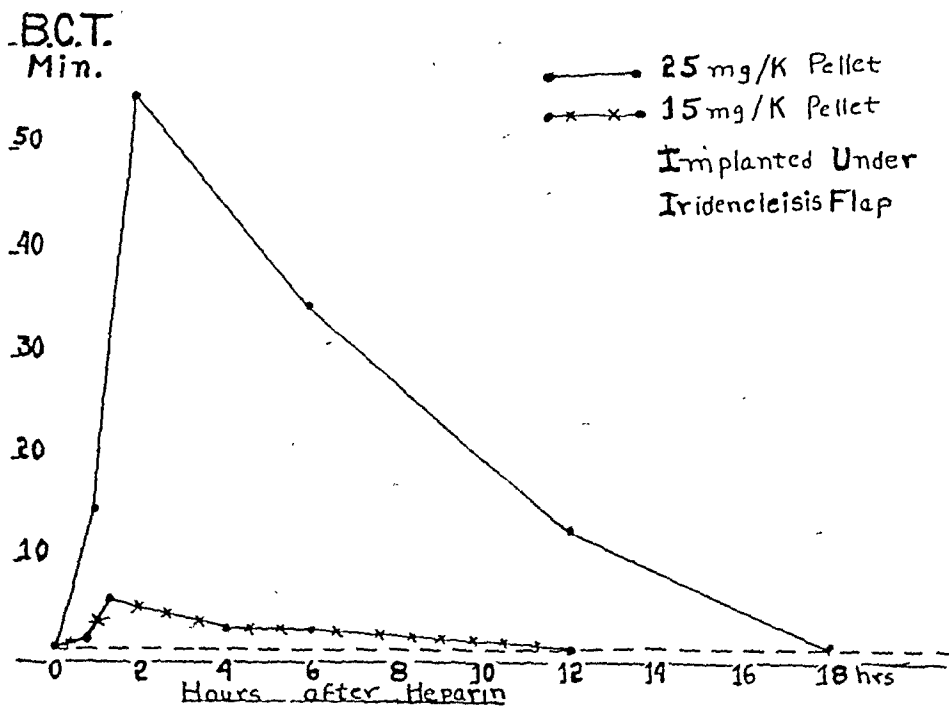
Fig. 2 (Bick and Haines). Anticoagulant activity of heparin pellets placed at the site of an iris inclusion operation. The lower curve indicates tissue saturation with a slight excess of heparin. The upper curve shows a considerable excess of heparin.

than 30 mg., no anticoagulant effect is noted. Consequently, the tissue saturation dose for a pellet implantation is about 30 mg. For purposes of tissue saturation, pellets in excess of this may be regarded as wasted heparin.

It is interesting to study the rapidity with which the heparin enters the blood stream.
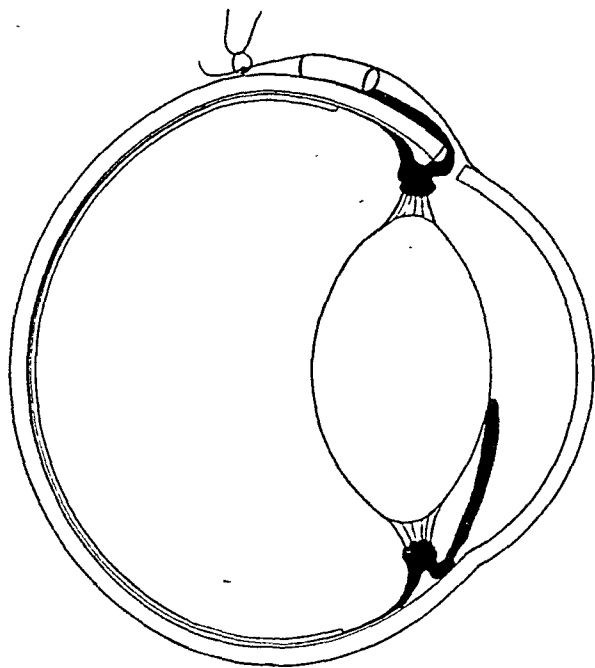
Fig. 3 (Bick and Haines). Heparin implant at site of filtering operation. The conjunctiva is sutured well behind the implant.

according to the site of implantation. If heparin is placed directly into the anterior chamber by injection of a saturated solution, a maximal effect is noted in the peripheral blood in one hour.[1] With pellet implantation at a filtering site (fig. 2), the time is lengthened to two hours; whereas, a simple subconjunctival implant (fig. 1) delays the maximal effect to six hours. It would appear, therefore, that the wash of aqueous through the filtering operation is instrumental in carrying heparin through the channels by which it is absorbed into the blood stream.

This wash of aqueous saturated with heparin is sufficient to prevent the local formation of fibrin in the absorbing channels for at least 18 hours and probably for several hours after the anticoagulant effect

of the heparin is no longer apparent in the circulating blood.

EXPERIMENTAL USE OF HEPARIN PELLETS

An experiment was undertaken to determine what effect, if any, the local use of heparin had on the development of postoperative fibrosis and filtration in the normal rabbit eye following a filtering operation.

Heparin pellets manufactured and stored as described above were used throughout. Albino rabbits were shaved closely about the lids with an electric clipper and were anesthetized with 300 mg. of nembutal per kilogram of weight by the intravenous route. The skin of the lids was painted with 3.5-percent iodine. Pontocaine was instilled into the conjunctival sac and, under sterile conditions, an iris inclusion operation was performed through a keratome incision. A large flap of conjunctiva extending well back to the equator was employed in each case. The optimal site for such a procedure was found to be the superior portion of the globe next to the lateral muscle. A fine running silk suture was used to close the flaps. In some cases, the sphincter of the iris was cut; in others, the iris was included without cutting.

In those eyes in which heparin implants were used, a milligram of heparin in 0.1 cc. solution was introduced into the anterior chamber as soon as the keratome incision was made. A heparin pellet was then placed at the site of the inclusion or right adjacent to it and the flap was closed (fig. 3). Sutures were removed during the second week under topical pontocaine.

The eyes operated upon fall into three groups: (1) Those in which heparin was implanted directly; (2) those in which no heparin was implanted and where the animal received no heparin; and (3) those in which no heparin was used directly, but where a heparin pellet had been placed under the conjunctival flap in the opposite eye within a half hour. In this way we were able to observe the effect of varying uncontrolled degrees of systemic heparinization and in-
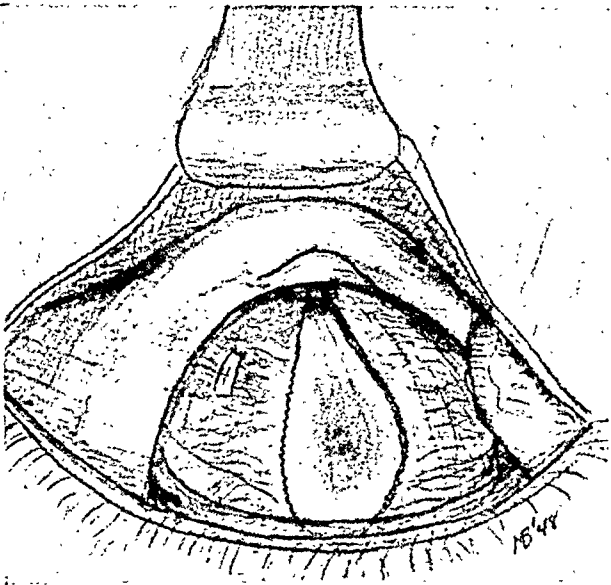
Fig. 4 (Bick and Haines). Appearance of rabbit eye prior to injection of trypan blue.

Fig. 5 (Bick and Haines). When the dye was confined to the bleb, filtration was considered to be poor.

tense, well-controlled local heparinization.

The weight of the heparin implant employed varied from 60 to 34 mg. and averaged about 45 mg. The average weight of the rabbits employed was 2.5 kilograms. The smallest dose used was sufficient to have some effect on the clotting time for 5 hours and the largest for 18 hours. Every pellet used exceeded the tissue saturation level.

The animals were observed for 6 weeks to 2 months and, after the eyes had whitened completely, the sizes of the blebs were compared, and filtration was observed.

Filtration was estimated by puncturing the cornea with a hypodermic needle, allowing most of the aqueous to escape, and then injecting 0.1 cc. of 1-percent solution of trypan blue. The rapidity of filling of the conjunctival bleb, the amount of filling, and the spread of the dye under the conjunctiva were observed for 15 minutes.

Filtration was classified in three groups: (1) Absent, (2) poor, or (3) good. If the bleb filled slowly and incompletely during the period of observation, the filtration was considered to be poor (figs. 4 and 5). If the bleb filled rapidly and the dye spread out under the conjunctiva around the bleb, filtration was considered to be good (fig. 6). The

size of the bleb in general corresponded to the degree of filtration present. There were exceptions, however, and grading was made solely on the basis of the spread of the dye.

After the filtration experiment, the rabbit was killed, and the eyes were fixed in Zenker's solution for histologic study.

RESULTS

The results of the filtration experiments in the three groups are summarized in Table 1.

If the absent and poor filtration are
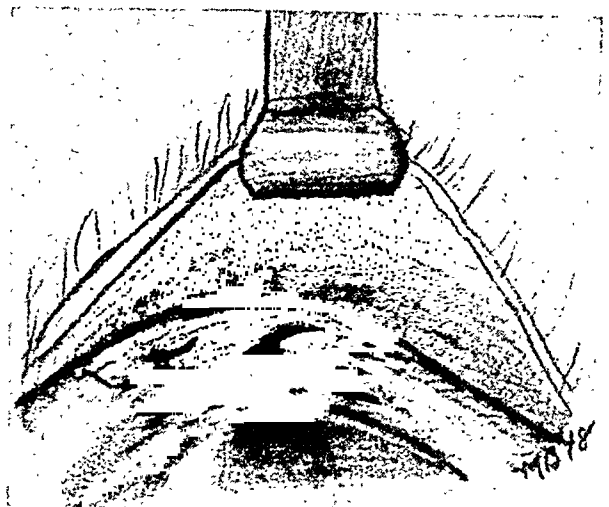
Fig. 6 (Bick and Haines). When the dye spread under the conjunctiva outside the bleb, filtration was graded as good.

Fig. 7 (Bick and Haines). Section taken from the control eye in which no filtration was observed. The heavy episcleral layer of fibroblasts (a) arising from normal sclera (b) which bridges over the iris (c) impeded the spread of trypan blue to the subconjunctival space (d).

grouped together, a statistically significant difference exists between Groups 1 and 3 which gives $x^2 = 5.49$.

Since $P = 2$ at 5.412, there are only 2 chances in 100 that the observations are a matter of chance.

The differences observed indicate that intense local heparinization with saturation of the tissues is of benefit in promoting filtration.

HISTOLOGIC OBSERVATIONS

In a correlation of the histologic picture with the degree of filtration recorded on our

TABLE 1

FUNCTION OF FILTERING OPERATIONS IN HEPARINIZED AND NONHEPARINIZED RABBIT EYES

Filtra-tion	Group 1 Heparin Implant (Locally)	Group 2 Heparinized (Remotely)	Group 3 Control
Absent	0	2	3
Poor	10	7	8
Good	7	4	1
	17	13	12

test, one is impressed that there are two critical points which determine the success or failure of filtration. These are: (1) The channels from the anterior chamber between the iris and the cornea on one side and sclera on the other, and (2) the organization and thickness of the fibroblastic layer overlying the iris under the conjunctiva. This fibrous layer bridges the iris from the cornea to the sclera.

In Figure 7, the normal sclera is seen in the lower right corner. The iris is in the lower left corner and, above this, is the very heavy layer of fibroblasts which bridges over the iris. Overlying this is the subconjunctival tissue. This heavy fibrous capsule impeded the spread of trypan blue so that no filtration was possible. This section was taken from one of the control eyes in which no filtration was observed.

In Figure 8, the channel between anterior chamber and subconjunctival space is closed by organization of the iris with episcleral fibrous tissue so that a free channel from the anterior chamber does not exist. Even though the iris is well incarcerated and the fibrous subconjunctival layer is not excessively thick, no filtration was observed.
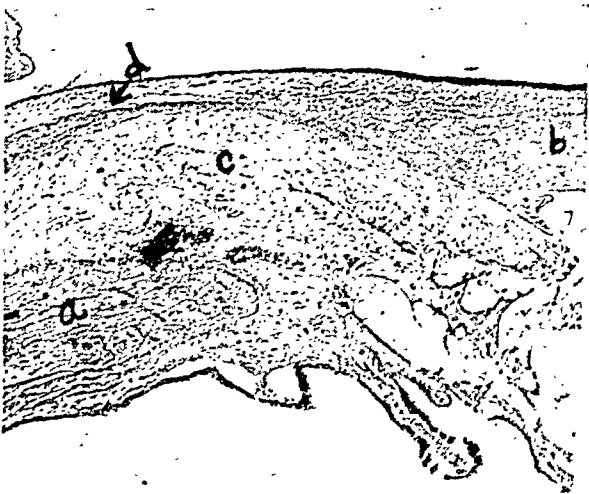
Fig. 8 (Bick and Haines). Section from control eye in which no filtration was observed. There is no free channel from the anterior chamber. The episcleral fibrous layer is not excessively dense. (a) Sclera, (b) cornea, (c) iris, (d) episcleral fibrous layer.

In Figure 9, taken from one of the eyes in which a heparin pellet was directly placed, we observe a free channel over the anterior but not the posterior surface of the iris. The fibrous layer extending from the episcleral tissue is of sufficient thickness to impede filtration. Filtration was rated as poor in this eye.

In Figure 10 one is able to see a free channel of flow from the anterior chamber. The fibrous layer is loosely organized and allows the formation of cystic spaces. Both of these sections represent eyes in which filtration was rated as good, and in which heparin implants were placed at the time of surgery.

DISCUSSION AND CONCLUSIONS

A heparin pellet dissolves somewhat more rapidly in the aqueous than under the conjunctiva. The high solubility of heparin in tissue fluids and its relatively slow appearance in the blood stream indicate that it remains locally in high concentrations even though the pellet has dissolved. This would seem to fit in with the known facts that heparin is nondialyzable and forms dissociable complexes with proteins.[2] We were able to follow the release of heparin into the

Fig. 9 (Bick and Haines). Filtration was rated poor. Despite a free channel over the anterior surface of the iris, a dense episcleral layer of fibrous tissue impeded filtration to the subconjunctival space. (a) Cornea, (b) sclera, (c) iris, (d) episcleral fibrous layer.

blood stream for almost 24 hours following local implantation. A pellet of 30 mg. is sufficient to saturate an implantation site and have a slight excess detectable in the blood stream of the rabbit.

How long heparin remains effective locally is still to be determined. From the present study, it would appear that heparin remains for a sufficient period of time locally to
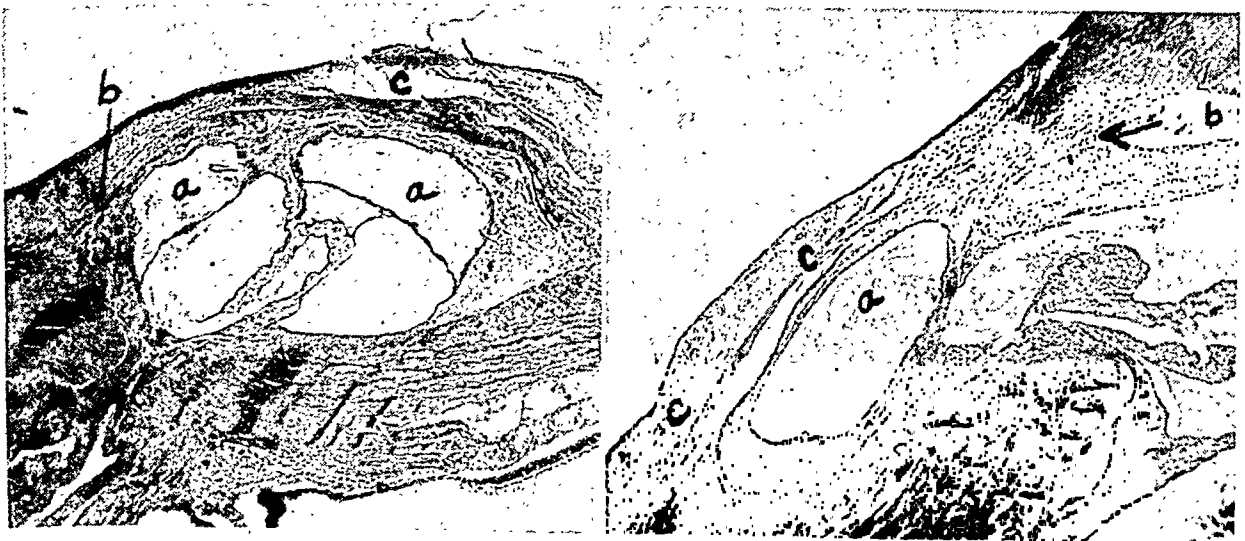
Fig. 10 (Bick and Haines). Sections taken from eyes in which heparin implants were used. The episcleral fibrous layer is loosely organized and permits the formation of cystic spaces (a). There are open channels between the anterior chamber (b) and the subconjunctival space (c).

modify in some manner the normal process of tissue repair. There is enough heparin present to prevent fibrin formation for at least a day, and this may be all that is required to improve filtration in the normal rabbit eye.

Heparin pellets implanted at the site of filtering operations caused no undue reaction and histologic observations made during the first week after subconjunctival implantation substantiated this gross observation.

There is no reason why heparin cannot be used locally in the human being in the same manner as in the rabbit. A pellet of 30 to 60 mg. should have little or no effect on the blood coagulation time in the human. On theoretical and experimental grounds, such implantation of heparin might be of value in those cases where fibrin formation and secondary fibrosis are to be avoided. It should be borne in mind that the eyes used in our animal study were not inflamed or congested, conditions where heparin might show its full usefulness.

SUMMARY

The preparation of heparin pellets was briefly described. The local absorption of heparin pellets placed in ocular tissues was observed. The experimental use of heparin pellets at a filtering site indicates that intense local heparinization is of benefit in promoting filtration in the normal rabbit eye.

Heparin causes no undue local reaction.
292 Worthington Street.
The Johns Hopkins Hospital (5).

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OPHTHALMIC MINIATURE

There are four varieties of protuberance of the iris. The first, resulting from rupture of the cornea, resembles the head of an ant, so that it may be mistaken for a pustule. I will in a short time speak of the difference between the two.

The second variety of prolapse is larger and more prominent than the first. It is called "fly's head." The third sort is still larger and may protrude so far as to come in contact with the eyelashes. This condition is a very serious bar to vision. Its appearance gives it the (vulgar) name of "berry," and it certainly has a grapelike shape. The fourth variety bears the vernacular name "nail-head." It is found in chronic cases, where the cornea has grown over the protrusion, thus giving the swelling the likeness attributed to it. Paulus calls it simply "finger nail."

Memorandum Book of a Tenth Century Oculist
Translated by Casey A. Wood.

THE EFFECT OF RETROBULBAR ALCOHOL INJECTION ON THE EYES OF EXPERIMENTAL ANIMALS*

WALTER KORNBLUETH,† M.D.

San Francisco, California

In the course of the study on the physiopathology of experimental corneal grafts in conjunction with Maumenee, it was found that all auto- and homografts inserted into a cornea made insensitive by a retrobulbar injection of alcohol prior to the operation either became cloudy, infected, or sloughed. The details of these findings will be recorded elsewhere. It suffices to note that 14 out of 14 grafts (100 percent) were total failures if 0.25 cc. of 95-percent ethyl alcohol was injected into the orbits of rabbits, 6 days, 9 days, 10 days, 11 days, 20 days, and 42 days before operation. This is in sharp contrast to the average percentage of successful homografts into clear corneas which, in our series, amounts to approximately 75 percent.[1]

The clarity of the graft did not seem to be appreciably influenced by performing the following procedures before operation: (1) Cutting the corneal nerves by an incision down to Descemet's membrane around the entire periphery of the cornea, thereby causing insensitivity of the cornea; (2) removal of both the Harderian and lacrimal glands; (3) removal of the superior cervical ganglion, thereby severing the sympathetic innervation to the cornea. It was therefore thought that the retrobulbar injection of alcohol might cause changes in the eye different from those which were produced by the procedures mentioned above.

As the clinical use of retrobulbar alcohol injections for painful blind eyes and even for various chronic conditions in seeing eyes becomes more popular, an experimental evaluation of changes in the eye following such injection appears appropriate. Very little experimental work on retrobulbar alcohol in-

jection has been reported. The only experimental approach was made by Weekers[2] who injected 1 cc. of an 80-percent solution of ethyl alcohol into the orbit of one rabbit. The author noted the hypotonic effect of this injection on the intraocular pressure of his animal.

EXPERIMENTAL STUDIES

The experiments to be reported here consist of clinical, histologic, and chemical studies.

TECHNIQUE

The technique for retrobulbar alcohol injection in rabbits was similar to that used in man. Albino rabbits weighing around 2,500 kg. were given general anesthesia by injecting nembutal intravenously. In spite of anesthesia the corneal reflex could still be elicited. A needle (24 gauge, ¾ inch) was inserted through the conjunctiva between the external and inferior rectus muscles pointing to the apex of the orbit. As soon as the optic nerve could be felt with the needle, the syringe was drawn back for a few millimeters and 0.25 cc. of 95-percent ethyl alcohol was injected slowly into the orbit. After a successful injection the corneal reflex was abolished immediately and the pupil became dilated and fixed to light. In the majority of the cases only one eye was injected; the other eye served as control.

CLINICAL OBSERVATION

The conjunctiva in the upper nasal part usually became injected and chemotic a few hours after introducing alcohol into the orbit. The chemosis persisted for 3 to 4 days. The deeper vessels in the episclera did not seem to be dilated and the bulk of the reaction was found in the conjunctiva only. The vessels of the iris were slightly more apparent during the first few hours. After four

Fig. 1 (Kornblueth). External eye muscle of rabbit three days after retrobulbar alcohol injection showing heavy round-cell infiltration, destruction of muscle fibers, and proliferation of fibroblasts. (Histologic section. Hematoxylin-eosin stain. ×100.)

days the eye usually looked entirely normal. It was noted that, if a larger amount of alcohol (0.5 cc.) was injected, a marked enophthalmos developed later.

The cornea stayed clear indefinitely unless some lesion was caused intentionally or unintentionally. The latter happened if, by technical mistake due to leakage of the needle, a drop of alcohol fell onto the cornea; an erosion developed thereafter which healed only after a long period of time. In cases where an extreme chemosis of the conjunctiva persisted for a longer time and the animal was unable to move its lids due to the swelling of the conjunctiva, an exposure keratitis developed.

The duration of the insensibility of the cornea varied with the amount of alcohol injected; if only 0.15 cc. of 95-percent alcohol was given, a corneal reflex could not be elicited for nearly 3 weeks. If 0.25 cc. to 0.3 cc. was injected, an average of 6 to

7 weeks passed until the sensibility of the cornea returned. In a great many, if not in all cases, the pupillary reaction to light was regained as the sensibility of the cornea returned to normal.

HISTOLOGIC STUDIES

The rabbits' eyes were enucleated following the orbital injection at intervals ranging from 3 days to 3 months, in order to study the histologic changes in the coats of the eyes, the optic nerve, and the orbital tissues. Care was taken to cut as long a piece of the optic nerve as possible. Three days after the injection the most marked changes were found in the muscle which showed a heavy round-cell infiltration, destruction of the muscle fibers, and early proliferation of fibroblasts (fig. 1). The orbital fat also was
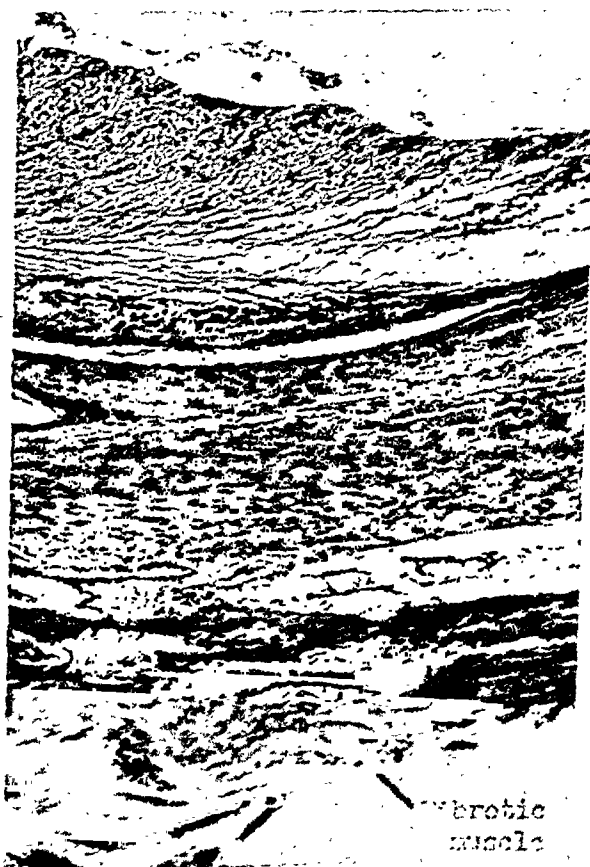
Fig. 2 (Kornblueth). External eye muscle of rabbit 57 days after retrobulbar alcohol injection showing fibrosis of the muscle fibers. (Histologic section. Hematoxylin-eosin stain. ×100.)

interspersed with lymphocytes. Neither the sclera, the optic nerve, nor its sheaths presented any sign of inflammation. Nine days after the injection the orbital tissue seemed almost normal except for proliferation of fibroblasts in the muscle which eventually led to fibrosis and adhesions to the globe (fig. 2). At no time did the optic nerve show any inflammatory reaction or signs of degeneration.

An interesting finding was observed in the corneal nerves. They were stained according to the silver impregnation method of Bielschowsky-Gros slightly modified by Campos. This method is reported in detail elsewhere.[3] Four days after the retrobulbar alcohol injection, the nerves still stained normally, but on the sixth day changes began to appear. Many nerves stained more faintly than normal, while other fibers still appeared to be normal (fig. 3). Twenty-seven days after the injection a majority of the nerves appeared pale, and at 48 days, the time when the sensitivity of the cornea started to return, most of the nerves again stained normally. At 57 days the nerves could not be differentiated from normal corneal nerves (fig. 4).

Fig. 4 (Kornblueth). Rabbit cornea 57 days after retrobulbar alcohol injection showing normally stained nerve fibers. (Histologic section. Silver impregnation. ×100.)

Fig. 3 (Kornblueth). Rabbit cornea six days after retrobulbar alcohol injection showing faintly stained nerve fibers. (Histologic section. Silver impregnation. ×100.)

FACTORS IN NORMAL HEALING

The poor results obtained with corneal transplants and the slow healing of minor injuries of the cornea after retrobulbar alcohol injection suggested that the various factors in normal healing which could be quantitatively assayed should be investigated. Therefore the following experiments were performed:

Determination of mitosis rate in the corneal epithelium of rats. White rats weighing 120 to 150 gm. were anesthetized with ether and 0.04 cc. of 95-percent alcohol was injected behind the globe. A high percentage of the rats thus injected developed an exposure keratitis and had to be discarded. In the remaining rats whose corneas stayed clear, a mitosis count on corneal epithelium was done after stopping the division of the cells in metaphase by injecting colchicine (5 mg./kg.) prior to enucleation. This method was devised by Buschke, Friedenwald, and Fleischmann.[4] The mitosis count showed a loss of 30 percent 3 days after the injection of alcohol, but increased to 30 percent above normal on the 4th day, and dropped to 31 percent below normal on the

6th day. After 14 days, the mitosis count was still 25 percent below normal and, 3 weeks following the injection, the loss amounted to 41 percent. After 5 weeks, the mitosis rate returned to practically normal (− 10 percent). See Graph 1.

Movement of epithelial cells in the healing of corneal wounds. The method of Friedenwald and Buschke[5] was used. This

the whole cornea was removed by scraping with a ring curette. Drops of penicillin solution (1,000 units/cc.) were instilled daily during the period of healing. While all the control eyes showed normal and clear epithelium after 7 days, only 3 of the 11 eyes (3 days, 9 days, and 10 days after retrobulbar alcohol injection) became covered with epithelium and showed a clear surface. In
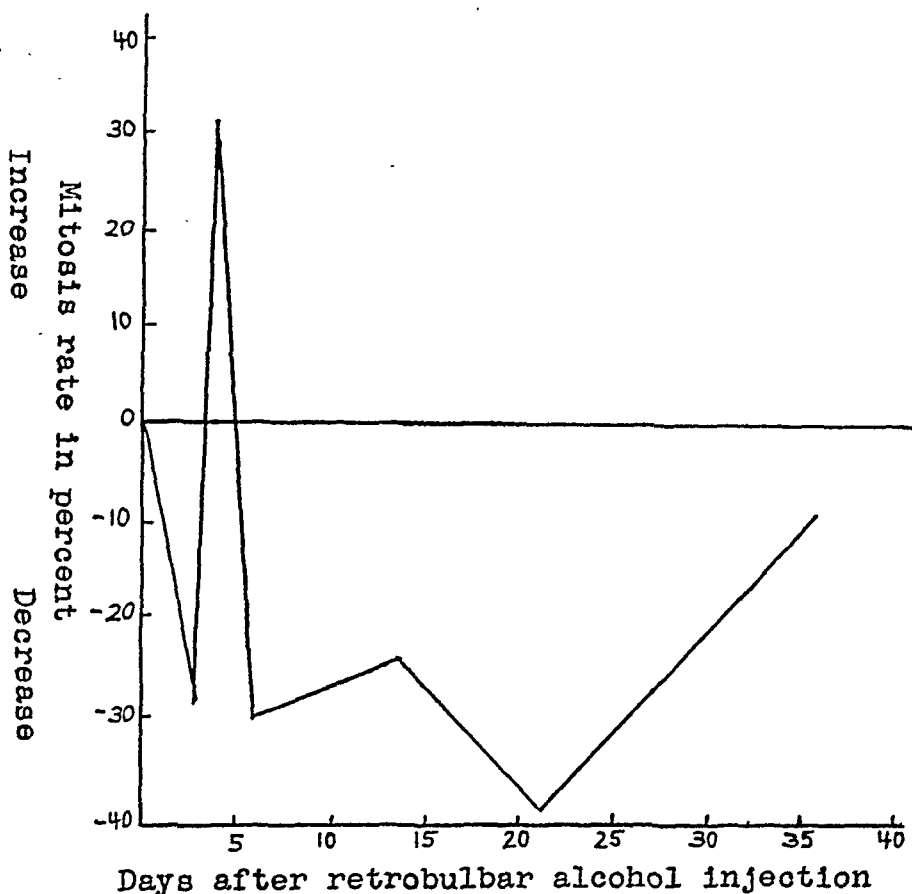
Graph 1 (Kornblueth). Mitosis rate of corneal epithelial cells of rats after retrobulbar alcohol injection. Each point on the graph represents a value of at least three eyes.

method was described as follows: "With a fine pointed needle about 30 small circular epithelial injuries are produced in the cornea of rats under ether anesthesia." The time required to fill the defect by cell movement in the retrobulbar alcohol-injected eyes compared well with the normal values.

Removal of epithelium of whole cornea of rabbits. In 11 eyes (3 days, 7 days, 9 days, 10 days, 18 days, and 19 days after retrobulbar alcohol injection) the epithelium of

these 3 it took approximately 3 weeks for reëpithelization. One of the corneas which became normal showed a recovery of sensibility in the course of healing. In 8 eyes the corneal epithelium remained irregular, was loosely adherent to the stroma, and had a tendency to slough. Vascularization and occasional secondary infection were noted in these eyes.

On histologic examination of the 8 eyes just mentioned, the epithelium often com-

prised only one layer and did not show any tendency to adhere to the underlying stroma. Fibrous tissue and newly formed capillaries were observed under the epithelium (pannus degenerativus) (fig. 5). In some of the corneas, the stroma became vascularized and infiltrated with leukocytes. In order to ex-

Destruction of corneal stromal cells. In a paper reported elsewhere[6a-6b] a method for destroying corneal stromal cells in a limited area by application of solidified carbon dioxide was given, and the mode of repair of the stromal cells described. With this technique, the corneas of rabbits (3, 6, 7, 11, 12, 14,
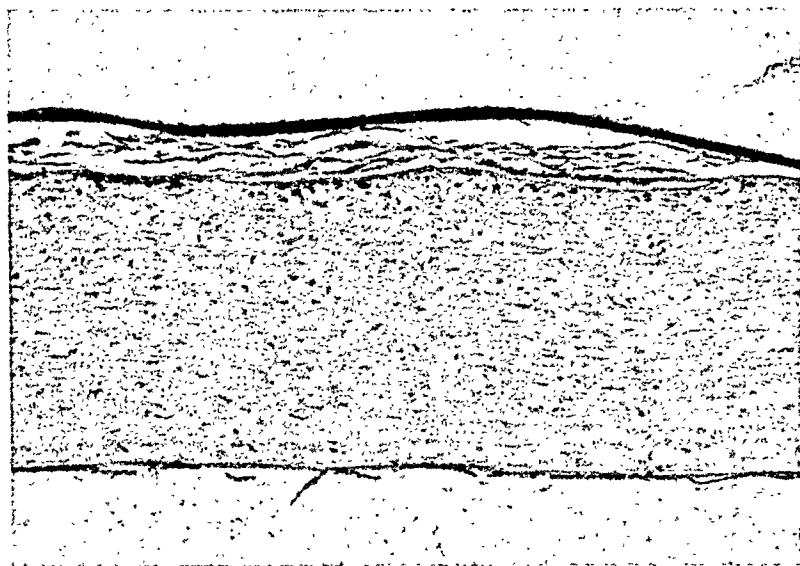
Fig. 5 (Kornblueth). Rabbit cornea 59 days after retrobulbar alcohol injection, 41 days after scraping of epithelium of whole cornea, showing fibrous tissue beneath the regenerated epithelium. Notice the thin epithelial layer. (Histologic section. Hematoxylin-eosin stain. ×100.)

clude the possibility that a secondary infection had inhibited the reëpithelization in these large denuded areas, experiments were performed with smaller lesions.

Removal of corneal epithelium in a circumscribed area. In 3 eyes (4 days, 14 days, and 25 days after retrobulbar alcohol injection) the epithelium of the cornea was removed in an area 4.5 mm. in diameter and the course of epithelization was followed. While the control eyes did not show any stain with fluorescein after 2 to 3 days, 2 of the retrobulbar alcohol injected eyes healed only after 8 days. One of these 2 eyes became sensitive 5 days after healing; the other showed a loosening and sloughing of epithelium 8 days after the originally injured area could not be stained with fluorescein. It was again covered with epithelium 10 days later. The 3rd eye healed only after 16 days. The 2 latter eyes regained some sensitivity before epithelization was complete. Nevertheless, this did not seem to promote normal healing of the wound.

and 18 days after retrobulbar alcohol injection) were injured by freezing an area of 6 mm. for 3 seconds.

When one compares normal and retrobulbar alcohol-injected eyes injured in the above manner, one finds fewer mitosis in the stromal cells of the latter eyes during the first 3 to 4 days. While normal eyes showed an average of 4 to 5 mitosis per vertical histologic section cut at 8μ. 3 days after the injury, the eyes which had received orbital alcohol injection gave an average of 2 mitosis per section. The same relation held true for the findings 4 days after the injury. The epithelium and endothelium were better developed in the control eyes.

At 6 days, the stroma at the area of injury in the control eyes was filled, although not very densely, with cells, while the eyes after retrobulbar alcohol injection showed large areas devoid of cells. These latter eyes still showed some acellular areas after 8 days, while the control eyes were filled completely with cells at that time (figs. 6a and 6b).
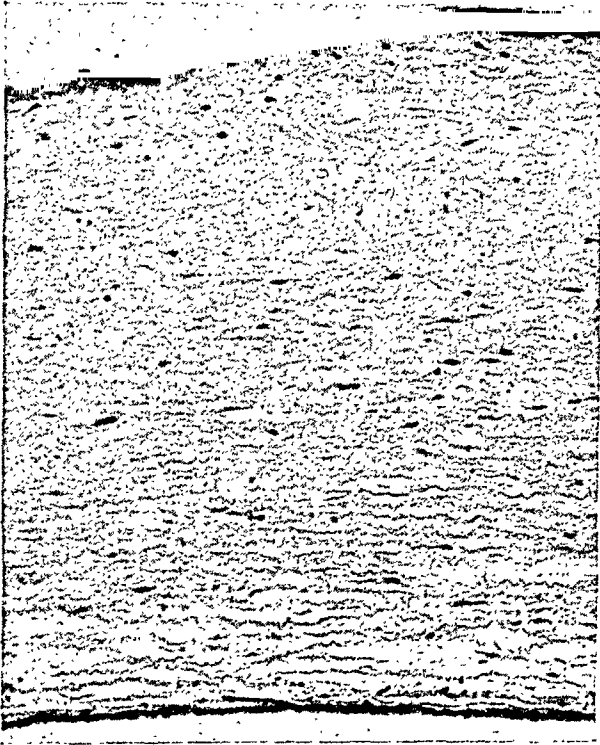
Fig. 6a (Kornblueth). Rabbit cornea 14 days after retrobulbar alcohol injection, eight days after application of 6-mm. brass rod (—78°C.) for three seconds, showing regenerated corneal stromal cells. Notice the acellular areas and the still persisting edema. (Histologic section. Hematoxylin-eosin stain. ×125.)

Fig. 6b (Kornblueth). Rabbit cornea eight days after application of 6-mm. brass rod (—78°C.) for three seconds, showing regenerated corneal stromal cells. Compare the density of the regenerated corneal stromal cells with those in Figure 6a. (Histologic section. Hematoxylin-eosin stain. ×125.)

Of the 5 eyes observed for 6 weeks or longer, 3 cleared up entirely after a period of 3 weeks (average normal 7 to 10 days). In 2 eyes, the edema of the stroma failed to subside. One of them also showed fibrous tissue and capillaries beneath the epithelium.

Nonperforating trephine cuts into the cornea. Nonperforating wounds were cut into the cornea 5 days after the retrobulbar alcohol injection with a 4.5-mm. trephine. The wound healed nicely, the cornea stayed clear, but the epithelium did not become firmly adherent where the trephine perforated the cornea.

Water content of cornea. In order to study whether the abolishment of the nervous control over the cornea might have some influence on the water-binding power of the cornea, the water content of this tissue was determined. Pieces of cornea (9, 10, 13, and 14 days after retrobulbar alcohol injection) were dried at 120°C. over calcium chloride and the loss of water was determined by the difference in weight before and after drying.

Although there was a slightly higher water content in the eyes following retrobulbar alcohol injections, the difference did not seem to be statistically significant.

Studies on the toxicity of aqueous in rabbits' eyes after retrobulbar alcohol injection. In order to see whether there was a toxic material in the aqueous of eyes after retrobulbar alcohol injection which inhibited wound healing in perforating wounds, the influence of the aqueous on the growth of rats' fibroblasts was studied. Pooled aqueous taken from 6 eyes, 0.2 cc. from each, from 3 days to 3 weeks following the retrobulbar alcohol injection, was added to a tissue culture of rats' fibroblasts. There seemed to be no difference in the rate of growth as compared with the normal control.

Protein determination in aqueous following retrobulbar alcohol injection. The protein content of the aqueous was determined on 0.2-cc. samples in 5 eyes from 3 days to 13 days following retrobulbar alcohol injection. The method used was the Micro-

Days after retrobulbar
alcohol injection
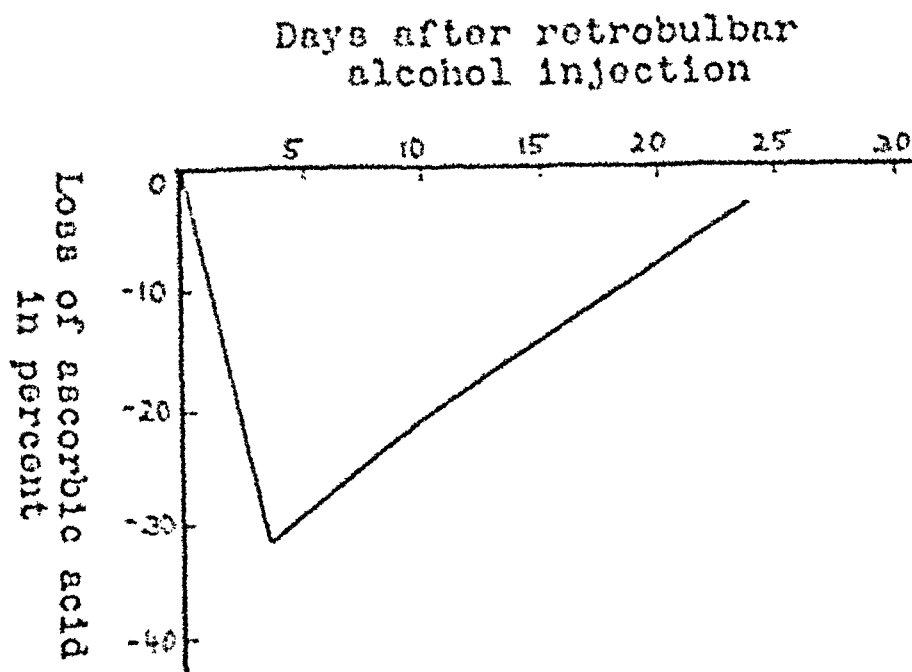
method of Birch, Harris, and Ray as modified by Buschke.[7] The results are given in Graph 2. Three days after the injection there was a loss of 30 percent of vitamin C in the aqueous which recovered to 21 percent loss at 9 days and returned to normal after 23 days.

Determination of glucuronidase in the ciliary body. The next step was to examine one of the enzymatic activities of the ciliary body. A method has been described by Talaly, Fishman, and Huggins[9] for the quantitative determination of glucuronidase, an enzyme which catalyzes the hydrolysis of the glucuronide linkage. The method which was used in this study was recently adapted

on the 29th day (graph 3). A similar but sharper increase in the activity of glucuronidase was found in the lacrimal and Harderian glands during the first few days after alcohol injection. These levels fell to normal around the 20th day (graphs 4 and 5). On inspection neither the lacrimal nor Harderian glands appeared atrophic following retrobulbar alcohol injection.

Rate of flow of aqueous in rabbits' eyes following retrobulbar alcohol injection. It seemed that a clue on the secretory activity of the ciliary body could be found by determination of the rate of flow of the aqueous according to the method described by Friedenwald.[11] "Under nembutal anesthesia
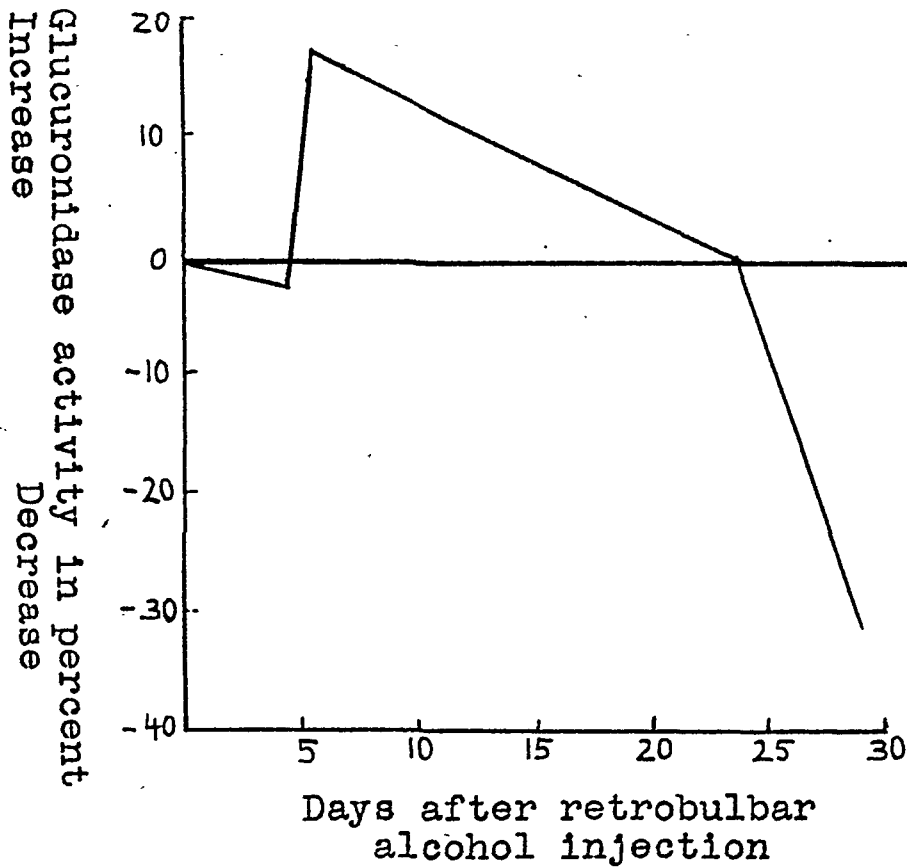
Graph 3 (Kornblueth). Glucuronidase activity in ciliary body of rabbits after retrobulbar alcohol injection.
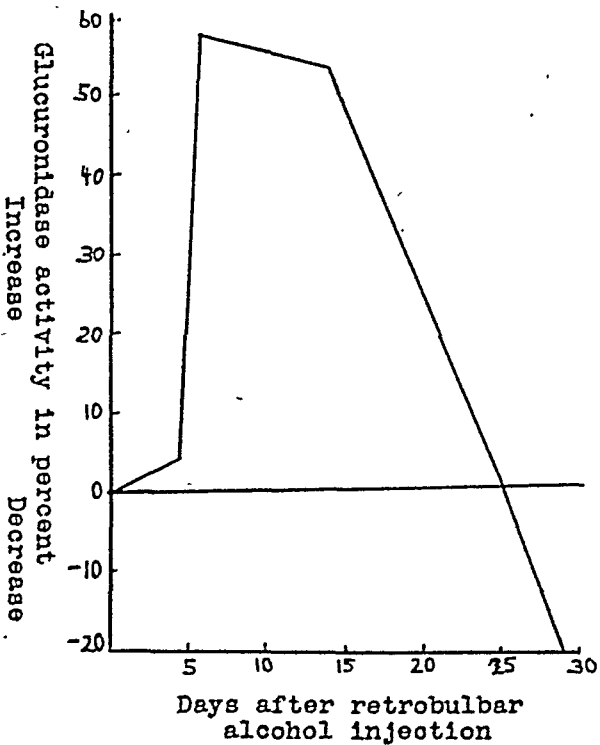
Graph 4 (Kornblueth). Glucuronidase activity in lacrimal gland of rabbits after retrobulbar alcohol injection.
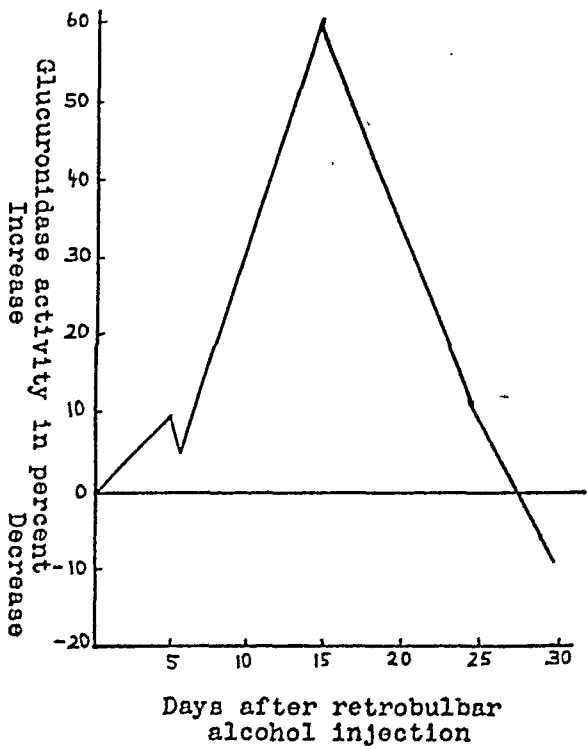
Graph 5 (Kornblueth). Glucuronidase activity in Harderian gland of rabbit after retrobulbar alcohol injection.

with local instillation of 0.5-percent ponto-caine a compensatory manometer was con-nected with the anterior chamber of one eye of a rabbit. As soon as the pressure reached a stable equilibrium 0.143 cc. of aqueous was withdrawn and the subsequent course of the intraocular pressure observed."

In untreated animals the intraocular pres-sure returned to normal after 5 minutes (graph 6a), while in one animal (3 days after retrobulbar alcohol injection) the tension came back only after 10 minutes (graph 6b), and in a 2nd animal (3 days after retrobulbar alcohol injection) the eye did not reach its original tension even after 25 minutes.

Tension curves of eyes after retrobulbar alcohol injection. The hypotonic effect of a retrobulbar alcohol injection on the treated eye and a concomitant ophthalmotonic effect

in the other untreated eye has been men-tioned by Weekers.[12] Since Weekers used a relatively large amount of alcohol (1 cc. of 80 percent) in his rabbit, it seemed impor-tant to see how a small amount of alcohol injected into the orbit would influence the
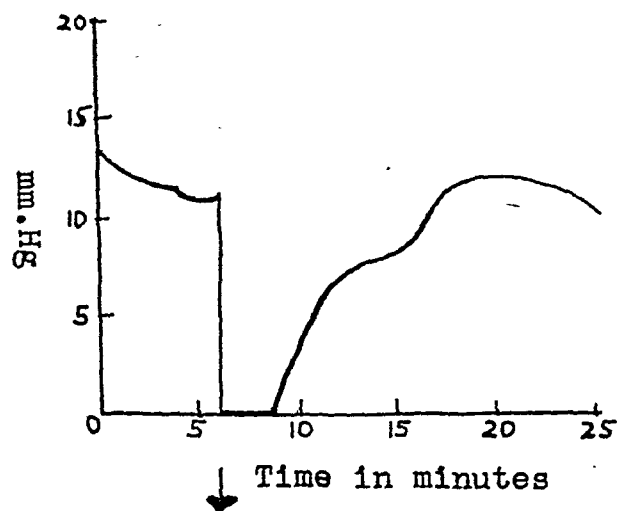
Graph 6b (Kornblueth). Rate of flow of aqueous in rabbit three days after retrobulbar alcohol in-jection. ↓ —0.143 cc. of aqueous withdrawn.

tension in the treated as well as in the fellow eye.

A series of 10 animals were given a retro-bulbar alcohol injection of 0.25 cc. of 95-percent alcohol on one side. The ocular ten-sion was compared in the normal and treated eye. The tension was measured with a Schiøtz tonometer. It is realized that the curvature of the rabbit's cornea varies from the curvature of the human cornea and the foot plate of the tonometer does not, there-fore, fit. However, the measurements give a comparative value. The tension dropped sharply one day after the injection and re-covered slowly to normal after 14 to 20 days. The typical change in the ocular tension after treatment is presented in Graph 7. No lower-ing of tension could be observed in the un-treated eye.

The tension was also measured in eyes in which the orbital alcohol injection was given on the nasal side of the muscle cone. In these eyes the corneal sensitivity remained intact. The eyes receiving retrobulbar alcohol in-
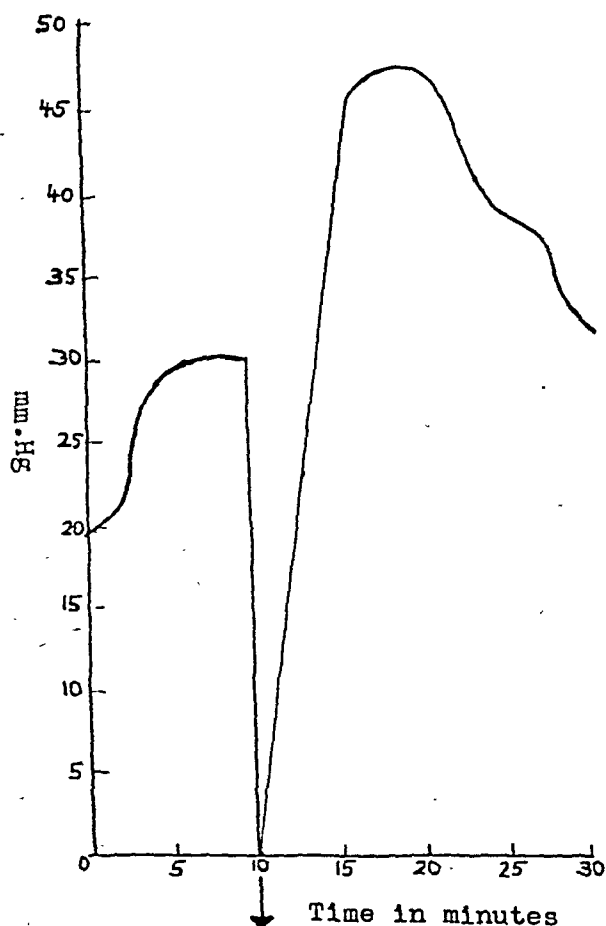
Graph 6a (Kornblueth). Rate of flow of aqueous in normal rabbit. ↓—0.143 cc. of aqueous with-drawn.

jections in the nasal side of the muscle cone showed an external inflammatory reaction similar to that found in eyes for which the injection was made in the region of the ciliary ganglion. However, the drop in ocular tension was not as marked and was only

rabbits, which have just been described, are probably similar to those in man following such injections. The amount of alcohol chosen for injection into the orbit of rabbits, 0.25 cc. of 95-percent alcohol, compares well with that given clinically to humans, 1 cc.
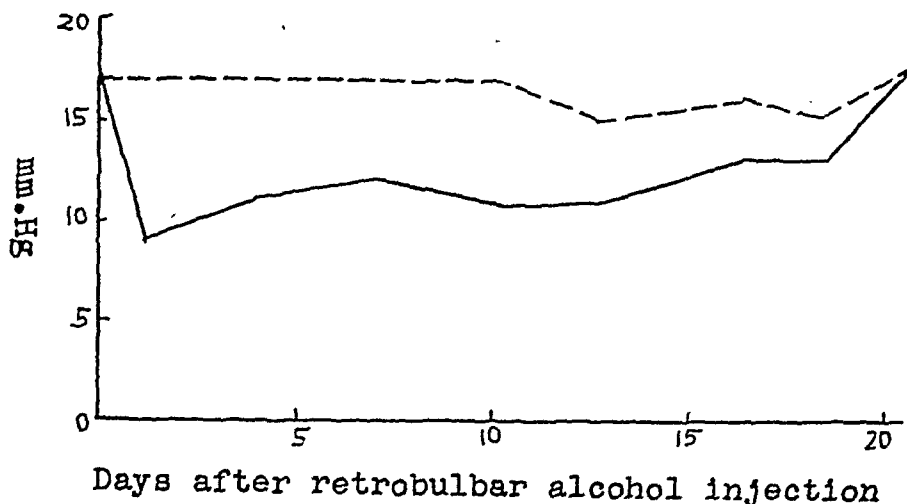
Graph 7 (Kornblueth). Tension curve of rabbit eye after alcohol injection into right orbit. R.E.: ———; L.E.: ----.

transitory. It took 3 to 5 days for the ocular tension to return to its original level (graph 8).

DISCUSSION

The reactions in the eyes and orbits, following retrobulbar alcohol injections in
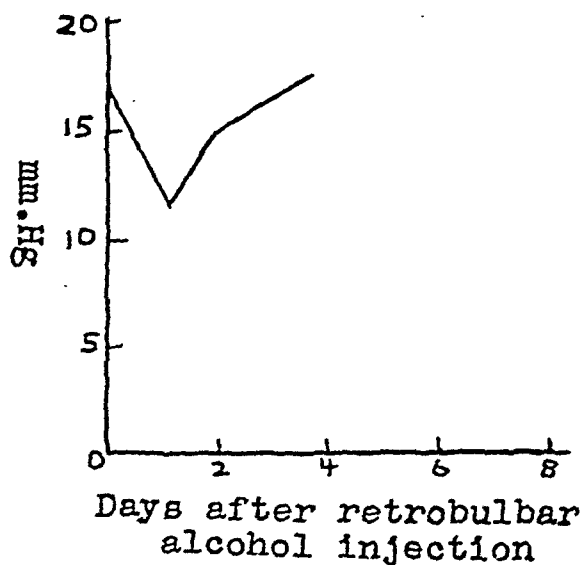
Graph 8 (Kornblueth). Tension curve of rabbit eye after retrobulbar alcohol injection into the orbit without interrupting the nervous supply to the eye.

of 95-percent alcohol. The volume of the human orbit is approximately 4 times that of a 2.5 to 3 kg. rabbit. If, however, 1 cc. of novocaine is used prior to the retrobulbar alcohol injection, as has been described by some workers,[16] the immediate concentration of the injected alcohol is probably diluted to some extent. This dilution may eliminate some of the sclerosing effect of the more concentrated solution.

Some of the rabbits' eyes showed a slight deviation to the temporal side following retrobulbar alcohol injection. This was not due to a paralysis of the muscles but to fibrous adhesions between the external rectus muscle and the globe which formed as a result of the inflammatory reaction caused by the injection.

The healing process of trivial injuries (stippling of the cornea with a fine needle, nonperforating cuts with a trephine into the corneal stroma) did not seem to be affected by the injection. In larger injuries, however, the defect was covered by epithelium very slowly and even then the newly formed epi-

thelium did not exhibit the vitality of normal epithelium. The regenerated epithelium often comprised only one layer and did not adhere normally to the underlying stroma. Thus, large bullæ were frequently formed and a pannus degenerativus occurred as a result of the chronic irritation.

The reciprocal relation of vitamin C in the aqueous and the glucuronidase activity of the ciliary body is interesting. As the value of vitamin C of the aqueous decreases, the glucuronidase in the ciliary body increases. This, according to Friedenwald[13] might be due to the decrease of an inhibitor (ascorbic acid) rather than an active increase in glucuronidase. Friedenwald and Becker[14] have shown that ascorbic acid inhibits the enzyme in vitro.

A comparison of Graphs 7 and 8 shows a marked difference in the degree of lowering of the intraocular pressure and the duration of the decrease if the injection was given in such a way as to interrupt the nervous supply to the eye. This would suggest that the reduction in tension is not only "due to provocation of an active hyperemia first in the orbit, then indirectly in the eye" (Weekers[15]) but due to some neurogenic influence. No concomitant fall in the tension in the other noninjected eye was observed.

Although no explanation for the peculiar action of the retrobulbar alcohol injection can be given, some possible single factors may be excluded. Cutting the nerves around the entire periphery of the cornea deprived the cornea of its nervous supply and, therefore, of its sensibility. It might be argued that not all the nerves were destroyed. Even if only 90 percent of the nerves were cut (serial sections in selected cases showed a degeneration of nearly all the nerves) some effect on the clarity of corneal transplants and healing of the surgical wound should have occurred if sensibility of the cornea was a deciding factor. However, such lesions healed without complications.

It might be theorized that retrobulbar alcohol injections destroyed the function of

the Harderian and lacrimal glands. However, removal of these organs before performing a keratoplasty did not affect the final clarity of the graft. The glucuronidase activity in the ciliary body remained normal after the glands had been excised.

Removal of the superior cervical ganglion before operation had no adverse effect on a graft which was inserted on a cornea thus deprived of its sympathetic supply. The glucuronidase activity of the ciliary body, Harderian and lacrimal glands showed normal values after superior cervical ganglionectomy; nor was the rate of flow of the aqueous changed as shown in a previous paper by Friedenwald.[11]

Notwithstanding the difference in behavior of the rabbit and human corneas as regards the return of sensitivity following orbital alcohol injections (the human cornea stays insensitive only for a few days, while the rabbit cornea regains sensitivity in 6 to 7 weeks), one important conclusion can be drawn. During the period of action of the alcohol injection, the tendency of corneal wounds to heal seems to be diminished in rabbits. This should serve as a warning against clinical use of retrobulbar alcohol injections in cases of chronic ulcerative processes of the cornea.

SUMMARY

The effect of retrobulbar alcohol injections in the eyes of rabbits and rats was examined. The influence of the injections on the clarity of corneal grafts, sensibility of the cornea, corneal nerves, optic nerve, orbital tissue, pupillary reaction, mitosis rate and cell migration of the epithelial cells, wound healing in regard to epithelial and stromal wounds, regeneration of corneal stromal cells, water content of the cornea, toxicity of the aqueous, protein and vitamin-C content of the aqueous, glucuronidase activity of the ciliary body, Harderian and lacrimal glands, rate of flow of the aqueous, and ocular tension was studied.

The action of the retrobulbar alcohol in-

jection could not be explained, but neither cutting the corneal nerves around the entire periphery of the cornea, nor removal of the lacrimal and Harderian glands, nor extirpation of the superior cervical ganglion showed an effect on the eye equivalent to the one of retrobulbar alcohol injection.

A marked inhibition in wound healing in larger injuries of the cornea was observed. The conclusion was therefore drawn that the clinical use of retrobulbar alcohol injections in cases of chronic ulceration of the cornea might be detrimental to the process of wound healing.

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HISTOPATHOLOGY OF INTERSTITIAL KERATITIS DUE TO CONGENITAL SYPHILIS*

CARLOS WESKAMP,† M.D.

Rosario, Argentina

For the last 20 years, excepting the one case of Malinin-Scharkowsky[1] no reports on the histopathology of interstitial keratitis of congenital syphilitic origin have been recorded. The case of these authors refers to a girl, 12 years of age, with parenchymatous keratitis and congenital lues, whose left eye was enucleated after a severe trauma. The histopathologic picture was that of deep hemorrhagic proliferative interstitial keratitis and iritis.

The few previous cases we found in the literature refer almost all to interstitial keratitis of several months' duration. Stanculéano[2] studied the cornea of a patient with pulmonary tuberculosis. The patient had an old ulcus internum in both eyes, with destruction of the deep layers, while the superficial layers were only slightly altered. Watanabe[3] enucleated, on the patient's request, one eye that was blind due to interstitial keratitis which had appeared 7 months before.

Jäeger[4] could study the histologic appearance of the cornea in a case of keratitis with a clinical course of five months; the patient had died of hemorrhagic encephalitis. Elschnig[5] is the only one who made the histologic study of a more recent keratitis. That was the case of a girl, eight years of age. The interstitial keratitis had developed two months previously in one eye, and three weeks before examination in the fellow eye.

Stock[6] studied one eye of a 5-year-old boy, idiotic, with saddle nose and Hutchinson's teeth, who had been blind since infancy, following interstitial keratitis. Igersheimer's case,[7] described by Kunze, dealt with an old keratitis which relapsed shortly

before the patient died. There was a small necrotic focus in the parenchyma; and the lesions in the endothelium were not very marked.

Since interstitial keratitis is an inflammatory process of the cornea, which usually subsides leaving more or less satisfactory vision, one cannot enucleate the eye for the sake of histologic study only. This explains the difficulty in obtaining enough material for histopathologic examination of the different stages of the disease. This reason influenced us to take biopsy specimens from the cornea.

Keratectomies were performed in very different stages of the disease, varying from 25 days to several months after onset of the keratitis. Keratectomy is obviously an incomplete method, since it does not permit the cornea to be analyzed in its total thickness, especially in its deeper layers. This method, however, allows one to obtain better knowledge of the changes taking place in the anterior layers and in the epithelium. Since the whole parenchyma has the same structure throughout and the same source of nutrition, however, there is no biologic reason to suppose that the changes of the deeper layers should be different from those of the upper rows. By means of keratectomy or laminectomy we can gather material enough for our study and compare the histologic appearance of the corneas of different patients in the same stage of the disease. We started to make biopsy keratectomies on different corneal diseases many years ago.

The cases herein reported are of patients with congenital lues in whom the diagnosis of interstitial keratitis was confirmed. We performed 7 keratectomies in 5 patients. Treponema pallidum was searched for by Jahnel's method, but could never be found. For histologic examination the sections were

fixed in formaldehyde or Bouin's solution (twice in Ruffini's), imbedded in paraffin, and stained by routine methods (hematoxylin-eosin, trichromic, methanil yellow, and so forth).

CASE REPORTS

CASE 1

Irene B., aged 18 years, came to our clinic in early August, complaining of troubles that appeared two months previously in her left eye.

seen, especially among the cells of the basement layer.

Bowman's membrane. Bowman's membrane was normal in its whole length, keeping its homogeneous appearance. It followed a wavy course at certain portions, according to the various thickenings of the epithelium.

Parenchyma. The stroma beneath Bowman's membrane was formed by fascicles of sharply demarcated fibrils, enhanced by interstitial edema. Between the fascicles lymphocytes and proliferated parenchymatous cells were found.
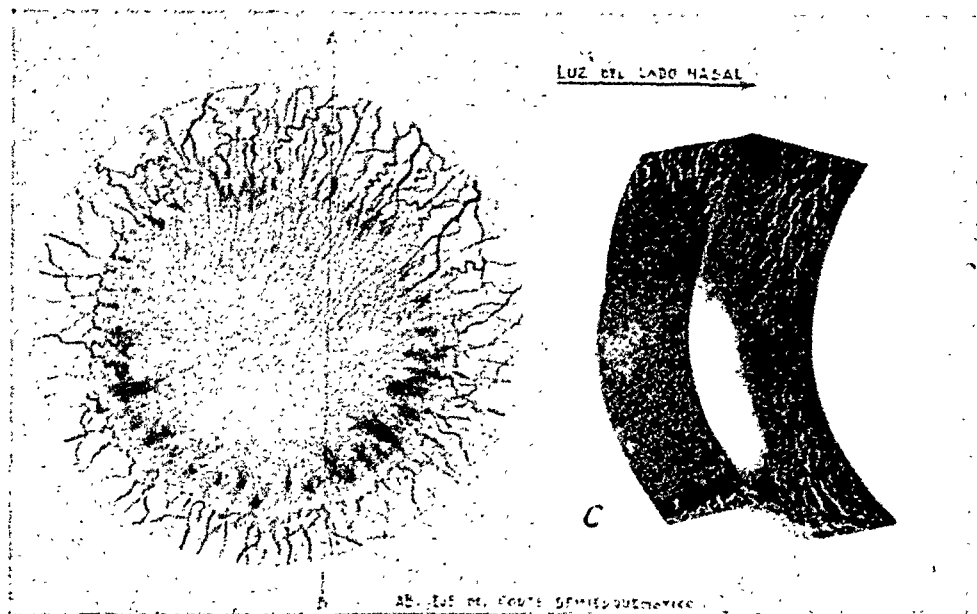
Fig. 1 (Weskamp). *Case 1.* (A-B) Gross appearance of the lesion. (C) Semischematic optic section of the damaged cornea of the left eye.

Her parents were syphilitic. The patient showed positive Wassermann and Kahn reactions (3 plus). On ocular examination we found the clinical characteristics of interstitial keratitis in full infiltrative stage. The cornea was infiltrated almost totally, mainly in its deeper layers. In the upper portions of the anterior layers a slight bedewing was seen at several points. Vascular loops were very abundant (fig. 1).

Histologic examination. Keratectomy of the left eye, external upper sector, was performed. This specimen for biopsy was taken on September 11, 1942, about 3 months after the onset of the inflammatory process in that eye.

Epithelium. Four to five layers were counted. It appeared of uneven thickness, for the cells were flattened at certain points and swollen at others. In some places the basal cells were smaller than those of the middle layers.

In general, the epithelial cells were pale, their nuclei deformed, with the chromatic network difficult to detect. Some nuclei were surrounded by a halo of perinuclear edema. Some lymphocytes were

CASE 2

This case involves the right eye of the same patient as in Case 1. While the patient was under observation for the disease of her left eye, slight photophobia and very slight perilimbic vascularity appeared in her right eye.

On slitlamp examination a small portion of the deeper layers of the upper outer segment showed a very thin infiltrate formed by minute gray dots. Little by little the infiltrate extended until it covered almost the whole upper outer quadrant. It did not extend to the pupillary border, however. At the same time, in the lower section of the cornea, very near the limbus, a spot similar to that of the upper sector appeared; it lay in the deeper layers of the cornea.

Three weeks after onset of this process the bedewing appeared on the superficial layers of the cornea, on both the upper and the lower half. The central portion of the cornea was still transparent. The perilimbic vascularity, which had been very slight at the beginning, increased as it reached

the upper half of the cornea, but it did not penetrate the stroma at any point (fig. 2).

Histologic examination. Keratectomy of the right eye, involving a piece of adjoining conjunctiva, was performed 25 days after the onset of the symptoms.

Epithelium. It appeared of varying thickness, its

were elongated in the horizontal axis. This was especially noted in the basal cells (fig. 3).

The area next to the corneoscleral limbus, which seemed to be the most seriously altered, showed the epithelial cells not in layers but in disorderly arrangement. The infiltrative elements had altered the orderly arrangement of the normal epithelium.
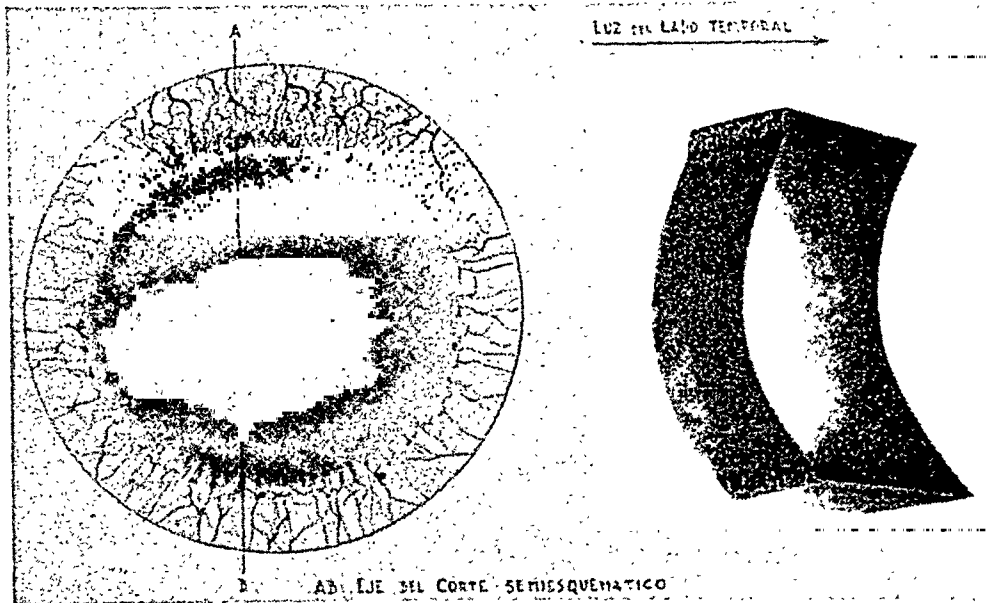
Fig. 2 (Weskamp). *Case 2.* Right eye of the same patient as in Case 1 (fig. 1).

Fig. 3. (Weskamp). The varying thickness of the epithelium and the decrease of the cellular infiltrate at the parenchyma are observed.

thicker portions being at the periphery of the cornea. Here the number of invading cells was increased and an interstitial edema which formed microvesicles was present. As the infiltrative process thinned toward the center of the cornea, the epithelium also became thinner because the proper cells flattened and their number diminished. At some places the epithelium was extremely thin, only 1 or 2 rows of very flattened cells being counted. They were so flattened that their nuclei

The nuclei of the scattered epithelial cells stained well, but their cytoplasm was pale and it was difficult to outline each epithelial cell. Hematocytes, sometimes isolated, sometimes in groups or on the way to form a channel, were mingled with the flattened epithelial cells. Lymphocytes were encountered, too (figs. 4 and 5). It was difficult to identify the basal cells because they were out of place and had lost their shape.

At the central area of the cornea the epithelium

regained its orderly arrangement and the cells were distinctly outlined. The basal cells had their nuclei surrounded by a halo of intracellular edema.

Bowman's membrane appeared intact throughout: in several places it was detached from the epithelium by vesicles containing cellular elements, principally hematocytes and lymphocytes. This detachment was very marked at certain parts, as if it followed a cleavage plane. The presence of lymphocytes and red blood cells proved that the

the stained sections are actually the layers of half the thickness of the cornea.

Approaching the center of the cornea from the infiltrative focus, the infiltrative elements became scantier. The deeper layers were less invaded and their reaction was less marked. The stroma was formed by broad lamellae, as if their fibers were swollen and slightly wavy. The nuclei of the fixed cells were well stained: some of them were enlarged. Between the lamellae a hematocyte or a lymphocyte was observed. In areas still farther from the lesion, the tissular reaction consisted of swelling of the lamellar fibers and thickening of the nuclei of the fixed cells (fig. 4).

Fig. 4 (Weskamp). Epithelium disorganized and infiltrated. Adjacent to Bowman's membrane is a cyst containing hematocytes and lymphocytes. The lamellae of the parenchyma are formed by swollen fibers. Clear spaces of interstitial edema are present.
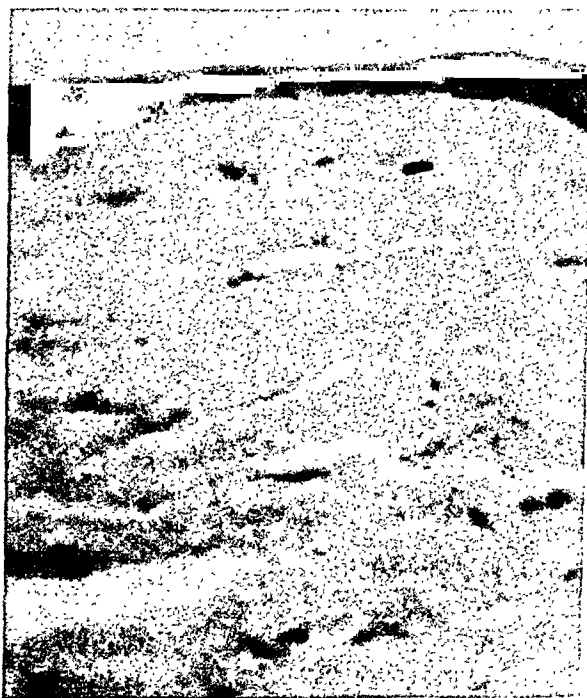
Fig. 5 (Weskamp). The very thin epithelium is formed by two layers. The parenchyma is edematous, the lamellae being formed by swollen fibers.

detachment was not an artefact. In other sites Bowman's membrane widened and merged with the underlying stroma.

Parenchyma. It was invaded by the same cells which invaded the epithelium. They were more numerous at the superficial layers. Here the lamellae formed thin fascicles with serrated borders and microvesicles of interstitial edema. Between the fascicles, hematocytes, lymphocytes, a few swollen fixed cells, and cellular detritus were encountered. At this point, the deeper the layers, the more they resembled the normal tissue, but the lamellae seemed to be formed by swollen fibers, and the lymph spaces were enlarged by interstitial edema. We must keep in mind that the deeper layers of

The histopathologic changes just described corresponded to the "dusted" appearance which was evident on slitlamp examination. As shown in Figure 2, at the optic section the bedewing extended through the superficial and through the deeper layers of the cornea, but the middle layers were normal or only slightly altered. In other words, in optic section the lesion was shaped like a great "V" with its vertex at the limbus and its opening toward the center of the cornea.

CASE 3

Zunilda Raquel C., a girl, aged 9 years, had had interstitial keratitis for three months prior to our examination. Wassermann and Kahn reactions were positive (3 plus). Biomicroscopic examination revealed an infiltrative process of the

posterior layers, but there was also haziness in the anterior layers.

Histologic examination. Keratectomy of right cornea was performed on September 4, 1942.

Epithelium. The epithelium was of varying thickness due to edema of the basal layers. This edema was mainly intracellular. The cells in general were not ruptured. The edema reminded one of Leloir's degenerative cavitary condition. This condition has been encountered in various diseases of the skin, in secondary syphilis for instance. Sometimes it has been observed as occurring technically. Several nuclei were shrunken and hyperchromic.

Small foci, formed by rests of Bowman's membrane and migratory nuclei, were seen between the epithelium and Bowman's membrane. The overlying epithelium was raised and the neighboring epithelial cells presented cariocytoplasmic changes (vacuolation, alteration of staining conditions, pyknosis, cariolysis, and so forth). In other sections the same area appeared as a cavity within Bowman's membrane and contained cellular debris and infiltrative fluid.

Bowman's membrane was present throughout and its staining properties were normal, but its thickness was not even and its anterior and posterior borders were serrated. In places it looked as if Bowman's membrane was fused with the underlying stroma.

Parenchyma. In general, its lamellar appearance was greatly altered. The deeper layers had lost their normal appearance and looked almost homogeneous, as if the lamellae had swollen and merged; it was difficult to outline them. The superficial layers adjoining Bowman's membrane, presented in some areas their fibrillar appearance. The parenchymatous cells were scarce and pale (fig. 6).

Fig. 6 (Weskamp). *Case 3.* Intracellular edema of the epithelium. Bowman's membrane is of varying thickness, and the appearance of the parenchymal lamellae is very altered.

CASE 4

Angela A., aged 40 years, complained of interstitial keratitis which had appeared 4 or 5 months
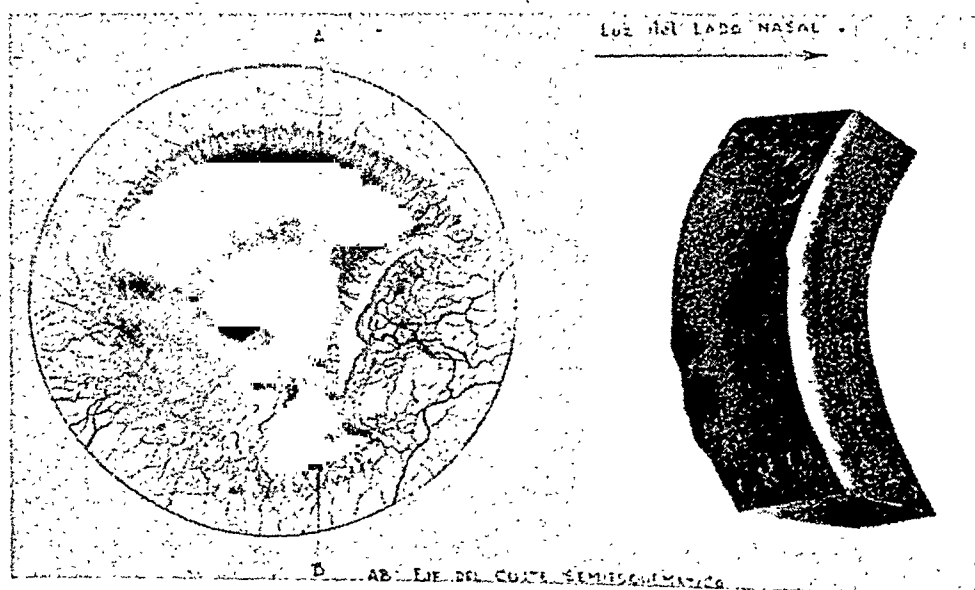
Fig. 7 (Weskamp). *Case 4.* The lesion, in the left eye, was most marked at the outer and middle layers of the cornea. There was rich vascularization with active circulation of blood.

before. Wassermann, Kahn, and Chediak reactions were positive (3 plus). She came to our clinic in April, 1942, showing a lesion in her left eye (fig. 7). In optic section we saw that the lesion was most marked at the outer and middle layers of the cornea. Rich vascularization with active blood circulation was noted.

remained normal. At the basal layer the nuclei of some cells were displaced by intracellular edema.

Bowman's membrane had disappeared.

Parenchyma. Areas were found where the parenchyma was sclerosed; in other regions it presented edema. The parenchyma was formed by thin trabeculae with wide meshes. Between these one
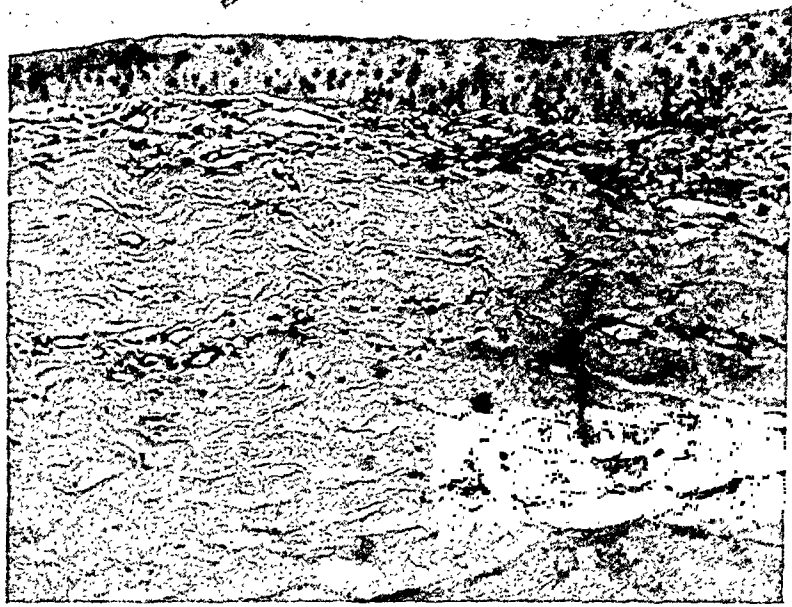
Fig. 8 (Weskamp). Broad meshes beneath the epithelium. Lymphocytes and capillaries are interspersed.
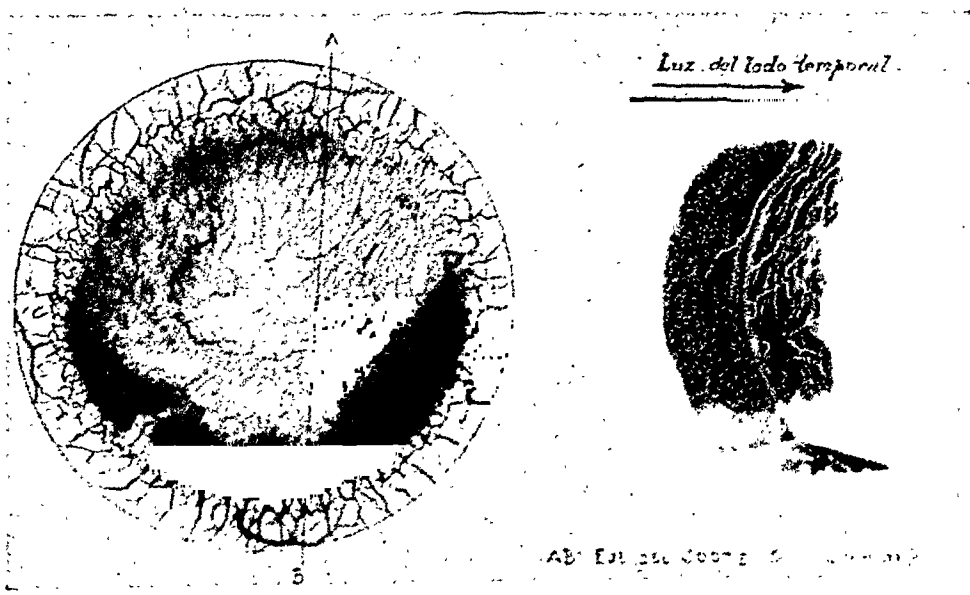
Fig. 9 (Weskamp). *Case 5.* Semischematic optic section of the damaged cornea of the right eye and the gross appearance of the lesion.

Histologic examination. Keratectomy was performed on May 13, 1942.

Epithelium was formed by 4 to 8 layers. Its inferior border was wavy; at certain points it formed a sort of papilla. It lay directly upon the parenchyma. The epithelial cells seemed to have

encountered vessels filled with blood, newly formed capillaries, fixed cells, and lymphocytic infiltrates. The lymphocytes surrounded the vessels (fig. 8).

CASE 5

Raul T., a boy, aged 20 years, showed inter-

stitial keratitis on his right eye. The lesion involved the cornea almost totally and throughout its thickness (fig. 9). The disease was of 6 to 7 months' duration. Wassermann, Kahn, and Chediak reactions were positive.

Histologic examination. A biopsy section of the cornea was taken on December 24, 1942, fixed in Ruffini's solution, and embedded in paraffin.

Epithelium. The epithelium was almost normal and its layers were in normal orderly arrangement. Interstitial edema was present in certain areas and intercellular bridges were visible. The

Between the fibers and the capillaries, fixed cells and lymphocytes were observed but, as the limbus was approached, the infiltrate became denser. This infiltrate was formed by histiocytes, lymphocytes, fixed cells, and a few polyblasts. Areas were seen in which the parenchyma was replaced by the infiltrate, mainly at the vicinity of the epithelium. In other regions very fine fibers of the stroma wove a fine network between the cells.

Vascularization in general was more marked at the subepithelial zone and through the superficial layers. The deeper layers of the biopsy presented

Fig. 10 (Weskamp). Bowman's membrane appears very thin. Immediately beneath it, the lamellar tissue has been replaced by bundles of fibers among which vessels and cellular infiltrates are seen.

border of the basal layer presented a slightly wavy contour but did not form papillae.

Bowman's membrane. In most places had disappeared, although the area next to the limbus remained and presented its normal appearance. It became thinner as it approached the conjunctiva, looking sometimes like a vitreous membrane. It would not have been possible to delimitate conjunctiva from cornea if one had had to follow the contour of Bowman's membrane only (fig. 10).

Parenchyma. The subépithelial stroma and the underlying layers were formed by bundles of wavy fibers which ran parallel to the surface. Between these fibers capillaries were observed that had proper walls, tumescent endothelium and the lumen totally occupied by blood elements. Most of these capillaries ran parallel with the fibers, but others had been cut crosswise and these seemed almost adherent to Bowman's membrane.

no vascularity and no infiltrate. The parenchymal lamellae were slightly tortuous and somewhat inclined to disrupt (fig. 11).

CASE 6

This case involves the left eye of same patient as in Case 5. In this eye, interstitial keratitis was 4 to 5 months old. The infiltrate was denser at the external upper and internal lower sector (fig. 12).

Histologic examination. Corneal layers of left eye were excised on December 5, 1942. The biopsy section was fixed in Ruffini's solution and imbedded in paraffin.

Epithelium was of varying thickness, 2 to 3 up to 5 to 6 rows of cells being counted. Its course was wavy and sometimes showed a wedgelike penetration of the parenchyma.

Bowman's membrane followed all the irregulari-
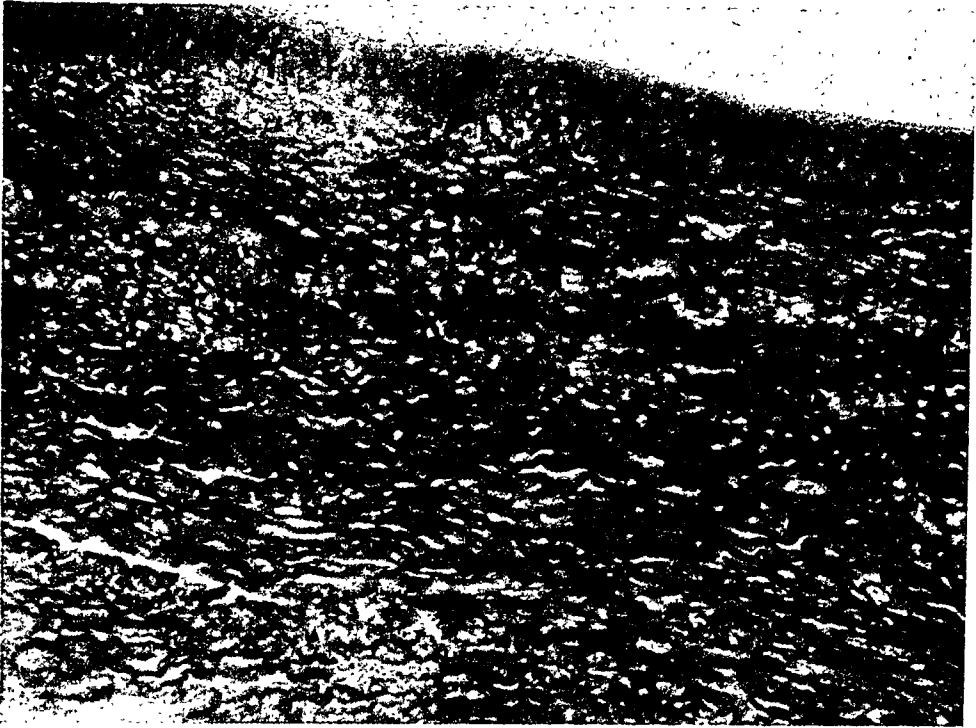
Fig. 11 (Weskamp). The varying thickness and irregular course of Bowman's membrane is observed. In the parenchyma, the lamellae have been replaced by bundles of wavy fibers. Vessels which have their own walls are shown.

ties of the epithelium and, at certain places, a sharp zig-zag was noted.

Parenchyma. Its normal appearance had totally changed. It was built up by a tissue of fine, sinuous fascicles intermingled like hairs on a head with numerous vessels which ran parallel to the fascicles and whose own walls were engorged.

Infiltrative elements were scattered among the interstices.

Observing the stroma with low magnification in order to obtain a panoramic view, one saw the fibrous fascicles lying immediately below Bowman's membrane; but the presence of vessels was the most marked variation from the normal noted in
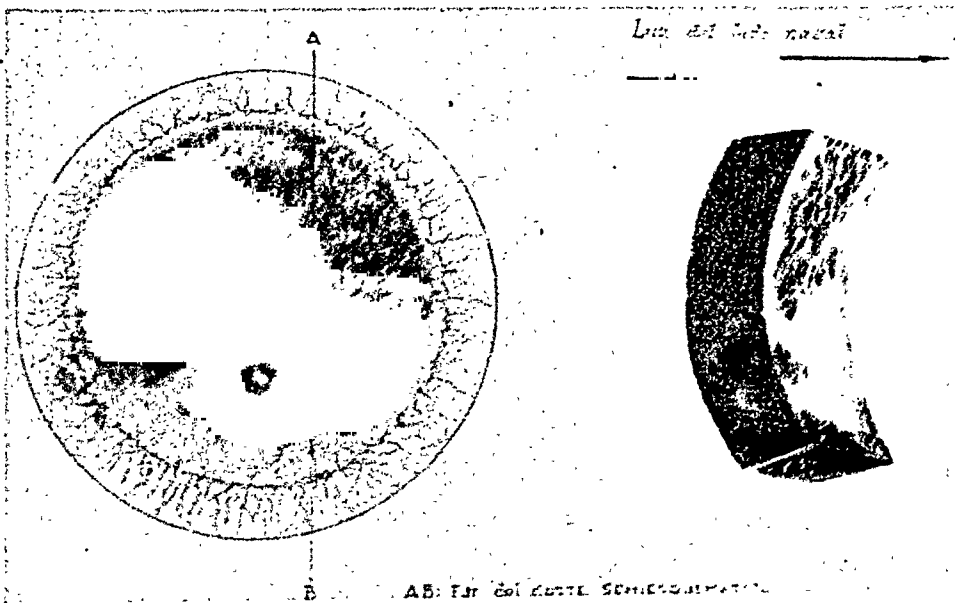
Fig. 12 (Weskamp). *Case 6.* Left eye of the same patient as in Case 5 (fig. 9).
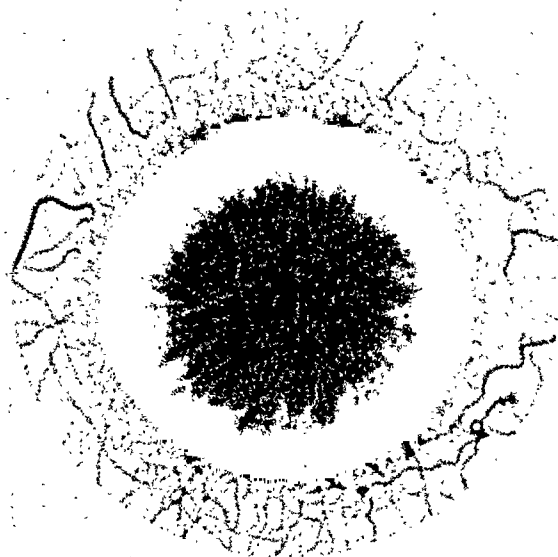
Fig. 13 (Weskamp). *Case 7*. Drawing of the left eye.
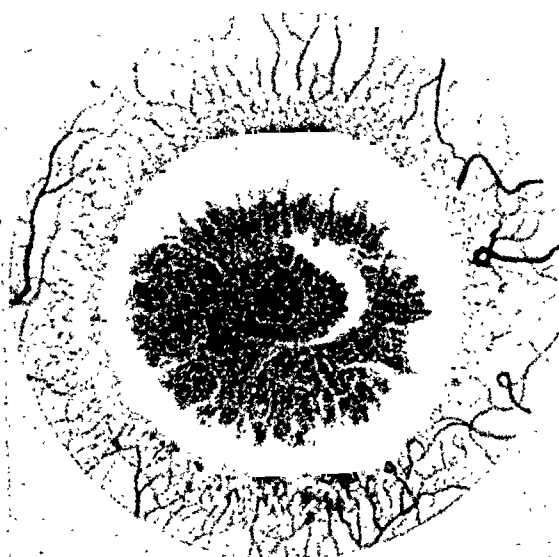
Fig. 14 (Weskamp). *Case 7*. Drawing of the right eye.

the tissue. These vessels formed a close network in the middle layers of the section. From these layers fine capillaries rose toward the upper layers. This interposed vascular network divided the parenchyma into two parts—one upper, or subepithelial, part of fine, firmly packed fibrous fascicles, among which fine capillaries were scattered; a second, lower part, situated below the vascular network. In this inferior portion the fiber fascicles were wider than on the upper part and more closely

resembled normal tissue. The middle layer, as has been said, was more vascular and exhibited many cellular elements among which were found plasmocytes, polyblasts, lymphocytes, fixed cells, and polymorphonuclear cells.

CASE 7

Juan G., a man, aged 28 years, with Hutchinson's teeth, had been given antisyphilitic treatment since childhood. His paternal uncle, a doctor, had been
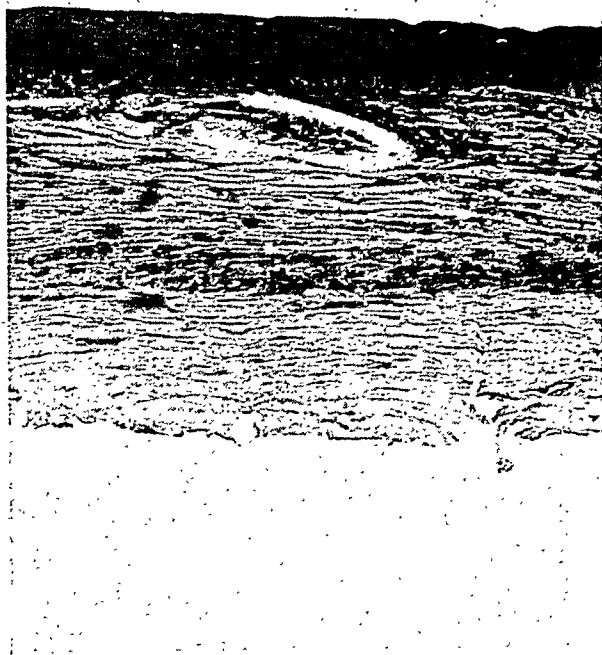
Fig 15 (Weskamp). The general structure of the epithelium remains. Bowman's membrane has disappeared in some places; in others, it appears thinner. The upper layers of the stroma are replaced by repair tissue. The inner layers are becoming normal.

the physician who administered intense and regular antiluetic treatment all through his life. Wassermann reactions at different intervals were always positive. In December, 1941, the first ocular symptoms appeared, characterized by soreness of left eye and slight decrease of vision in the same eye. An ophthalmologist diagnosed interstitial keratitis. Three months after onset of the disease the same symptoms appeared on the right eye. Vision decreased progressively to nearly total blindness in both eyes. In this condition, the patient was brought to our clinic by his physician in March, 1944, 2 years and 3 months after onset of the first symptom. The clinical appearance of the corneal lesions is illustrated in Figures 13 and 14.

Under low magnificaiton and with full front illumination the infiltrate was seen to involve almost the entire cornea, being more condensed at the pupillary area. In the right eye the infiltrate was whitish, looking like a calcareous deposit. Innumerable, glassy, radiating lines were seen in both corneas. The optic section exhibited Bowman's membrane interrupted at several points, the subepithelial tissue protruded until it reached the epithelium through those spaces where Bowman's membrane was absent. In addition, the infiltrate

occupied chiefly the posterior layers of the cornea, while at the anterior layers it was not so abundant. The middle layers appeared less changed. Arterial vessels with blood circulation were found in the deeper layers together with the whitish infiltrate. The disease was classified as residual interstitial keratitis.

Histologic examination. A biopsy of left eye was taken on March 10, 1942.

Epithelium. The structure of the epithelium seemed to remain normal (fig. 15), but its thickness was irregular, being thicker at both ends of the section where 10 rows of cells could be counted. In the center of the cornea, only 4 layers were counted. At one end the epithelium was trying to penetrate the stroma in form of a wedge. At certain regions the epithelium rested upon a repairing tissue which we shall describe later.

The epithelial cells were seemingly unaffected although they lay upon a tissue that differed from normal. Their protoplasm stained well and their appearance throughout was normal except for some nuclei that appeared faded. In places, basal cells appeared flattened and elongated, with spindle-shaped horizontal nuclei; some of these cells were so flat that they resembled thick fibers. In other parts, the row of basal cells was displaced toward the surface by a group or nest of histiocytes.
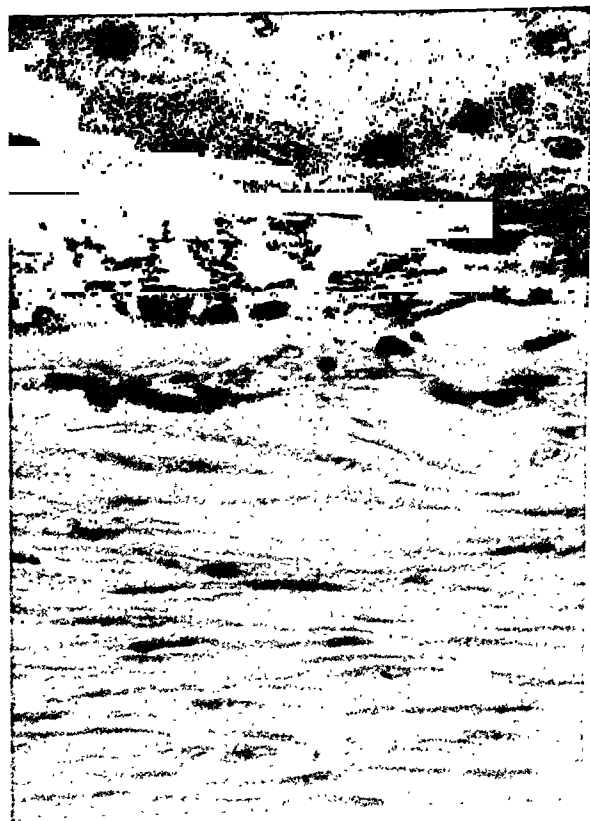
Fig. 16 (Weskamp). High-power view of the section in Figure 15. The repair tissue is penetrating the epithelium. Fibroblasts are noted among the fibers. Basal cells are flattened.

Bowman's membrane. Areas were observed where Bowman's membrane (fig. 15) was absent; in other places it appeared disrupted.

Parenchyma. The anterior layers of the parenchyma were replaced by the repairing tissue already mentioned. This tissue penetrated between Bowman's membrane and the epithelium at certain regions. It was formed by thin connective fascicles running parallel to the surface. Between its interstices, stellate cells (fibroblasts) were present. It was a *repairing connective tissue* (fig. 16). Immediately below the epithelium this tissue showed cells very much like lymphocytes and macrophages (histiocytes). Cellular debris were also found. As the deeper layers were approached, the stellate connective cells changed into spindle-shaped; the fascicles widened; in other words, the tissue began to have the appearance of cicatricial connective tissue. Blood vessels and red blood cells were absent. Below this scar tissue, the parenchyma appeared more normal the closer one approached the deeper layers.

COMMENT

In cases of recent interstitial keratitis we observed an exudate of lymphocytes, hematocytes, and fluid (probably fibrinous) running from the limbal region through the epithelial layers and corium of the conjunctiva toward the cornea. As this exudate invades the epithelium and the parenchyma, both disintegrate and become edematous. Thus the structure and the thickness of both are altered.

The epithelium is detached from the basement membrane in long stretches, as following a cleavage plane. The detachment looks like an artefact, but the presence of red corpuscles and lymphocytes in these spaces shows that the separation is pathologic. Places are seen where edema forms vesicles containing cells with round nuclei and scanty protoplasm.

The number of epithelial layers is decreased, only 2 or 3 rows of cells are counted in places. In other spots 4 rows are seen. These cells are flattened and their nuclei lie horizontally. The basal layer does not differ from the other layers. Where the invasion is most marked, the epithelium is thicker but loses its arrangement of orderly layers, and it becomes difficult to recognize the basal cells. The epithelial cells undergo different changes. Cariocytoplasmic modifications are observed, such as perinuclear edema, hyperchromic nuclei, nuclear distortion, pyknosis, and so forth.

In advanced stages, the epithelial cells are arranged in orderly layers. The number of these is not always normal but is increased in different places. Furthermore, in cases of long-standing keratitis the basal cells have lost their characteristic features and it is difficult to distinguish them from other epithelial cells. The epithelium has a wavy contour, sometimes wedgelike, as seen in Case 6, because the structure of the parenchyma is altered, with subsequent differences of curvature of the cornea.

We have found vesicles between the epithelium and the basement membrane containing histiocytes and lymphocytes. These vesicles were also observed by Jaeger[4] in congenital luetic keratitis, and by Pieskergen (cited by Jaeger) in scrofulous keratoconjunctivitis.

Bowman's membrane is intact throughout in recent cases of luetic interstitial keratitis. In cases of longer course Bowman's membrane is disrupted when not absent in places.

Parenchyma. The intensity of the damage decreases from the surface toward the deeper layers. (One must keep in mind that the analyzed pieces were obtained by keratectomy; therefore, when speaking of "deep layers" we refer to those of the biopsy. They are not the deepest layers of the cornea, but of more or less half its thickness.) We may conclude, then, that the middle layers of the cornea are less altered. This finding is consistent with the biomicroscopic picture, where the lesions appear in the inner and in the outer layers of the cornea, leaving a less-altered middle zone.

These changes may be classified chronologically as: (1) Infiltrative and edematous stage; (2) cellular necrosis and vascularization; (3) atrophy of the parenchyma; (4) organization of fibrous tissue.

1. In recent cases of syphilitic keratitis, the parenchyma is invaded by an exudate

which comes from the limbal area carrying cells of the lymphocytic type and erythrocytes. The parenchyma is disintegrated by these infiltrates and the proper cells become swollen. The fibers appear edematous. In areas near the invaded site the parenchyma no longer appears lamellar but almost homogeneous, as if the edematous fibers were no longer demarcated. Even the nuclei of the fixed cells disappear as shown in Case 3. Here the parenchyma looks as if it had a serous inflammation.

2. After the infiltrative and edematous stage, cellular necrosis, vascularization, and invasion of macrophages follow.

3. Later on there appears atrophy of the parenchyma characterized by decrease of fixed cells and a fibrillar appearance of the corneal lamellae.

4. The most advanced stage is characterized by the organization of fibrous tissue.

The histologic structure in these different phases explains perfectly the peculiarities of the biomicroscopic appearance. In the initial phase a bedewing is observed in a sector of the cornea near the limbus. This appearance is given by an infiltrate of very small cells (red blood cells and lymphocytes) and the interstitial fluid.

As the disease progresses, the bedewing becomes condensed and gives rise to dense spots; this is due to the presence of necrotic foci and of bigger cells (histiocytes) and to the organization of capillaries.

Still more condensed areas of compact structure are observed. This picture is probably given by the presence of newly formed fibrous tissue and of vessels with active blood circulation.

CONCLUSIONS

We find that our observations are rather consistent with those of Stanculéano, Elschnig, Stock, Watanabe, and Jaeger. For an accurate comparison of the findings observed by us at the outer layers of the cornea and those observed by these authors in enucle-ated eyes, we selected the cases of short duration reported by Elschnig and Jaeger and our own Case 1 and Case 2 which had a clinical course of 3 months and 25 days, respectively.

Epithelium. In Elschnig's case the epithelium was atrophic and was formed by the outer layer of flattened cells and a row of cubic cells. In the epithelium an infiltrate of numerous round cells was found.

In Jaeger's case the epithelium was also thinner than normal, the basal cells could no longer be distinguished from the cells of other layers. Vesicles with lymphocytes were lying between the epithelium and Bowman's membrane.

In our own cases, the epithelium was also thinner than normal, infiltration of round cells (probably lymphocytes) was present, and the basal cells had lost their characteristic features and were flattened. As in Jaeger's case we, too, found little foci of debris of Bowman's membrane and migratory nuclei lying between the epithelium and Bowman's membrane (Case 3). Some sections showed a cavity in Bowman's membrane containing fluid and migratory cells.

Bowman's membrane, which remained in Elschnig's and in Jaeger's case, was also present in our own Cases 1, 2, and 3. The little foci of lymphocytic deposits within Bowman's membrane described by those authors have been found by us as well.

Parenchyma. Elschnig noted the parenchyma infiltrated with migratory cells and with necrotic processes of the same kind of cells, and the lamellae as well. He also found a repairing process consisting of division of the fixed corpuscles in the vicinity of the necrotic foci. The lymph spaces were dilated and contained an exudate of detritus, fine grains, and nuclear fragments. The lamellae were more or less normal.

Jaeger also noted an infiltrated parenchyma, especially near the epithelium and Descemet's membrane, but he observed only slight damage to the layers of the middle third of the cornea. The infiltrate consisted

mainly of lymphocytes and newly formed vessels. The lamellae of the parenchyma were only slightly altered, but the lymph spaces were edematous and contained nuclei of different kinds.

In our cases, the superficial layers of the cornea showed the most marked alterations and the middle layers exhibited less change, exactly as in Jaeger's case. As for the rest, we encountered the same changes as described by Elschnig and Jaeger at the parenchyma, namely cellular infiltration of lymphocytic type, interstitial edema, and dilated lymph spaces containing nuclei and cellular detritus.

In their older cases Stanculéano, Stock, and Watanabe made these observations:

The epithelium was almost normal, only swollen and with prongs penetrating the parenchyma. This picture coincides with that of our older Cases 4, 5, and 6.

Bowman's membrane followed the contour of the epithelium. Sometimes it was absent and sometimes thinner than normal. The defects of the membrane were replaced by groups of lymphocytes. We encountered exactly the same changes in our older cases.

In short, in recent cases of syphilitic interstitial keratitis, the number and shape of the epithelial cells is altered but Bowman's membrane remains. In older cases, the epithelium has regenerated but Bowman's membrane undergoes destructive processes.

The parenchyma in older cases undergoes several changes. Newly formed vessels which have their own walls appear; cellular infiltration is present; the lamellae are altered and replaced by wavy fibers. Sclerotic foci and newly formed tissue are encountered. The appearance of our own cases, studied by means of keratectomies, is consistent with those of the authors[2-6] who studied the cornea throughout in enucleated eyes.

SUMMARY

In five patients with luetic interstitial keratitis, 7 keratectomies were performed for biopsy material which was used to analyze the histologic changes taking place in several stages of the disease ranging from a clinical course of 25 days to 2 years.

Keratectomy is not an ideal means of investigation since it does not permit examination of the entire thickness of the cornea. However, since it can be performed without fear of damage to the patient, keratectomy provides a useful means for studying congenital syphilitic interstitial keratitis, a disease that has not been studied exhaustively yet.

The findings at the epithelium, Bowman's membrane, and parenchyma are analogous with those of other authors.

In the early stages, between 25 and 90 days, marked changes of the epithelium occur, characterised by infiltration of an exudate containing lymphocytes and erythrocytes which disarrange the orderly architecture of the epithelial cells. The epithelium is formed by 1 or 2 rows of cells in those places where the exudate had decreased or disappeared.

Bowman's membrane is not altered during this stage. It remains perfectly normal and stains evenly.

The parenchyma is also infiltrated by the same elements as the epithelium. The lymph spaces are enlarged and contain fine detritus. The lamellae appear to be not greatly altered, but edematous. Their fibers seem often to be swollen, giving thus a homogeneous appearance to the lamellae. In this stage, the nuclei of the normal cells of the parenchyma are swollen or show cariokinetic changes.

In more advanced stages, the epithelium seems to be repaired, since it either shows a normal or an increased number of layers. Epithelial prongs are seen within the parenchyma. Bowman's membrane undergoes marked changes; in places it has disappeared, or is disrupted, or has been reduced in thickness.

The parenchyma shows vascularization. The vessels have their own walls and some

of them present active blood currents; others have their lumen clogged following degenerative processes of their walls. A few lymphocytes and histiocytes are observed in the most advanced stage of the disease. The lamellar tissue is sometimes replaced by scar tissue.

Laprida 1159.

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PRESENT CONCEPT OF THE THERAPY OF OCULAR SYPHILIS*

DAVID O. HARRINGTON, M.D.
San Francisco, California

AND

RANDALL W. HENRY, M.D.
Spokane, Washington

The dire need of a rapid and effective therapy of syphilis, brought on by the war years, stimulated intensive study and research along these lines, the results of which are far-reaching. A new interest in syphilis has been awakened and a new concept of its therapy is being established. In the midst of this evolution, it behooves us to survey the opinions of leading men in this field and to formulate conclusions which will guide us to a better understanding of its treatment.

TREATMENT OF SYPHILIS

PENICILLIN

In this treatment, penicillin plays a leading role. Its effectiveness as a treponemocidal agent has been definitely established. Its acceptance has been universal and enthusiastic and its evolution, since its inception, has been rapid.[1] However, this antibiotic is still in its infancy and it would be unwise and even hazardous, at this time, to arrive at any definite and dogmatic decisions. During the past year, a pure form of the drug has become available to us as a calcium and sodium salt, and just recently it has been synthesized by Du Vigneaud and his fellow workers.[2] The various species of penicillin, namely: F, G, K, and X, are under carefully controlled investigation.[3, 4, 5]

At the present time most of our commercial fractions are of the G species. All fractions of penicillin are rapidly excreted in the urine and attempts are constantly being made to maintain its concentration in the blood over a longer period of time. The most effective and successful method has been the Romansky and Rittman formula.[6, 7] Hydrogenated oil is also used as a vehicle, but here the maintenance of high blood levels is less pronounced.

Caronamide, a drug which exerts an inhibitory effect on renal excretion by action on the tubules, is under observation.[8] At-

tempts by Kolmer and Rule[9] to develop a strain of Treponema resistant to penicillin have been unsuccessful. Experimentally, Eagle and others[10] found that fever therapy enhanced the action of penicillin, but this has not been borne out clinically.[11]

The effect of penicillin is lost in acid solutions, even as weak as a pH of 5 or 7. Thus combinations with adrenalin hydrochloride and boric acid should be avoided.[1] Herxheimer reactions occur very commonly with penicillin, but are mild in degree and generally manifest themselves as an increase in temperature, headache, and general malaise. Local manifestations may be more severe.

ARSENICALS

Likewise, observations made during the rapid 20-day and the 25-week treatment of syphilis, with arsenicals, have enlightened us on their use. It was noted that mapharsen was a safe and therapeutically effective arsenical, and that the toxic reactions, in spite of the rapidity of administration, were not marked. On the other hand, the use of pentavalent arsenicals (tryparsamide) has been abandoned because pharmacologic studies showed that it had to be reduced to the trivalent form to be effective; that it had no greater penetrability or affinity for the central nervous system than the trivalent form; and that it often caused permanent visual damage in spite of precautionary measures.[12]

BAL is reported by Eagle and Magnuson[13] to be quite effective in controlling the many toxic reactions which do occur in the heavy metal therapy, and it has been recently postulated by Friedham and Vogel[14] that the combination of arsenicals and BAL may give us a nontoxic drug for syphilis therapy.

THERAPY OF OCULAR SYPHILIS

To facilitate generalizations, we have divided the therapy of ocular syphilis into the treatment of the acute ocular conditions and that of the chronic ocular conditions. Thus,

before taking up the treatment of individual lesions in the eye we may say that the more acute the syphilitic lesion, the more effective penicillin or chemotherapy will be and, likewise, the more acute and severe the lesion, the more severe the Herxheimer reaction will be, if large doses of the antisyphilitic drug are used. This latter reaction is to be avoided in treatment, especially so in the eye, because it leads to intensification of the inflammation locally and to too rapid a tissue destruction with increased fibrosis, thus burdening recovery.

From these generally observed facts, our results will depend on how early we can institute treatment in the more acute lesions of syphilis, and upon avoidance of a therapeutic paradox by the use of too large an initial dose in the more severe acute lesions.

ACUTE OCULAR CONDITIONS

Interstitial Keratitis. Interstitial keratitis is included in the classification of acute conditions, although the question still remains as to whether it is due to the presence of the spirochete in the cornea or to allergic or toxic reaction. The lack of dramatic response to penicillin and the absence of any noticeable reaction when large initial doses of penicillin are used would lead us to believe that other factors, besides syphilis, play an important role. Comparative results of treatment can be noted in the recent statistical study made by Klauder[15] (Table 1). In this same survey it was shown that penicillin does not prevent an initial attack of interstitial keratitis, nor does it prevent involvement of the second eye or recurrences of the disease. In spite of the resistance of this condition to antisyphilitic therapy, it is generally agreed that intensive therapy is indicated, as soon as the diagnosis is made. This immediate and early treatment has continued to show better response and results according to most observers.

Since penicillin is as effective as any other drug and can be given in a shorter period of time without danger of toxic reactions,

it becomes the drug of choice. Local penicillin therapy by iontophoresis, subconjunctival injections, and penicillin packs have ardent exponents, but at the present time there is insufficient data to warrant any definite conclusions.

We know of impressive results obtained by the use of iontophoresis, and this was especially noted in the earlier cases in which treatment was started immediately. Fever therapy is widely accepted as favorably influencing the outcome of interstitial keratitis and can be used in any of its forms as an adjunct to penicillin. Of course, mydriasis must be maintained by atropine or scopolamine throughout the treatment. Tradition and lack of noticeable response to penicillin have turned some observers back to the use of the heavy metals.

Syphilitic Uveitis. Syphilitic involvement of the uveal tract occurs in the secondary or late secondary stage of syphilis. The difficulties encountered in proving the syphilitic etiology of uveitis have caused considerable variation in the interpretation of the results of therapy. Benedict[16] and others have shown that antisyphilitic therapy exerts a non-specific action on uveitis, which may further complicate the evaluation of treatment. However, if more than a positive Wassermann reaction or a history of an old syphilitic infection were required for the basis of our diagnosis, our therapeutic results might be more uniform.

Klauder and Dublin[17] suggest that the most important criteria are: "(1) Demonstration of, or evidence pointing to, an early stage of syphilitic infection, (2) an inflammatory process of such character as to exclude, as far as is possible, other etiologic factors, (3) prompt effect of antisyphilitic treatment."

They observed a local intensification in the iritis in 70 percent of their cases following the administration of penicillin and neoarsphenamine. They purposely avoided large initial doses to prevent therapeutic paradox, and their observations were made by slitlamp examination.

The reaction followed within 8 to 24 hours after the drug was administered and consisted of an increased haziness in the cornea, an increase in the corneal precipitates, and an increase in the number of cells in the anterior chamber or an increase in the swelling of the iris.

Nodular iritis may be confirmatory evidence, but it does not occur frequently. It is more apt to be seen in cases in which the primary syphilis was insufficiently treated.

If the diagnosis of syphilitic uveitis is based on these considerations, the response to penicillin is dramatic; the inflammation disappearing in one or two weeks, without recurrence. It is important to initiate treatment with caution in the more severe cases, beginning with 5,000 to 10,000 units for the first 4 to 6 doses and then stepping up the dosage quite rapidly to the 50,000 unit dose. Less dramatic results are obtained with chemotherapy, but it is likewise very effective.

Fever therapy may be used in conjunction with penicillin, but Klauder[17] feels that it shows no definite advantage. In all cases, the treatment should be carried through its

TABLE 1

COMPARATIVE RESULTS OF TREATMENT OF INTERSTITIAL KERATITIS FROM
A STATISTICAL STUDY MADE BY KLAUDER[15]

Method of Treatment	No. of Eyes	Percentage of Final Visual Acuity		
		6/6 to 6/21	6/30 to 6/60	Less than 6/60
Untreated	185	55.1	37.0	12.0
Fever and Chemotherapy	95	84.2	8.4	7.4
Penicillin	97	84.5	11.3	4.2

entire course and not stopped when the uveitis had abated. Here again, mydriasis must be maintained.

Syphilitic Optic Neuritis. Syphilitic optic neuritis occurs more commonly in the late secondary stage of syphilis. It may occur with a syphilitic menigitis or be associated with a retinitis. It may also occur as a retrobulbar neuritis. If adequate antisyphilitic therapy is instituted early, the therapeutic results are good. We definitely feel that extreme caution should be taken to prevent too rapid a retrogression of the process with resulting increased fibrosis in the optic nerve. Herxheimer reactions should be avoided. Tryparsamide should not be used. Arsenicals have proved a satisfactory form of treatment, but more recently penicillin is being used with excellent results.

The initial dose of penicillin should be 10,000 units for the first 4 to 6 doses and then increased by 10,000 units with each successive dose until the 50,000- or 60,000 -unit dose is reached. This dosage is maintained until a total of at least 2½ million units has been given. Since appearance of optic neuritis may be the first sign of involvement of the nervous system, the patient should consult the syphilologist for the plan of his future treatment.

Many observers feel that fever therapy is definitely indicated at this stage of treatment and that it, with the penicillin, may check further progress of the neurosyphilis.

CHRONIC OCULAR SYPHILIS

Taboparesis with Ocular Involvement. Penicillin has been very effective in improving spinal-fluid abnormalities and certain of the clinical manifestations of neurosyphilis (more so than the results experienced by chemotherapy alone). Stokes[18] and Kateen and others[19] considered it equal to the effects of fever therapy. It offers many advantages over the induced fever techniques and has been substituted for it in many instances. However, it is generally felt that in the case of primary optic atrophy,

the combination of fever and penicillin should be employed.

The efficacy of penicillin therapy in the treatment of optic atrophy has not been established, and, until more evidence is obtainable, patients with this condition should receive immediate treatment with fever. The Kettering hypertherm has been advocated by some (Knight[20]). Epstein[21] has had excellent results with "blanket fever therapy," but malaria is generally believed to be the most effective (Moore,[22] Levin,[23] and Clark[24]).

It is logical to assume that, in the treatment of optic atrophy, the initial doses of the drug should be low and that treatment should begin as early as the diagnosis can be made. The therapeutic paradox may explain some of the cases of rapid loss of vision during the course of antisyphilitic therapy.

Perhaps, the greatest benefit that penicillin will offer in the therapy of primary optic atrophy will be the prevention of its occurrence by adequate and effective therapy in the primary stages of the disease, and the prevention of further involvement of the nervous system.

Syphilitic Optochiasmatic Arachnoiditis. There is a great deal of confusion in the literature concerning this condition. It is regarded by some to be the cause of primary syphilitic optic atrophy. The arachnoid adhesions are known to exist and have been demonstrated at autopsy and in exploratory operations. There is some question, however, as to whether or not the adhesions are responsible for the optic nerve atrophy. The clinical picture is not clearly defined and the symptomatology varies.

In all cases, there is a reduction of visual acuity. This loss of acuity may be rapid or insidious, unilateral or bilateral, and a central scotoma may or may not be present. The visual fields show variable changes, more commonly peripheral constrictions with a central scotoma.

Some observers present convincing evi-

dence of the occurrence of the arachnoid adhesions which tie down the optic nerves and compress the chiasm. One is more convinced when, after surgical freeing of the adhesions, the vision improves or the defect does not progress. It is difficult to understand why the adhesions do not reform in abundance after surgery and perhaps the improvement may be explained by mechanical stimulation of circulation in the optic nerve.

Bruetsch[25] has just recently published a very convincing paper in which he presents histologic and clinical evidence that primary syphilitic optic atrophy is essentially the result of inflammation in the optic nerve and chiasm, originating from a basilar syphilitic meningitis, which may or may not cause optochiasmal arachnoiditis, and that surgery is of little value. His suggested treatment is malarial therapy with a concomitant and subsequent course of penicillin, each course to consist of at least 5,000,000 units.

PITFALLS OF PENICILLIN THERAPY

Certain disadvantages in the use of penicillin must be realized.[26] Its widespread use in many minor conditions may mask an early syphilitic infection. This is particularly true in the routine treatment of gonorrhea. Sensitization reactions occur, according to Anderson,[27] in 2 to 5 percent of patients, varying from mild skin erythemas to the more serious exfoliating forms of dermatitis. Rare cases of laryngeal edema are recorded. In the more severe sensitization reactions, the drug must be discontinued, as it aggravates the patient and the disease.

Relapses have been reported to occur by Moore and others[28] in 3.2 percent of patients with seronegative primary syphilis,

5.0 percent in those with seropositive primary syphilis, and 9.8 percent in those with secondary syphilis. This fact necessitates a careful follow-up of the patient every 3 months for the first 2 years, and then yearly for 5 to 10 years. The "lulling of the patient into complacency"[26] by the rapid effect of penicillin therapy must be avoided.

SUMMARY AND CONCLUSIONS

Penicillin is an effective and convenient nontoxic antisyphilitic drug. In view of its recent synthesis and the probability of the development of therapeutically more active side chains, or of combining it with some of the heavy metals, its possibilities are far reaching. The results of its use in the early and acute lesions of syphilis involving the eye are very encouraging. Following the initial doses of penicillin, the intensification of the inflammatory process (constituting the Herxheimer reaction) in the eye is greater in the more acute and severe lesions, and should be avoided by small doses of the drug in the early stages of therapy.

Fever therapy still holds an important place in the therapy of ocular syphilis, being unsurpassed in the treatment of primary optic atrophy. Combined fever and penicillin therapy may prove to be the most effective method, especially in the late stages of syphilis.

It is important to keep in mind the necessity for careful follow-up treatment on all cases of syphilis regardless of the method of therapy and to remember that lapses, relapses and reinfections occur, which may be hazardous to the patient and to the public-health program.

384 Post Street (8).
Paulsen Medical Building.

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DISCUSSION

DR. NORMAN N. EPSTEIN (San Francisco): Dr. Harrington and Dr. Henry have presented an important and timely paper on the present concept of the therapy of ocular syphilis. While we, as individuals, may see only an occasional case of ocular syphilis, when such a case appears it is of utmost importance that we understand how to manage it promptly and effectively. Mismanagement or delay may be catastrophic as far as that patient is concerned.

The authors have stressed the place of

penicillin in the treatment of syphilis and there is no doubt that it is the greatest addition to the armamentarium of antisyphilitic drugs. It is now in its fifth year of use and, although a tremendous amount of research has been done upon its clinical application, the optimum time-dose relationship to this disease has not been determined. We know that it is a potent spirocheticide. The G fraction has this spirocheticidal property which is now available as crystalline penicillin G.

Penicillin G may be expected to be most effective in syphilitic processes where there are large numbers of Treponema pallida present and less effective in the degenerative and allergic effects of syphilis.

The rapid spirochete-killing property of penicillin G is emphasized clinically by the frequent development of the Herxheimer reaction as pointed out by the authors. Its importance in ocular syphilis is great. This reaction may be prevented or minimized by preparing the patient with a few weeks' treatment with bismuth therapy or by instituting penicillin therapy conservatively. It is our practice, when we wish to prevent the Herxheimer reaction, to institute penicillin therapy according to the following schedule: 1,000 units of aqueous penicillin G every 2 hours intramuscularly for the first 12 hours; 2,500 units every 2 hours for the second 12 hours; 5,000 units every 2 hours for the third 12 hours. If no untoward reaction occurs, the full dosage of 50,000 units every 2 hours for a total dose of 4.8 million units is given.

Ambulatory treatment with crystalline penicillin G in 4.5-percent beeswax and peanut oil may be used after the first 36 hours that aqueous penicillin has been given; 600,000 units as a single dose may be given for 10 to 20 days.

Frequently, it is advisable to combine artificial fever therapy with penicillin therapy in ocular syphilis, especially in interstitial keratitis and primary optic atrophy.

Inasmuch as we have had excellent results with artificial fever produced by mechanical means (the blanket method) I can see no reason for using malarial therapy. Engrafting one disease upon another in order to elevate body temperature is entirely unnecessary. The value of fever therapy in the treatment of ocular syphilis is well established clinically. Eagle has recently shown that elevation of temperature enhances the spirocheticidal effect of penicillin many times, both in vitro and in experimental animals. Clinical experience and experimental studies amply indicate that fever therapy has an important place in the treatment of ocular syphilis.

Penicillin should be most effective in acute arachnoiditis, optic neuritis, and acute iritis. In these conditions, spirochetes are present in abundance and penicillin should destroy them rapidly. In interstitial keratitis, where we are probably dealing with few organisms and an allergic reaction, and in primary syphilitic optic atrophy, where the process is degenerative, fever therapy will do the most good.

When it is possible to combine fever therapy with penicillin, we may expect our best results. The more rapidly this therapy is instituted the less residual damage we will have to deal with. This is especially true when progressive optic atrophy is present.

Something should be said about tryparsamide. This drug is contraindicated in ocular syphilis. Its position in the treatment of neurosyphilis has been almost entirely usurped by penicillin. We believe that tryparsamide has only a minor place in the syphilitic armamentarium.

Our neurosurgeons have treated a few cases of optic atrophy by release of arachnoidal adhesions. The results have not been striking. However, we have used this method of therapy only as a last resort and, therefore, the method has not been given a fair trial.

STREPTOMYCIN IN CLINICAL OPHTHALMOLOGY*

ARTHUR E. SCHULTZ, M.D.
East Lansing, Michigan

AND

JOHN R. GRUNWELL, MAJ. (MC), U.S.A.
Denver, Colorado

This study on the use of streptomycin in the eye clinic at Fitzsimons General Hospital, Denver, was not limited to a specific type of eye disease. It was felt that a greater knowledge of streptomycin activity could be obtained by treating more than one condition.

Recent medical literature has reported the successful use of streptomycin in ocular affections. Being a relatively recent therapeutic agent, this antibiotic has been used, thus far, predominantly on experimental animals. It cannot yet be said that streptomycin has won a place for itself in the treatment of ocular diseases; only further work with this drug will justify its use in these cases.

It is significant that streptomycin is more bacteriostatic or bactericidal than penicillin for Gram-negative bacteria. Streptomycin is also effective against some of the Gram-positive organisms. Among the Gram-negative organisms that may be found in the conjunctival fornices are: Koch-Weeks bacillus, Bacillus influenzae, Morax's diplobacillus, Petit's diplobacillus, Neisseria gonorrhoeae, Neisseria catarrhalis, Neisseria intracellularis meningitis, pneumonia bacillus, pseudomonas pyocyaneus, and Brucella tularensis. Some of the Gram-positive organisms are: Pneumococcus, Staphylococcus, Streptococcus, Corynebacterium diphtheriae, Corynebacterium xerosia, Mycobacterium tuberculosis.

Leopold and Nichols[1] have shown that streptomycin will penetrate the ocular tissues quite readily when administered systemically and by iontophoresis. Abrading the cornea will permit penetration when the drug is applied locally in drop form. Holt and Cogan[2] have shown that the corneal stroma offers little resistance to the passage of ions; whereas, the epithelium offers a relatively enormous resistance. Thus it is consistent that Leopold and Nichols should find increased penetration through the abraded cornea.

Alberstadt and Price[3] used streptomycin locally by instillation in a concentration of 10,000 μg. per ml. They found that the corneal ulcers treated with streptomycin healed in an average of 13 days, while those in the control group, treated without streptomycin, healed in 20 days.

Flippin[4] has also found that, when administered parenterally, streptomycin is detected in the intraocular fluids in concentrations approximating that level found in the circulating blood. This is important because penicillin penetrates poorly from the blood stream into the vitreous.[5]

Bellows and Farmer[6] report that streptomycin injections into the vitreous are well tolerated in concentrations of 500 μg. in 0.1 ml. saline. Local application of streptomycin in concentrations greater than 10,000 μg. per ml. delay the regeneration of the epithelium and promote scarring and corneal vascularization.

METHODS OF ADMINISTRATION

This report is a delineation of several methods of streptomycin administration in clinic and hospital patients. The methods are:

Local administration by iontophoresis of 50,000 to 100,000 μg. streptomycin per ml. of normal physiologic saline solution. A pad of cotton was placed over the eye and saturated

with the streptomycin solution. A 2 ma. galvanic current was used for 4 minutes, the positive electrode being applied to the eye pad. This was used in external and anterior-segment inflammations.

Parenteral administration by the intramuscular route. Parenteral administration of streptomycin, 1 to 2 gm. daily in 2 to 4 divided doses, given intramuscularly, was used in the more severe cases.

CASE REPORTS

BLEPHAROCONJUNCTIVITIS

Case 1. Infection was controlled with two treatments of streptomycin iontophoresis. A 30-year-old white man developed contact dermatitis of the lid margins following the use of an underarm deodorant. A severe secondary blepharoconjunctival infection developed disclosing hemolytic Staphylococcus on culture. After the second iontophoretic treatment with 50,000 µg. streptomycin per ml. the condition was greatly improved and the culture was negative.

Case 2. A recurrent lid infection of two years' duration in a 45-year-old white man resisted all treatment including sulfathiazole and penicillin ointment. The culture was negative. Eleven treatments of iontophoresis with 100,000 µg. streptomycin per ml. showed temporary improvement during the time of treatment but relapsed immediately on cessation of therapy.

ACUTE CONJUNCTIVITIS

Ten cases of acute conjunctivitis were treated with streptomycin iontophoresis using 50,000 µg. per ml. on an eye pad. Cultures disclosed 2 cases each with Gram-positive nonhemolytic Staphylococci and hemolytic Staphylococcus aureus and 2 with nonhemolytic Streptococci; 1 case with hemolytic Staphylococci and diphtheroids, 1 with hemolytic Staphylococcus aureus and another with nonhemolytic Staphylococcus albus. Three cases were negative.

In 8 of the cases the symptoms and ob-

jective evidence of the conjunctivitis subsided in an average of 2 treatments apiece. In the 9th case a sensitivity reaction occurred with marked blepharoedema, but the infection was controlled. In the 10th case the condition progressed to an oculoglandular syndrome, wherein the cultures and smears were negative and streptomycin therapy was ineffective. The condition was thought to be of viral etiology. However, it resolved after 10 days of parenteral penicillin therapy.

Cultures were negative in 48 to 72 hours in 7 of the cases.

CORNEAL ULCER

Case 1. This ulcer developed in two days in a 23-year-old white man following an abrasion by a Christmas-tree branch. The culture revealed hemolytic Staphylococcus aureus. In spite of conservative therapy, which included hot-boric compresses, 1-percent atropine drops once daily, and sulfathiazole ointment, the ulcer increased in depth and diameter. After the third treatment with 100,000 µg. streptomycin by iontrophoresis, the pain disappeared and there was no further staining with fluorescein. The culture became negative in 48 hours. Healing was uneventful.

Case 2. A blow with the fist to the right eye of a 25-year-old white man produced an abrasion which progressed to form a corneal ulcer in 5 days. The culture revealed nonhemolytic Staphylococcus albus. The ulcer healed after the third streptomycin treatment with iontophoresis, using 50,000 µg. per ml. of streptomycin.

Case 3. A third breakdown at the site of an old ulcer in a 22-year-old white man was completely healed with 6 treatments of streptomycin iontophoresis, using 50,000 µg. per ml. The culture was negative before therapy was begun. However, a 4th breakdown occurred three weeks later. This, likewise, was controlled by streptomycin iontophoresis, this time in 7 treatments, with no further recurrences in 3 months. The etiology of this ulcer was not known. Although a herpetic

type was considered, the corneal sensitivity was not altered.

KERATITIS

Case 1. A case of sclerotic keratitis over the lateral limbal margins of both eyes was seen in a 33-year-old Negro (fig. 1). Although the keratitis was of 5 years' duration, he complained of a dull ache, pruritus, and redness in both eyes for two months. The first strength Mantoux reaction was 2 plus. The culture was negative. At the time of the first consultation, the patient was using sulfathiazole ointment. He was given 2 gm. streptomycin parenterally daily for one month. In one week the eye ache, pruritus, and redness disappeared. At the end of a month, the conjunctival vessels were less congested and the limbal granulation tissue was greatly reduced (fig. 2). Streptomycin was then discontinued.

Within a week after cessation of treatment, a relapse occurred. Streptomycin therapy was resumed for another month with resulting complete quiescence of the lesions with minimal granulation tissue remaining at the limbus. The Mantoux reaction continued to be 2 plus. Visual acuity before and after therapy was 20/20 in each eye. Five months' observation showed no recurrence of the lesions or symptoms.

Case 2. A case of interstitial keratitis of one month's duration was seen in a 22-year-old American Indian. It was thought to be tuberculous. The culture was negative. The patient had been given penicillin ophthalmic ointment at a station hospital. He complained of a constant dull ache, photophobia, and epiphora in both eyes. Visual acuity was: O.D., 20/60; O.S., 20/25, uncorrectible. The cornea showed cloudy opacification and deep neovascularization of the propria, bilaterally. The first strength Mantoux reaction was 3 plus; Kahn test was negative. Streptomycin iontophoresis was begun, using 100,000 µg. per ml. Within one week photophobia, epiphora, and eye ache were greatly diminished. After one month of therapy, the lesions were

smaller and less dense. The blood vessels had begun to obliterate. The lesion in the left cornea cleared very well, while the right cornea was somewhat scarred in its deeper layers. Visual acuity was: O.D., 20/80; O.S., 20/20, corrected. The first strength Mantoux reaction was still 3 plus. A total of 42 treatments had been given.

Case 3. This 54-year-old white woman complained of moderate pain and loss of
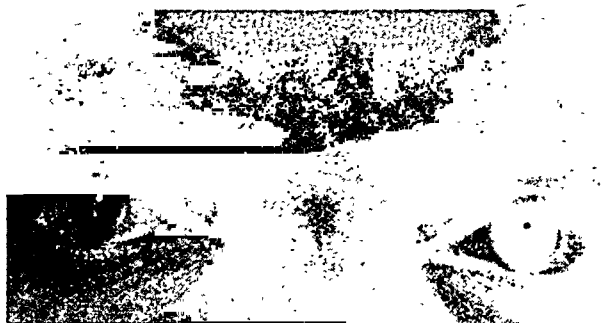
Fig. 1 (Schultz and Grunwell). A case of sclerosing keratitis before streptomycin therapy.

Fig. 2 (Schultz and Grunwell). The same case as in Figure 1 following streptomycin therapy.

vision in her left eye of two weeks' duration. Examination disclosed disciform keratitis with corneal anesthesia. The culture was negative and the first strength Mantoux reaction was 4 plus. Therapy included 1-percent atropine drops used once daily and iontophoresis with 50,000 µg. streptomycin per ml. in normal saline once daily. At the end of 6 treatments, the pain had disappeared and the lesion had become smaller. In fact the patient felt that her eye was so much improved that she decided to return to her Christian Science practitioner for further healing.

IRITIS

Case 1. Pain and slight visual loss in the left eye for 3 days was the complaint of a

35-year-old white man, who had recently recovered from pulmonary tuberculosis. Examination showed many mutton-fat keratic precipitates with many cells in the anterior chamber; the iris was edematous and sluggish in action. Because the patient had been up and around a short time, hyperpyrexia was considered unsafe.

Conservative therapy including 1-percent atropine drops once daily and hot-boric compresses was of no avail. One gm. streptomycin hydrochloride was given intramuscularly. That night the patient developed severe chills, fever, hemorrhagic bullae on his hands, and was practically prostrate. The patient had two such attacks. One hundred mg. of pyribenzamine and 10 cc. of calcium gluconate were given 3 times daily. Eight days later, all evidence of the previous iritis, including the keratic precipitates had disappeared.

The remarkably favorable results should be attributed to the patient's streptomycin allergy which caused the severe fever reaction. He had not been given streptomycin for tuberculosis. His general condition was unaffected. The iritis did not return during one month's observation.

UVEITIS

Case 1. This 55-year-old white man was operated for removal of a completely luxated Morgagnian cataractous lens. Upon attempted removal, the tense capsule ruptured just as the lens passed through the lips of the corneoscleral section. One week after surgery, corneal edema was quite marked. There were many cells in the anterior chamber and there was an increase in keratic precipitates from day to day. A retropupillary membrane which was present became quite dense at the end of two weeks. The patient complained of pain and tenderness of the eye. The culture and smear were negative.

Treatment consisted of 1-percent atropine drops, once daily. At the beginning of the third week, daily streptomycin iontophoresis, using 100,000 µg. per ml. was begun. After

10 treatments, the corneal edema and aqueous flare was less marked. The retropupillary membrane became thinner and, in 16 treatments, this membrane had completely disappeared. The subsequent course was uneventful.

Case 2. This 27-year-old white man complained of pain, tenderness, and photophobia in the left eye of 5 days' duration. He had had two such attacks previously, the first 20 years ago, the last one 4 years ago. Examination showed visual acuity in the left eye to be 20/50, uncorrectible, and signs of acute iridocyclitis with evidence of previous inflammation in the form of posterior synechias. The first strength Mantoux reaction was negative. Iontophoresis with 100,000 µg. streptomycin per ml. was begun 2 times daily. One-percent atropine drops once daily and hot-boric compresses three times daily were also begun. After five treatments of streptomycin iontophoresis, pain and tenderness were greatly relieved, corneal edema was reduced, keratic precipitates were fewer, and the aqueous flare was less marked. After 21 treatments, examination showed that the acute inflammation had subsided. Visual acuity was 20/30 in the left eye, uncorrectible.

Case 3. This 21-year-old white man, a patient with a minimal pulmonary tuberculosis, complained of hazy vision in each eye of one month's duration. Examination showed a visual acuity of 20/40 in each eye, correctible to 20/20. The slitlamp examination of the right eye disclosed a moderate number of keratic precipitates and many cells in the anterior chamber and vitreous. The left eye showed a small number of cells in the vitreous. The fundi were normal.

The presence of pulmonary tuberculosis contraindicated the use of hyperpyrexia. Therapy consisted of 1-percent atropine drops once daily, hot-boric compresses 3 times daily, and 1 gm. of streptomycin in 2 divided doses given parenterally. After one month of therapy, the patient no longer complained of hazy vision. Visual acuity was

20/30 plus in each eye, correctible to 20/15. Slitlamp examination of the right eye showed only a few remaining cells in the anterior chamber and the vitreous. No cells were found in the left eye.

Case 4. This 32-year-old white man complained of redness and blurring of vision in the right eye for a period of 3 weeks. Visual acuity of the right eye was 20/25, uncorrectible. The first strength Mantoux reaction was negative. Examination disclosed the presence of an anterior uveitis and a secondary glaucoma. Therapy consisted of cycloplegia and hyperpyrexia. It was finally necessary to resort to surgical intervention and an Elliot trephining operation was performed to control the tension. One month after surgery there was recurrence of the anterior uveitis with rise in tension. Thirteen treatments of streptomycin iontophoresis, using 100,000 μg. per ml. showed no regression of the uveitis. The condition was finally brought under control with the use of epinephrine bitartrate and adequate massage.

Case 5. This 42-year-old white man complained of loss of vision of the left eye 13 years ago following trauma. He had had a dull ache in this eye for several weeks. Visual acuity in the left eye was light projection. Examination disclosed the presence of many old and new keratic precipitates and a small number of cells in the anterior chamber; however, there were no synechias present. The iris was atrophic and a mature cataracta complicata was apparent. Intraocular pressure was 29 mm. Hg (Schiøtz). The first strength Mantoux reaction was 1 plus. Treatment consisted of 1-percent atropine drops and iontophoresis with 50,000 μg. streptomycin per ml. once daily. After the third treatment, the dull eye ache subsided and the tension dropped to 16 mm. Hg (Schiøtz). No positive findings were noted with the slitlamp although, after 28 treatments, there were fewer keratic precipitates and these were old. No cells were seen in the anterior chamber. The patient stated that his eye was subjectively much improved.

CHOROIDITIS

Case 1. Circumpapillary choroiditis in a patient with minimal pulmonary tuberculosis responded very well to parenteral streptomycin. This 21-year-old Negro complained of blurring vision in each eye of one week's duration.

Visual acuity was 20/20 in each eye. Slitlamp examination showed the anterior segment to be normal, but there were many cells in the vitreous of both eyes. Ophthalmoscopic examination disclosed hyperemia of both papillae with peripapillary edema worse in the left eye. There was exudate around the left disc. Moderate venous engorgement was present. Bilateral perimacular edema was also present. Visual field changes were consistent with findings of circumpapillary choroiditis. Hyperpyrexia was contraindicated because of the presence of pulmonary tuberculosis.

Treatment consisted of 1-percent atropine drops once daily, hot-boric compresses 3 times a day, and 50,000 units of penicillin intramuscularly every three hours. The condition was definitely worse after one week.

At the beginning of the second week, 2 gm. streptomycin were given daily in 4 divided doses. Within two weeks, improvement was noted, and there was regression of the peripapillary and perimacular edema. Peripheral and central fields showed marked recovery. The vitreous opacities cleared considerably. Streptomycin was continued for a longer period than the ocular disease indicated because of a subsequent improvement in the pulmonary tuberculosis. The choroiditis showed complete recovery in one month, but streptomycin was continued for 42 days. Visual acuity was 20/20 in each eye, uncorrected. No recurrence of the ocular condition was noted in 5 months.

EALES'S DISEASE

Case 1. A case of recurrent retinal periphlebitis was treated with parenteral streptomycin without improvement. This 22-year-old Negro, a patient with questionable pul-

TABLE 1

RESULTS OBTAINED WITH STREPTOMYCIN THERAPY IN VARIOUS OCULAR DISEASES

Condition Present	Case Number	Age	Duration of Complaint	50,000 μg./ml.	100,000 μg./ml. (Iontophoresis)	No Rx for Improve	No. Rx for Recovery	Not Improved	Parent. Strep. Dosage	Recovery Time	Complications	Culture	Hem. Staph. Aureus	Nonhem. Staph. Albus	Hem. Staph. & Diphth.	Nonhem. Strep.	Nonhem. Strep. & Hem. Staph.	Mantoux	Recurrence	Observ. follow. Rx.
Blepharoconjunctivitis	1	30	1 wk.	X	X	2	5	X			None	—	X							1 mo.
	2	45	2 yrs.								Cont. Derm.									2 mo.
Acute conjunctivitis	1	19	2 da.	X		2	4				None	—								2 mo.
	2	32	4 da.	X		1	2				None	—								3 wk.
	3	32	2 da.	X		1	3				None	—		X						1 mo.
	4	8	1 da.	X		1	1				None	—			X					1 mo.
	5	30	1 wk.	X		2	4	X			None					X				2 mo.
	6	30	1 da.	X		2	4				None									2 mo.
	7	43	1 mo.	X		2	4				None						X			2 mo.
	8	10	1 wk.	X		3	5				None									1 mo.
	9	25	2 da.	X			Dis-con.				Cont. Derm.									1 mo.
	10	25	1 da.	X		1														
Corneal ulcer	1	23	2 da.		X	3	4				None	—	X							2½ mo.
	2	25	5 da.	X		3	6				None			X						1½ mo.
	3	22	1 da.	X		6					None									2 mo.
Keratitis	1	33	5 yrs.		X	12	42		2 gm. daily	2 mo.	None	—						2+		5 mo.
	2	22	1 mo.	X		6		Incomplete			None	—						3+	X	1 mo.
	3	54	2 wk.								None	—						4+	(X)	1 wk.
Iritis	1	35	3 da.				Dis-con.		1 gm. daily		Severe system. react.	not done								1 mo.
Uveitis	1	55	3 wk.		X	10	16		1 gm. daily	1 mo.	Pain Edema	"								2 mo.
	2	27	5 da.		X	5	21				None	"								1 mo.
	3	21	1 mo.								None	"					Pulmon. TB		4 mo.
	4	32	3 wk.	X	X	3	28?	X			Sl. Corn. stain.	"						1+		3 mo.
	5	42	3 wk.								None									2 mo.
Choroiditis	1	21	1 wk.					X	2 gm. daily	2 wk.	None	"						Pulmon. TB		4 mo.
Eale's disease	1	22	2 wk.					X	2 gm. daily		Facial derm.	"						3+		5 mo.
Intravitreal foreign body	1	21	8 hr.	X					1 gm. daily	2 wk.	None			X						1 mo.

monary tuberculosis, complained of poor vision in the left eye of 2 weeks' duration. Visual acuity was 20/20 in the right eye and 6/400 in the left eye, uncorrectible. Ophthalmologic examination showed the right fundus to be normal while the left showed peripheral venous perivasculitis. The first strength Mantoux reaction had been 3 plus when the patient was admitted to the hospital 6 months previously.

The patient was given 2 gm. streptomycin parenterally daily for 26 days. Following this period, the right eye began to show venous perivasculitis and hemorrhages increased in the left eye. Vision in the right eye was 20/20; hand movements in the left eye. The condition became progressively worse in spite of streptomycin and strict bed rest. Rutin was begun, but this too proved ineffectual. At the last examination, 6 months after the onset of symptoms, massive vitreous hemorrhages in each eye had reduced visual acuity to light projection in the right eye and the ability to count fingers at one meter with the left eye.

INTRAOCULAR FOREIGN BODY

Case 1. This 21-year-old white man was hammering a chisel when a fragment from the hammer flew into his left eye. Examination disclosed a jagged perforation of the sclera through the internal rectus muscle. The vitreous was presenting. Ophthalmologic examination disclosed air bubbles in the vitreous and massive vitreous hemorrhage. No foreign body was seen. Following X-ray localization, removal of the intraocular foreign body through the perforation was successfully performed. Cultures revealed a nonhemolytic Staphylococcus albus.

Further therapy consisted solely of strict bed rest and 1 gm. daily of streptomycin hydrochloride given parenterally. The medication was continued for two weeks. There was no evidence of intraocular infection and the eye had begun to whiten. Three days after stopping streptomycin, a massive vitreous hemorrhage occurred, obscuring the pre-

viously visible fundus. At the last examination, 6 weeks after the injury, the sclera of the injured eye was almost as white as the normal eye and the vitreous hemorrhage was absorbing slowly; there was no evidence of inflammation nor of phthisis.

COMMENT

The advent of a new drug in the field of ocular therapeutics is often similar to a chain reaction. First there is skepticism, then acceptance, followed by over-enthusiasm, ending in indifference.

Those who work with a new drug often fail to realize that many ocular diseases are self-limiting. It follows, then, that cures attributed to the drug at hand should be viewed with caution because the error of clinical observation is high. The enthusiasm of the experimenter should be tempered by the criticism of the skeptic.

The clinical use of streptomycin herein presented is significant in that the course of ocular disease was favorably altered in the majority of cases studied.

The rational in using streptomycin in concentrations of 50,000 and 100,000 μg. per ml. of normal saline solution, 5 and 10 times greater than that recommended by Bellows and Farmer,[6] lies in the fact that a pad saturated with streptomycin is placed over the partially closed lids. Thus, the tears diluted the streptomycin as it came in contact with the cornea and conjunctiva. It was felt that not only was local application achieved but that the tarsal glands, so often the nidus for infection, were in some measure penetrated by the antibiotic.

The first case of acute secondary blepharoconjunctivitis culturing hemolytic Staphylococcus responded very well to streptomycin. The second case of chronic blepharoconjunctivitis was only temporarily improved while on treatment. This latter patient developed a contact dermatitis of the lids after the 11th treatment; this is not uncommon, as indicated by Strauss and Warring.[7]

The 10 cases of acute conjunctivitis were treated with iontophoresis using 50,000 μg. of streptomycin per ml. of normal saline. All but 3 cases showed positive cultures. Marked improvement was noted after an average of 2 treatments in 8 of the cases. The 9th case developed contact dermatitis of the lids, but the culture was negative after the first treatment. The 10th case was thought to be viral in etiology; no response was obtained. The ideal condition would have been to run a series of control studies without any treatment and another series using penicillin, but this was not possible. All we can surmise is that, on the basis of clinical observation and bacteriologic studies, improvement was not only achieved but accelerated.

The satisfactory results obtained in the healing of corneal ulcers indicated that our streptomycin concentrations did not discourage epithelization, and were apparently effective against Gram-positive organisms. We agree with the findings of Alberstadt and Price[3] in that the "duration of pain was shortened, healing of the ulcer was accelerated, and total hospitalization was shortened."

Parenteral streptomycin was effective in controlling a case of sclerosing keratitis— the etiology very likely was tuberculous. The tuberculin skin test was positive and unchanged before and after therapy. Is it possible that the allergenic focus was altered by the streptomycin and thus changed the type of tuberculoprotein produced? Or was the lesion on the eye tuberculous per se? Further investigation is certainly indicated along these lines.

It is pertinent at this point to recognize the activity of streptomycin against the tubercle bacillus. It had been demonstrated by Fisher[8] and other investigators[9] that tubercle bacilli isolated from a total of 130 patients prior to therapy were uniformly inhibited by 1 μg. or less streptomycin per ml. The literature[1, 4] and our own studies give ample

evidence of the high intraocular concentration of streptomycin. Therefore, is it not conceivable that streptomycin may favorably affect the course of the ocular tubercle or of ocular disease due to tuberculin sensitivity? Several of our case studies indicate that this may be so. Streptomycin iontophoresis appeared to improve the course of a tuberculous interstitial keratitis and a disciform keratitis. First strength Mantoux tests in these cases were 3 and 4 plus, respectively.

A patient with healed pulmonary tuberculosis was found to have iritis with muttonfat keratic precipitates. A single dose of one gram of parenteral streptomycin produced a very severe and dangerous anaphylactoid reaction, characterized by high fever (105°F.), morbilliform rash, blotchy erythema, and generalized malaise. To avoid a reaction such as this, it would be advisable to skin test each patient prior to therapy.

Five cases of uveitis were seen. Four were treated with streptomycin iontophoresis and one, a patient with pulmonary tuberculosis, was treated with parenteral streptomycin. Four of the cases improved under therapy.

One case of circumpapillary choroiditis in a patient with pulmonary tuberculosis responded favorably to parenteral streptomycin wherein previous conservative therapy had failed.

A patient with Eales's disease did not respond to parenteral streptomycin after 26 days of treatment. The disease progressed to cause almost complete blindness.

A patient was seen with an intravitreal metallic foreign body, with vitreous presenting at the point of entrance through the sclera. The culture was positive for nonhemolytic Staphylococcus albus. Parenteral streptomycin was given for two weeks after removal of the foreign body. No vitreal infection or phthisis had occurred after one month's observation.

119 East Grand River Avenue.

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FUNDUS LESIONS IN TUBERCULOUS MENINGITIS AND MILIARY PULMONARY TUBERCULOSIS TREATED WITH STREPTOMYCIN

M. A. DOLLFUS, M.D.
Paris, France

Translated by MICHEL LOUTFALLAH, M.D.
Santa Barbara, California

AND

CLARENCE H. ALBAUGH, M.D.
Los Angeles, California

As early as 1942, I had called attention to the frequency with which chorioretinal tubercles are found in miliary pulmonary tuberculosis and in tuberculous meningitis.[1] These lesions had been fully described in 1867 by Bouchut[2] but they had been apparently forgotten by some, and their existence denied by others.

As treatment with streptomycin was started on such cases in the hospitals of Paris, I suggested the importance of ophthalmoscopic examination from the diagnostic, prognostic, and even therapeutic standpoints. It was indeed possible to think that the evolution of the chorioretinal tubercles, following treatment with streptomycin, could be similar to that of the meningeal or pulmonary lesions.

At the same time as Debré, Monbrun, and Laval[3] were studying (in the Hôpital des Enfants Malades) the fundi of 135 such cases, I carried on a similar study in the specialized departments of the Hôpital de la Pitié and the Hôpital de la Salpétrière, in the services of M. Decourt and M. Fouquet. At the Pan-American Congress of Ophthalmology at Havana, I reported the first results; but, since then, I have examined a great number of cases with lesions either in the chorioretina or in the optic nerve.

CHORIORETINAL LESIONS

The chorioretinal lesions are of three main types, all of which represent miliary tuberculosis, as described long ago by Bouchut. If these lesions have not been seen by some observers, it is due to the fact that the examination of young, severely ill, semicomatose, and photophobic patients is quite difficult. A complete mydriasis, repeated examinations in the course of the disease, and a great deal of patience are essential.

The first type of lesion seen is the small miliary tubercle. It is round, situated near the bifurcation of vessels, white or yellowish, with indistinct edges, and with a diameter rarely exceeding one-half disc diameter. It may be found anywhere in the retina but most often is located near the posterior pole, in contact with or close to the disc. This tubercle is slightly elevated above the level of the retina; it may be single, but is more often multiple, and distributed in both eyes. The optic nerve is somewhat hyperemic, with blurred margins. Functional signs are almost absent. Since there are usually no

subjective symptoms, even in conscious patients with miliary pulmonary tuberculosis, only a systematic search for the lesions will disclose them.

In the second type, more often noted than the tubercles, the retinal lesion is formed by one or more small white spots with blurred edges, not elevated above the retina, of more irregular shape than the tubercles. They may be round but are generally more or less triangular. In certain cases, especially in miliary tuberculosis with meningitis, the whole posterior pole of the eye is spotted with such lesions which may number as many as 10 or 20. More commonly, however, only 5 or 6 are noted and present equally in both eyes.

The third type of lesion is found more rarely. It is a single, isolated tubercle, measuring 1 to 2 disc diameters in size. It is rounded and somewhat elevated above the retina. This tubercle is yellowish-white in color, and its edges are fairly well defined.

One should mention, in addition (as has been observed by Monbrun and Lavat), the occasional presence in these patients of small chorioretinal patches of the atrophic type, with some pigmented edges, which may be considered as healed tubercles.

OPTIC-NERVE LESIONS

Lesions of the optic nerve are less frequent than those in the retina. However, as I have already stated, the presence of a chorioretinal tubercle is often associated with a certain degree of papillary edema characterized by congestion of the nervehead and blurred edges. More rarely, the appearance may be that of a choked disc, especially in the cases of tuberculous meningitis where streptomycin treatment has led to partitioning by meningeal adhesions. In these cases with meningitis, the choked discs often resemble those with intracranial tumor. Finally, in a few isolated cases, I have noted the presence of an optic atrophy, with well-defined margins. I am not sure what the pathogenesis of these cases may be.

EVOLUTION OF THE CHORIORETINAL LESIONS

Before streptomycin therapy was introduced, death occurred quite rapidly and, therefore, healing of the tubercle of the choroid was seen only exceptionally. Since the use of streptomycin, however, it has been possible to follow these lesions for weeks or months.

Contrary to what was expected, streptomycin seems to have a very irregular action on the evolution of the chorioretinal tubercles. In some cases, I have seen the tubercles become paler, then disappear completely without leaving a trace; in others, the evolution started with a pigmentation at the center of the lesion as a black spot, then extended toward the periphery, finally leaving a small atrophic area edged with pigment or centered by a black spot. This evolution of the tubercle toward healing was noted in only a small number of cases, and paralleled improvement of the general health.

In 5 of 16 cases, the tubercles disappeared or became healed with pigmentation as the condition of the patient improved after several weeks of treatment. In 9 cases, the lesions were not modified by the use of streptomycin, and the tubercles remained without apparent change 3 or 4 months after the start of the treatment, even though 2 gm. of streptomycin were used daily. Finally, in 2 cases there was dissociation between the evolution of the chorioretinal tubercles, which disappeared, and the general condition which declined and ended in death.

Tubercles of the choroid were even seen to appear in the course of the treatment. In a case which had been checked and treated for several weeks, with improvement in the general condition, several tubercles observed at the first examination healed or disappeared, then suddenly multiple tubercles developed in both eyes as the treatment was continued regularly.

In some patients, dismissed from the hospital after apparent cure of their meningitis or miliary pulmonary tuberculosis and in whom tubercles disappeared or even in whom

none were seen during the course of the treatment, who were reëxamined several weeks after discontinued treatment, chorioretinal tubercles were noted later. This proves that the tuberculous process was not entirely extinguished and that a recurrence was imminent.

FREQUENCY OF THE CHORIORETINAL LESIONS

In my preceding article,[1] I reported that chorioretinal tubercles had been noted in 72 percent of the cases of miliary tuberculosis without meningeal symptoms, and 40 percent of the cases of tuberculous meningitis. These examinations, however, were made on severely ill patients, often in the last days of life, when an efflorescence of miliary lesions occurs. In addition, the statistics were derived from a limited number of patients.

The centralization of the cases in specialized departments, for treatment with streptomycin, has enabled me to observe a larger number of patients, adults as well as children.

My study was made on 226 patients (103 adults and 123 children). I noted tubercles in 79 cases (35.0 percent; 29 percent in adults, 39.9 percent in children). I have further divided my cases, as follows:

1. Pure miliary tuberculosis without meningeal signs—37 cases of this type were examined; 18 had tubercles (48.7 percent; 33 percent of adults, and 65.7 percent of children).

2. Military tuberculosis with meningitis— 29 cases were observed, of which 20 presented chorioretinal tubercles (68.9 percent; 75 percent of adults, and 61.5 percent of children).

3. Tuberculous meningitis without pulmonary signs—160 cases were examined; 31 presented choriorentinal tubercles (19.3 percent; 17.4 percent of adults, and 20.8 percent of children).

The appearance of tubercles is a little more frequent in children, as compared with the adults. If the frequency of the tubercles found in meningitis is smaller than that of published accounts, it is due to the fact that the cases of meningitis are now directed earlier to a specialized department for streptomycin treatment at a stage when tubercles of the choroid are rare and, under the influence of the treatment, do not develop.

There is no appreciable difference in frequency between the sexes.

FREQUENCY OF OPTIC-NERVE LESIONS

The fairly frequent observation of a slight blurring of the disc margins, when tubercles of the choroid are present, has already been mentioned. However, not infrequently, in addition to the slight edema, a real papillitis or choked disc has been observed. In 5 cases of tuberculous meningitis, I noted the development of optic atrophy during the course of treatment.

It is obvious that, in miliary pulmonary tuberculosis, involvement of the optic nerve is exceptional. Only one case was noted (2.7 percent) and it is probable that the patient might have developed meningeal signs, if follow-up had been complete.

In miliary pulmonary tuberculosis with meningeal involvement, the optic nerve was affected in 10.3 percent of cases.

In tuberculous meningitis, this complication is much more frequent. In 160 cases, 45 had such lesions, or 28.1 percent; and in 5 cases (3.1 percent), an optic atrophy was present. These cases of optic atrophy may give rise to a discussion as to the etiology. In my communication to the Pan-American Congress at Havana, I introduced the hypothesis that the lesion may be due to the toxicity of streptomycin, similar to neuritis of the eighth cranial nerve which is known to develop. Four such cases were in children aged 3, 3½, 5, and 6 years. I examined these children upon their admission; their fundi were considered normal. Three of these cases had tuberculous meningitis, and the fourth miliary pulmonary tuberculosis with meningitis. The dosages of streptomycin were 1.5

to 2 gm. daily, by intramuscular injections, and 0.2 gm. intrathecally. In all 4 cases, after 2 weeks of treatment, a pallor of the disc was noted without preceding papillitis. Slowly the discs became atrophic, with loss of sight. In 1 of the cases, treatment with streptomycin was stopped, with a resulting slight improvement in the visual acuity; but in the 3 others blindness with optic atrophy became permanent. Since formulation of the hypothesis of toxic optic neuritis, anatomic evidences were obtained in 2 cases. The optic nerves were sheathed by a false membrane, thus forming a real optico-chiasmatic arachnoiditis. The possibility of toxic neuritis due to streptomycin cannot be dismissed entirely; but the fact that this complication is not seen in the large group treated and having no meningeal signs leads one to believe that the etiology of these cases of neuritis may be the meningitis. The presence of this complication in these patients is due to the extension of life afforded by the treatment of meningitis by streptomycin.

Conclusion

The systematic examination of the fundus oculi, in tuberculous patients treated with streptomycin, can bring out significant observations on the course of the disease.

The appearance or the discovery of chorirentinal tubercles has considerable prognostic importance, as it forecasts a meningeal complication in miliary pulmonary tuberculosis and is an index of severity of the form of the disease in tuberculous meningitis.

It is necessary, after discontinuation of the treatment with streptomycin, in patients considered as cured, to have periodic ophthalmoscopic examinations. The appearance of a chorioretinal tubercle preceding a recurrence of the systemic disease, by days or weeks, leads thereby to the earlier resumption of treatment.

In a fairly large number of cases, evolution of the chorioretinal tubercles paralleled the evolution of the pulmonary or meningeal tuberculosis; but the relation is not constant and, from the state of the fundus lesions, one cannot deduce the state of the systemic lesions.

The lesions of the optic nerve, especially choked disc which is fairly frequent, lead one to believe that, in these cases of meningeal blocks by adhesions or in cases of block of the third ventricle, an operation may become necessary to place in situ the drug which cannot pass through the meningeal partitions.

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REMOVAL OF INTRAOCULAR NONMAGNETIC FOREIGN BODIES*

WITH A REPORT OF SIX CASES

JAMES S. SHIPMAN, M.D.
Philadelphia, Pennsylvania

Any type of intraocular foreign body may test the skill and patience of most ophthalmologists. This is doubly true when the foreign body is nonmagnetic. In many cases the surgeon is perplexed and at a loss as to what procedure to follow, particularly when the patient still has useful vision present in the injured eye.

This problem was particularly important during the recent world war when the incidence of nonmagnetic intraocular foreign bodies was very high. This was pointed out in Wilder's[1] report concerning 150 enucleated eyes which had been sent to the Institute of Pathology, U. S. Army Museum. The increased use of alloys in industry and in civilian life also increases the incidence of inocular nonmagnetic foreign bodies and makes this problem more important to the ophthalmologist.

Jackson[2] has said "the earliest possible removal of the foreign body is the first thing to be considered in nearly all cases and it usually should be done at any cost, even to the removal of the eye." de Schweinitz[3] stated that "while foreign bodies in the background of the eye may be tolerated for long periods of time with retention of good vision they never can be trusted, as they are liable to cause degenerative changes." Knapp[4] felt very much the same as these two authors. This feeling has become more or less universal among ophthalmologists, particularly when the foreign body is copper which is believed to cause irritative and later degenerative changes, including chalcosis, when left in an eye. This was first pointed out by Leber[5] over 50 years ago. Purtscher,[6] in 1918, called attention to chalcosis lentis or copper cataract. Schultz[7]

more recently has described this condition as bilateral. Sympathetic ophthalmia has been considered a very likely complication in these cases; however, I am not so sure that this danger is as great as we formerly thought it to be.

Bulson[8] doubted the necessity for removal of all foreign bodies. He felt that every case should be considered separately. Of course, there are many types of inert nonmagnetic foreign bodies such as glass, stone, zinc, wood, and so forth, the removal of which from the eye is not always essential, but depends upon the localization and size of the foreign body.

I have had under my observation for over 16 years a man who has had a small piece of zinc embedded in one eye. This is in the retina near the optic disc, with no evidence of any ocular irritation or degeneration. Nevertheless, I think we can all agree that, if a foreign body is present in an eye and if it can be removed without too much destruction to the eye, its removal should be attempted. I feel that this is especially true when the foreign body appears to be copper.

I have had two cases under my observation for the past 3 or 4 years, one of which has a small piece of copper (dynamite cap) in the lower anterior vitreous as localized by the Sweet localizer. This cannot, however, be seen with the ophthalmoscope. This case showed a definite chalcosis lentis with an irregular starlike yellow pigmentation on the anterior capsule of the lens when it first came under my observation. After several consultations, it was decided to make no attempt to remove the foreign body, since it was not visible with the ophthalmoscope and also since the vitreous in the lower portion was so very cloudy. However, if

and when the vitreous clears enough to afford a view of the foreign body, we will attempt its removal, using the first method about to be described.

The second case has a piece of copper (a fragment of a 22-caliber cartridge shell) which is localized in the sclera far posteriorly. Again, the foreign body cannot be seen with the ophthalmoscope. Dr. Zentmayer has seen this case in consultation and advised conservative treatment and observation which has been followed to date. The eye remains quiet.

METHODS OF REMOVAL

Numerous methods for the removal of nonmagnetic foreign bodies from the eye have been attempted in the past. The five principal ones which have been reported are: (1) Direct observation with the ophthalmoscope while using forceps through a posterior sclerotomy; (2) use of the biplane fluoroscope; (3) removal with the ophthalmic endoscope; (4) removal by use of transillumination; (5) removal of small foreign bodies from soft lenses by means of a large needle and suction.

FORCEPS THROUGH A POSTERIOR SCLEROTOMY

The first of these methods is unquestionably the oldest and has probably been used by more ophthalmologists than any of the others. Greenwood[9] stated that he used this method to extract copper from the eye in two cases more than 20 years ago. He also stated that the forceps he used had cup-shaped ends.

Technique. The Parker electric hand magnet is applied to the globe while observing the foreign body with the ophthalmoscope. The current is turned on and off and the foreign body is carefully observed to detect any response. In the absence of any response, it is concluded the foreign body is nonmagnetic.

A retrobulbar injection of 1.5 cc. of 2-percent novocain is then given and a small amount of the same solution is injected subconjunctivally in the quadrant under examination.

An incision is then made in the bulbar conjunctiva parallel to and 10 mm. back of the limbus. The sclera is exposed and cleaned of all episcleral tissue. A point on the sclera, which we feel is nearest to where the foreign body is localized, is selected and marked. This area is then surrounded by diathermy micropins, the number depending on the length of the sclerotomy to be done. A scleral incision is then made with a Graefe knife in a radial direction from the limbus. The length of this incision will depend on the size of the foreign body.

It has been recommended by Thorpe[10] that this incision should be I or T shaped and that only the sclera should be incised with the knife, the uvea being incised with the cutting diathermy current. This seems logical but not necessary. I use a linear incision and cut through the uvea as well as the sclera with the Graefe knife. If one is fortunate, the foreign body may be seen in the vitreous by direct view when the uvea is opened and if so, it can be grasped with a forceps and removed. In the sixth case to be described later, it was my good fortune to have this happen.

If this does not occur, the foreign body is then observed through the dilated pupil with the ophthalmoscope held in one hand while the forceps, of a type similar to those devised by Thorpe[10] or Cross,[11] are held in the other hand and inserted through the scleral opening into the vitreous chamber. While observing the blades of the forceps and the foreign body with the ophthalmoscope, it is possible to grasp the foreign body and remove it through the opening in the sclera. The scleral incision is then superficially coagulated with the Lacarrere electrode; the opening is closed with interrupted fine black silk 6-0 sutures; and the conjunctival incision is closed with a running black silk suture.

The type of forceps which we have used in this procedure was similar to a Hess iris

forceps with flat corrugated tips. However, in view of Thorpe's[10] contribution on this subject, I feel that his varied and most adaptable forceps might be preferable for this type of work.

I claim no credit for the procedure although, at the time I saw the first case reported here, I had not seen or read of the procedure but followed it because it appealed to me as logical and practical. This first method was the one which was followed in the five reported cases of copper in the vitreous.

USE OF BIPLANE FLUOROSCOPE

The second method mentioned, namely, that in which a biplane fluoroscope is used, was first described by Cross.[11] He has written several articles on this subject and, in 1931, reported that up until that time he had done seven cases by this method. In one of these cases the resulting vision was 6/6. In most of his cases the foreign body was a lead shot and, in a few, a large piece of copper in the vitreous. He devised a special type of cross-action forceps which were made of No. 18 German silver wire, the ends of which were flattened and bent in the form of a circle and filed out to fit the size of shot which might be present in the eye.

Technique. A conjunctival incision is made parallel to and 8 or 10 mm. back of the limbus in the quadrant where the foreign body has been localized. The sclera is then bared and a posterior sclerotomy 6 to 8 mm. long is done at a point as near the location of the foreign body as possible. The forceps are then inserted through the incision at an angle so that their long axis corresponds to that of the wound and are then turned at right angles so that their action corresponds to the long axis of the incision. The tips of the forceps are then placed over the approximate position of the foreign body in the vitreous as located on the X-ray film. The speculum is removed and all the lights are turned out. The remainder of the operation

is carried out in darkness with the roentgenologist directing the surgeon.

USE OF OPHTHALMIC ENDOSCOPE

The third method of extraction with the ophthalmic endoscope was devised by Thorpe.[10] The instrument is a special inverted Galileon telescope, similar to those used in cystoscopy, pharyngoscopy, and so forth. It permits a view of a field 10 mm. in diameter at one inch distance. The telescope is 2.5 mm. in diameter. There is a miniature lamp, adjacent to and in front of the telescope, which is operated by a battery handle or by a cord from a rheostat. The forceps are attached behind the telescope by means of an adjustable sheath. In all, the total width of the instrument at its widest part is 6 to 6.5 mm.

Technique. It is necessary to make an incision of 8 mm. in the sclera to use this instrument. Thorpe[10] reports that he has used it successfully in five cases. Spaeth[12] also reports a certain degree of success with this instrument. I have always felt, however, that the incision necessary to use this instrument was too large and was inviting a considerable loss of vitreous, although I can see that in some cases this method might have to be resorted to in order to save the eye even though satisfactory vision might be lost.

TRANSILLUMINATION

Transillumination as described by Schultz[7] is the fourth method.

Technique. The sclera is bared as in the other procedures except over a wider area and further back so that two strong lights similar to those used in the Lancaster transilluminator can be inserted back of the globe, and gently but firmly placed against the eyeball at two different points opposite the foreign body and opposite the incision in the sclera which has been made as near to the localization of the foreign body as possible. A third and similar light is then used to illuminate the wound area. A pair of Hess

iris forceps is then used to grasp and extract the foreign body which is seen as a shadow outlined against the illuminated area behind it.

The use of this method appears logical when the foreign body cannot be seen with the ophthalmoscope. I have tried it in one case in which a large piece of copper was localized by X ray in the vitreous but could not be seen ophthalmoscopically. Unfortunately, there was a considerable amount of purulent exudate in the vitreous which interfered to some extent with the transillumination. We were unable by this method to get a definite shadow of the foreign body and were unsuccessful in its removal. The eye was lost.

LARGE NEEDLE AND SUCTION

The fifth method of removal of small nonmagnetic foreign bodies, when located in the lens, by means of a needle and suction was described by Donovan.[13]

Technique. This is done by making a small incision in the cornea just anterior to the limbus and near the 12-o'clock position. A large needle, such as that used for spinal puncture, with a rubber tube and syringe to supply suction, is then inserted through this opening and into the soft cataractous lens. The opening of the tip of this needle is kept face upward so that it can be observed by the operator and is placed underneath the foreign body in the lens at which time suction is applied and the foreign body, when small enough, is engaged in the needle and extracted. Naturally, this method is limited to children with soft lenses.

CASE REPORTS

CASE 1

History. A white woman, aged 21 years, was first examined at Wills Hospital on July 14, 1932. She stated that while operating a coil winding machine, about one hour before, a piece of fine copper wire broke off and struck her in the left eye. Visual acuity without correction was 6/9 plus in each eye.

External examination. Right eye: Entirely normal. Left eye: There was a small laceration, 1 mm. in length, in the bulbar conjunctiva on the nasal side. This was in the horizontal plane about 12 mm. from the limbus. There were no corneal abrasions or perforations. The anterior chamber was of normal depth and clear. The iris was of good color and the pupil was round, regular, and equal in size to that of the right eye. The direct and consensual light reaction, as well as the convergence reaction, were normal.

Ophthalmoscopic examination. Right eye: The media was clear and the fundus was normal in appearance. Left eye: A highly refractile, metallic-looking foreign body could be seen in the anterior vitreous. This was "S" shaped and gave the appearance of fine copper wire. It moved slightly but did not float freely. A few stringy vitreous opacities were observed posterior to the foreign body. Two small fresh circular hemorrhages could be seen well forward in the nasal portion of the retina.

Roentgenographic findings. There was an opaque foreign body in the left eye which corresponded in size, shape, and position to that seen ophthalmoscopically.

Operation. The Parker electric hand magnet was applied to the upper portion of the left globe while the foreign body was observed with the ophthalmoscope. Application of the current produced no movement whatever of the foreign body. It was then concluded that the foreign body was copper and nonmagnetic and would, therefore, have to be removed by other means.

An incision was made in the bulbar conjunctiva parallel to the limbus and 10 mm. back of it in the upper nasal quadrant. A black silk suture was inserted in the conjunctiva on either side of the incision for traction. A posterior sclerotomy, 3 to 4 mm. long, was then made radially with a Graefe knife, 10 mm. back of the limbus. An old iris forceps with worn off teeth was then inserted through the lips of the sclerotomy wound.

While observing the blades of the forceps and the foreign body with the ophthalmoscope through the dilated pupil, it was possible to grasp the foreign body and remove it through the opening in the sclera. The ophthalmoscope was held in the left hand and the forceps in the right while the assistant, by grasping the bulbar conjunctiva with fixation forceps, helped the patient fix the eye temporally. Several attempts were necessary, however, before the piece of copper was finally engaged between the blades of the forceps.

The loss of vitreous was very slight and much less than might be expected. The sclerotomy wound was then closed with one fine black silk intrascleral suture, and the conjunctiva was closed over this with a continuous silk suture.

Postoperative convalescence. The patient made a very satisfactory recovery with no postoperative hemorrhage or infection. After one week she was discharged from the hospital with visual acuity of 6/9 in the left eye with a +1.0D. sph. ⊃ +0.25D. cyl. ax. 90°. The eye was entirely quiet and the media was remarkably clear. Examination with the ophthalmoscope revealed a small white area

surrounded by small hemorrhages, well forward in the superior nasal quadrant. There was no evidence of any detachment of the retina at this time.

About two weeks later, August 10, 1932, ophthalmoscopic examination of the left eye showed a small globular detachment of the retina in the upper nasal quadrant. There was a corresponding visual field defect in the lower temporal quadrant. The detachment of the retina progressed and the patient was readmitted to Wills Hospital on August 30th. On September 1, 1932, an electrocoagulation operation was performed with the Weve needles. This failed to relieve the detachment. The operation was repeated in October, 1932. This operation was also unsuccessful.

Finally in January, 1933, a third electrocoagulation operation was done and this time the Safar needles were used. The retina remained detached, however, and the patient refused further surgery. The detachment became complete and was complicated by the development of a cataract. The eye remained quiet although it finally became blind and divergent.

CASE 2

History. A white man, aged 25 years, was first admitted to Wills Hospital on August 29, 1933, with a history of the left eye being injured by a dynamite-cap explosion three days previously. Visual acuity, with correction, was 6/6 in the right eye and 6/21 in the left.

External examination. Right eye: Entirely normal. Left eye: There was a laceration about 2 to 3 mm. in length in the corneoscleral limbus at the 9-o'clock position, with a small prolapse of iris.

Ophthalmoscopic examination. Right eye: No evidence of any pathologic condition or injury. Left eye: There was a maple-leaf, posterior cortical cataract present with an irregular square refractile metallic-looking foreign body, about 2 by 2 mm. in size, behind it. This appeared to be floating in the posterior vitreous. The vitreous was otherwise clear and the fundus healthy.

Roentgenographic findings. X ray revealed an opaque foreign body in the posterior vitreous of the shape and size described above.

Operation. It was felt that the foreign body was copper and application of the magnet failed to cause any movement of the foreign body. The same procedure was then followed as in Case 1. An irregular square piece of copper, about 2 by 2 mm. in size, was successfully extracted through a posterior sclerotomy in the superior nasal quadrant with very little loss of vitreous. In this case, however, the lips of the sclerotomy wound were sealed by means of the actual cautery after the foreign body was removed. The intrascleral and conjunctival sutures were then inserted. In this case it was also necessary to excise the prolapsed iris and to cover the limbal wound with a conjunctival flap.

Postoperative convalescence was uneventful and the patient was discharged from the hospital on September 10, 1933. He was seen at intervals until August 22, 1934, at which time the injured left eye was entirely quiet and the lens changes were only slightly increased. Visual acuity at that time was 6/15 in the left eye, with correction. The vitreous showed one large opacity in the central portion. The fundus was healthy with no evidence of retinal detachment. The intraocular pressure was 22 mm. Hg (Schiøtz). The visual fields in each eye were normal.

CASE 3

History. A white man, aged 23 years, was first seen on November 15, 1935. He gave the history that two days previously, November 13, 1935, while winding fine copper wire on a machine, a piece of wire broke off and struck him in the left eye.

External examination. Right eye: Normal in all respects; vision, 6/7.5, without correction. Left eye: Vision 6/12—, without correction. There was a considerable amount of ciliary congestion. The pupil was not dilated and reacted sluggishly to light. A small penetrating scar could be seen in the center of the cornea. There was a small cut in the pupillary margin of the iris on the temporal side. Just behind this there was an opacity extending back through the entire lens and giving the appearance posteriorly of a typical rosettelike traumatic cataract.

Ophthalmoscopic examination. Right eye: The media was clear and the eye grounds healthy. Left eye: The corneal and lenticular changes already described were distinctly seen. The vitreous was clear and no foreign body could be seen. The eye grounds appeared to be healthy.

Roentgenographic findings. X ray revealed a small, wirelike, opaque foreign body in the anterior superior temporal quadrant of the vitreous.

Operation. On November 18, 1935, the foreign body could be seen easily with the ophthalmoscope through the dilated pupil in the anterior superior-temporal quadrant, where it had been localized by X ray. On that date the patient was admitted to Wills Hospital and the foreign body was removed by the same procedure employed in the first two cases. In this case, however, the lens was injured while attempting to engage the foreign body between the blades of the forceps.

Postoperative convalescence. On the day after the operation the lens showed a definite increase in the cataractous changes with considerable swelling of the cortex. There was marked ciliary congestion but no definite elevation of the intraocular pressure. Conservative treatment was employed until December 7, 1935, and the eye remained quite irritable. On this date a linear cataract extraction was performed. Two weeks later, December 21, 1935, the eye was much quieter and the patient was discharged from the hospital. Improvement continued and one month later the eye was entirely quiet. The vision at that time was 6/6—, with a +13D. sph.

Follow-up report. When the patient was last examined in March, 1948, the visual acuity in the

left eye was 6/9+ with a +13D. sph., and 6/5 in the right eye with +2.0D. sph. ⊃ +1.0D. cyl. ax. 180°. Both eyes were entirely quiet and the tension was 22 mm. Hg (Schiøtz) in the right eye and 19 mm. Hg in the left eye.

The left eye, externally, showed a horizontally linear perforating scar in the upper periphery of the cornea, the site of the old keratome incision which was made at the time of the linear extraction. The iris was slightly adherent to this, posteriorly, but it was not incarcerated. Some thin capsular remains, but no cortex, were present. There was a very good opening in the capsule and the vitreous appeared to be quite clear. The fundus, which could be seen easily, was entirely healthy with no evidence of any retinal detachment. Visual fields showed no gross defects in either eye.

CASE 4

History. A white man, aged 22 years, was first admitted to Wills Hospital on June 2, 1943. He gave the history that while soldering 22-caliber cartridges, the day before, one of the shells exploded and a fragment struck his right eye. Visual acuity, without correction, was reduced to counting fingers on the temporal side at 1.5 meters in the right eye, and was 6/6 in the left eye.

External examination. Right eye: A through and through obliquely vertical laceration 5 mm. in length could be seen extending through the margin of the lower lid in the outer third. There was a moderate amount of photophobia and lacrimation present with considerable congestion of the bulbar conjunctiva. In the 7-o'clock meridian, beginning just 2 mm. back of the limbus and extending horizontally for approximately 5 mm., there was a perforating wound of the bulbar conjunctiva and sclera. The cornea was clear and showed no wounds or foreign bodies. Left eye: Normal in all respects.

Ophthalmoscopic examination. Right eye: The cornea and lens appeared clear. With a +10D. sph., however, an irregular glistening mass could be seen in about the middle of the vitreous. This mass was silvery yellow in color, 3 to 4 disc diameters in length, and 2 to 3 in width. There was a massive subhyaloid hemorrhage which obscured the optic disc. It began at the 11-o'clock position and extended down on the temporal side and across the midline below to about the 5-o'clock position. The upper nasal portion of the fundus was seen with a —3.0D. lens and it appeared healthy. Left eye: Media was clear and the fundus was normal in all respects.

Roentgenographic findings. The Sweet localizer revealed a large opaque foreign body which was 6.5 mm. long and 4.5 mm. wide. The center of the foreign body was 17 mm. back of the center of the cornea, 1 mm. below the horizontal plane, and 6 mm. to the nasal side of the vertical plane.

Operation. On June 2, 1943, the foreign body was removed from the right eye. The same procedure was followed as in the previous three cases. Due to the size of the foreign body, however, the

scleral incision was found to be too small. When the foreign body was grasped and pulled up to the scleral opening, it could not be extracted and dropped back into the vitreous. The sclerotomy was then enlarged and more vitreous was necessarily lost when the foreign body was finally extracted.

An additional complication occurred in the form of a massive hemorrhage which immediately followed the removal of the foreign body. The patient received typhoid-fever therapy and intramuscular penicillin in addition to local treatment. The eye never regained its normal tension and remained irritable. The patient was discharged from the hospital on June 24, 1943, with the recommendation that the injured eye should be enucleated.

CASE 5

History. A white woman, aged 25 years, was first admitted to Wills Hospital on November 8, 1944. She stated that the day before, while winding coils of fine copper wire, a piece of wire broke off and struck her left eye. Visual acuity, without correction, was 6/5—2 in each eye.

External examination. Right eye: The lids, conjunctiva, and the anterior segment appeared to be entirely normal. Left eye: There was a slight amount of conjunctival congestion, lacrimation, and photophobia present. At the 8:30-o'clock position in the cornea, 2 mm. from the limbus, there was a wound which seemed to perforate into the anterior chamber. At the posterior edge of this wound one could see what appeared to be a fine piece of copper wire. The anterior chamber was normal in depth. The iris was normal in texture and the direct and consensual pupillary reactions to light were normal.

Slitlamp examination. This verified all the external findings and showed that one end of the wire was caught in the posterior lips of the corneal wound. The other end of the wire was bent almost at a right angle about 0.5 mm. from its posterior tip and this lay on the iris near its nasal periphery a little above the corneal wound. The length of the wire appeared to be 2 to 3 mm.

Ophthalmoscopic examination. This was essentially negative for both eyes, and, through the undilated pupil, no opacity could be seen in the lens of the left eye.

Roentgenographic findings. X-ray films revealed an opaque foreign body in the left eye corresponding in size, shape, and position to that seen by external and slitlamp examinations.

Operation. A small hand magnet was first applied over the left eye near the foreign body with no response. An incision into the anterior chamber was then made with a keratome, beginning 2 mm. back of the limbus and just above the position of the foreign body. This incision was then enlarged below with scissors. An iris forceps was then introduced into the anterior chamber and with this the piece of wire was engaged and removed. Some hemorrhage was encountered due to the iris be-

coming entangled, but it did not prolapse and no iridectomy was done. The iris was replaced with a spatula, pilocarpine ointment was instilled, and the eye was closed.

Postoperative convalescence. This was somewhat stormy due to the large hemorrhage in the anterior chamber which was slow in absorbing. There was some elevated intraocular pressure but this was controlled with miotics. Repeated injections of typhoid vaccine were also given. Subsequent X-ray examinations after operation failed to reveal any evidence of a foreign body. The pupil was drawn over to the nasal side and was pear-shaped, due to incarceration of the iris at the site of the paracentesis.

The patient was discharged from the hospital on December 1, 1944. The eye continued to improve and on January 2, 1945, the patient returned to work with 6/6—1 visual acuity, without correction, in her injured left eye. She had a slight flare-up in April, 1945, but this was quickly relieved by local treatment and the patient has had no trouble since. Today the vision in the left eye remains 6/6—2, without correction, and the eye is entirely quiet with normal intraocular pressure. The pupil is still distorted as described, and there are some lens changes which have remained localized in the nasal periphery. These appear to be limited to the anterior capsule and are apparently organized hemorrhage and pigment. The uninjured right eye has been and remains entirely free of any irritation, with normal vision without correction.

Case 6

History. A white youth, aged 18 years, was admitted to the Wills Hospital on April 12, 1948. Five days previously he had been tampering with a defective dynamite cap which suddenly exploded, and something struck him in the right eye causing a slight laceration of the right upper lid with a small amount of bleeding. Visual acuity at this time, without correction, was 6/6 in the right eye and 6/12, in the left eye.

External examination. The right eye revealed a healed laceration in the upper lid near the inner margin and, under the nasal bulbar conjunctiva, there was considerable hemorrhage which was undergoing absorption. No definite evidence of a perforating wound in the sclera could be seen at that time. The eye otherwise appeared to be quiet and the cornea was entirely clear. The anterior chamber was normal in depth, and the pupil was moderately dilated. The iris was healthy in color with no evidence of injury. Left eye: Entirely normal.

Ophthalmoscopic examination. Right eye: The cornea and lens were entirely clear. The vitreous showed a few stringy opacities. In the lower nasal periphery, just back of the equator, there was a large mass of exudate which extended from the retina into the vitreous. In the center of this, near the anterior edge, there was a highly refractile metallic-looking foreign body. This was somewhat square in shape with slightly irregular edges and

appeared to be slightly larger than 1 disc diameter in size.

Anterior to the foreign body, and slightly more to the midline and below, there was another mass of exudate which extended as far forward as one could see. There was no free hemorrhage present and no definite tear could be seen in the retina. There was no evidence of any retinal detachment. The optic disc and macula both appeared to be entirely normal. Left eye: The media was clear and the eye grounds appeared entirely healthy.

Roentgenographic findings. X-ray films showed a small opaque foreign body, the density of which suggested copper, in the right eye. This was localized 19 mm. back from the center of the cornea, 7.5 mm. below the horizontal plane, and 9 mm. to the nasal side of the vertical axis. The approximate size of the foreign body was 1 to 1.5 mm. in diameter.

Operation. The patient was prepared for operation in the usual manner. The hand magnet was then applied while viewing the foreign body with the ophthalmoscope. No response was noted. In view of this, we felt quite certain we were dealing with a piece of copper in the right eye. We decided to follow the same procedure in this case as we had in the previous ones.

The procedure was exactly the same except that, in this case, we were a little more careful in our localization of the foreign body, since it appeared to be lying close to the retina. We tried to localize it in the same manner as we have been localizing retinal tears in retinal detachments. In doing this, we had our assistant hold the Arruga spoon between the exposed sclera and the bulbar conjunctiva in the lower nasal quadrant while we focused on the foreign body with the ophthalmoscope. This was done with the operating room in darkness.

The assistant observed the light of the ophthalmoscope as it was transilluminated through the sclera and, when we were accurately focused on the foreign body, he marked the sclera with gentian violet at the point where the light was most concentrated. The assistant also exerted pressure on the sclera at this point with a squint hook while we observed the foreign body with the ophthalmoscope, and we could see the foreign body move forward each time the sclera was indented with the squint hook. After the posterior sclerotomy had been made, a bead of vitreous presented through the lips of the scleral incision. In this vitreous bead could be seen a small highly refractile foreign body which we immediately removed with a pair of small forceps.

This foreign body proved to be a piece of copper of the same size and shape as that which we had seen in the eye and which was shown on the X-ray plates. We then looked into the eye again with the ophthalmoscope and could no longer see the refractile body. The wound was closed in the manner as described in the other cases.

This patient made an uneventful recovery and, at the time of his discharge from the hospital, which

was about three weeks after the removal of the foreign body, the eye was quiet. The retina was in good position and the vision in the injured eye was 6/9 with correction. It has now been over one year since the patient's discharge from the hospital, and he has been seen at intervals since then. At the present time, the vision in the injured eye, with correction, remains 6/9+, and there is no evidence of any retinal detachment.

SUMMARY

Six cases of intraocular copper are presented. Nearly 16, 15, and 13 years, respectively, have elapsed since operation in the first three cases. In Cases 4 and 5 it has been over three years since operation. Case 6 has now been under observation for over one year.

In 5 of the cases the copper was in the vitreous and in one it was in the anterior chamber. The first, third, and fifth cases were similar in that they were all injured on coil winding machines at the same plant. The type of foreign body in these 3 cases was a fine piece of copper wire. The second and sixth cases were injured by a dynamite-cap explosion. The fourth case was injured by an exploding 22-caliber cartridge.

A technique is described for the removal of nonmagnetic foreign bodies from the vitreous and the anterior chamber, respectively.

The first 4 cases, all with copper in the vitreous, were operated by means of a posterior sclerotomy, through the lips of which a small capsule forceps was inserted. While looking with the ophthalmoscope through the dilated pupil, the operator was able to grasp the foreign body in the vitreous and extract it through the sclerotomy opening. In the first case the scleral opening was closed with interrupted black silk sutures with no cauterization. In the other 3 cases the same method was employed but the sclera was coagulated around the incision with diathermy before suturing.

The first case made an uneventful recovery and the vision was normal for five weeks following the operation. At the end of this time a retinal detachment was observed. This became more marked and, approximately two months after the original accident, a retinal detachment operation was done with the Weve needles. This was unsuccessful and two more retinal detachment operations were performed, Safar pins being employed at the last operation. These were all unsuccessful. Today, more than 15 years later, the patient's injured eye is divergent, has a complicated cataract, and no light perception.

The second case made an uneventful recovery. In spite of the fact that he had a partial posterior cortical cataract, from the time he was first seen, there has been no material progress in the lens changes and now, almost 15 years after the injury, he has useful vision, 6/15 with correction. There was no evidence of any retinal detachment at any time and the visual field has remained full.

The third case showed more reaction following operation than the first two cases. The partial cataract which was present before operation became complete shortly after this and a linear extraction was necessary. Following the cataract extraction, the patient made an uneventful recovery and has had no trouble since. Today, 13 years after the injury, the eye is entirely quiet with normal tension. The vitreous is clear and the fundus is healthy with no evidence of detachment. The visual field is full and the visual acuity of the injured left eye is 6/9 plus with +13D. sph.

The fourth case offered a poor prognosis due to the very large foreign body and the massive preretinal hemorrhage which was present when the patient was first seen. A considerable amount of vitreous was lost and more hemorrhage occurred at the time of the extraction of the foreign body. This hemorrhage persisted and eventually the eyeball became phthisical. Enucleation of this eye was advised.

The fifth case showed the copper wire to be present in the anterior chamber. This was removed by means of a paracentesis made with a keratome and enlarged with

scissors. The foreign body was then grasped with iris forceps and withdrawn. However, the iris became entangled and had to be replaced through the wound. This resulted in some incarceration but no prolapse of the iris. The pupil became pear-shaped and drawn to the nasal side. A localized opacity still remains on the nasal side of the anterior lens capsule. The media are otherwise clear, the fundus healthy, and both eyes are entirely quiet. The visual acuity without correction today is 6/5 in the right eye and 6/6 — in the injured left eye.

The sixth and last case reported was one in which the nonmagnetic foreign body was localized in the vitreous, and the same procedure was followed as in the other cases of nonmagnetic foreign bodies in the vitreous. However, in this case we were much more fortunate than in the others because, after the sclerotomy opening had been made, a bead of vitreous presented with the piece of copper glistening in its center. This was then extracted with forceps and the necessity for going any deeper into the vitreous was avoided. The scleral wound and conjunctiva were then closed in the same manner as in the other cases.

CONCLUSION

I feel that the results obtained in the 5 reported cases of copper in the vitreous, justify the technique followed. However, a special type of forceps, such as a modification of the alligator forceps used by otologists, or a smaller and stronger forceps similar to those of Thorpe,[10] but with the handles lower down, might aid in grasping and holding the foreign body.

I recognize the fact that if the lens is too opaque for one to see the foreign body, the procedure described cannot be employed. However, since removal of the cataractous lens would be indicated anyway, this could be done first and the technique described could then be carried out. I feel that, when it is possible to see the foreign body ophthalmoscopically, the method described provides

the best procedure for the average ophthalmic surgeon successfully to remove nonmagnetic intraocular foreign bodies.

Of course, when the vitreous is very cloudy, due to hemorrhage, the method of choice might be the use of the biplane fluoroscope as described by Cross.[11] This, however, is not without danger and there are very few of these instruments available. Also, small pieces of metal, particularly copper, are almost impossible to see with this method. Indeed, most of the cases which Cross[11] has reported were lead shot or large pieces of copper in the vitreous.

The method here described requires patience as well as perseverance throughout, but especially in approaching and grasping the foreign body with the forceps. It must be realized that the forceps, as well as the foreign body, are magnified by the ophthalmoscope. Except in cases of very large-sized foreign bodies, the sclerotomy opening need not be large. All scleral openings should be electrocoagulated with a small amount of current such as is used with a Lacarrere instrument. I also like to touch the edges of the sceral incision with 50-percent trichloracetic acid or 50-percent phenol just before closing the conjunctiva, as suggested by Stieren.[14]

It is now realized that, in the first case, the eye should have been saved. The retinal tear made by the posterior sclerotomy should have been sealed off and the detachment could have been prevented. Failure to do this was the result of a lack of sufficient knowledge about the method for, and the importance of, closing retinal tears 16 years ago.

In Cases 2, 3, and 5, the results were as satisfactory as one could expect from such drastic surgery. Case 4 was considered very unfavorable when first seen due to the large size of the foreign body, and the massive preretinal hemorrhage. However, a larger sclerotomy might have been done first and the foreign body could have been more easily extracted with less trauma. It is realized in retrospect that an iridectomy should

have been done in the fifth case, thereby avoiding the incarceration of the iris. The sixth case illustrates the importance of a very accurate localization of the foreign body and the advantage of making the sclerotomy as near it as possible.

255 South 17th Street (3).

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HISTORICAL MINIATURE

Egyptian Ophthalmology

We know from the writings of Clemens Alexandrinus (200 A.D.) that the first 36 of the 42 cannonical books of the Egyptian priests contained their entire wisdom and the last 6 were medical. They dealt with the organization of the body, diseases, instruments, drugs, the eye, and gynecology. It is noteworthy that a separate book was devoted to the eye. The primary document that has come down to us is the papyrus (1500 B.C.) which Ebers found at Thebes in 1872. It is chiefly a treatise on the management of disease. There is no indication that medicine was divided into specialized disciplines.

The theoretic knowledge of the ancient Egyptians was meager, despite their extensive experience in dissection and embalming, but their therapeutics was not to be despised. They knew the action of castor oil, the use of pomegranate bark for tapeworm, and of treatment by inhalation. The section of the Ebers's papyrus on ocular disease begins with a description of the commonest eye disease, conjunctivorrhea which is characterized by three striking manifestations: redness, exudation, and swelling. They recognized chronic trachoma and recommended a preparation that contained verdigris, myrrh, onion, and gazelle dung. It was to be brushed into the eye with the feather of a vulture.

Hirschberg, *Graefe-Saemisch Handbuch.*

EVALUATION OF ANISEIKONIC CASE REPORTS*

PAUL W. MILES, M.D.

Saint Louis, Missouri

The new space eikonometers make it practical for an ophthalmologist to measure aniseikonia without the necessity of a technician. The time required in testing is less than 15 minutes. Aniseikonia can be ruled out in 5 minutes.

There will be larger series of patients studied, and new evaluations of aniseikonia made. Although most of this work will be done by those already acquainted with aniseikonia, there are some who will report cases for the first time. Case reports in the past have elicited criticism on various points to be discussed in this paper.

To illustrate the difficulties in evaluating aniseikonic case reports recorded in the past, this paper describes 100 of the first patients treated with aniseikonic spectacles by the Washington University aniseikonic clinic. The patients were first seen in 1939 and 1940, and responded to a questionnaire in August, 1944. Thirty reported no improvement, 32 moderate improvement, and 38 complete relief. Twenty-six of the 70 reportedly improved have returned more recently for review and received new aniseikonic spectacles. All were private patients of ophthalmologists, and only 5 percent came from a distance of less than 50 miles.

INCOMPLETENESS OF DATA

Criticism of most case reports published to date applies to the present series, and is based on incompleteness of the following data:

1. A careful history, reviewing all the systems. General medical studies when indicated. At least the physician's opinion as to the patient's psychiatric state. Duration of symptoms.

2. Occupation, visual habits.

3. Keratometer readings.

4. Stereoscopic acuity.

5. Progress notes.

6. Sensitivity or precision of the patient.

7. The effect of change of prescription alone.

8. Meridional aniseikonic measurements have not been taken nor has the influence of oblique astigmatism on the prognosis been considered. The old ophthalmo-eikonometer was incomplete in this respect.

Data probably faulty were used when aniseikonia measured at 13 inches was not found at 15 feet. This aniseikonia for near is possibly due to physiologic exophoria, decreased sensitivity on the ophthalmo-eikonometer at near, the effect of unequal accommodation, and proprioceptive factors. This difference is not found in the space eikonometer.[1] Many prescriptions have been given for aniseikonia found only at 13 inches, and are reportedly beneficial. Three such cases appear among the improved group in this series.

SERIES OF CASES STUDIED

Most of the patients in this series came from a distance, and, to save money and time, prescriptions were given on the basis of a single examination. In difficult cases, this is unwise even in ordinary refraction.

Five of the unimproved patients reported in the follow up letter that diagnoses had been made: encephalitis, sinusitis, carotid sinus syndrome, uremia and nervous exhaustion. Symptoms in aniseikonia are not pathognomonic, but should be carefully considered. If headache is not related to use of the eyes, it is not aniseikonic. Records should state whether eyestrain, headache, or nausea follows reading, watching small moving objects, riding a vehicle, or seeing the movies.

Aniseikonic symptoms are rarely of recent onset, unless induced by new glasses. Visual acuity is usually above normal with glasses, and there may be anisometropia or unequal astigmatism. All patients with oblique astigmatism have oblique aniseikonia. History of relief upon monocular blurring or occlusion is diagnostic of a binocular anomaly. Photophobia is a common complaint in aniseikonia.

Just as small errors of astigmatism may not annoy a laboring man, aniseikonia does not always cause symptoms. Aniseikonic glasses should not be placed on every patient until the costs come down within reason. Even in the presence of low stereoscopic acuity, if the patient is comfortable, aniseikonic glasses are not indicated. If the patient is a surgeon and cannot get his hemostat near a bleeder, an exception may be made.

OCCUPATIONAL GROUPS

Aniseikonia is symptomatic in persons in certain occupational groups who make extraordinary demands upon their eyes. One must admit that the same occupational groups are notoriously subject to neurosis. In the present series, the occupation could only be obtained in some cases from the correspondence. Among those completely relieved were: 12 housewives, 3 students, 2 bank presidents, 2 attorneys, 1 physician, 1 writer, 1 treasurer, 1 minister, 1 insurance manager, 1 hardware dealer, 1 stenographer, 1 soldier, 1 navy officer, 1 oil manager, and 1 war worker.

Those moderately improved included 4 housewives, 1 oil engineer, 1 assessor, 1 sanitary engineer, 1 nurse, 1 physician, 1 stenographer, 1 brewer, and 1 navy-yard worker. Those unimproved included 9 housewives, 2 physicians, 1 minister, 1 sailor, and 1 radio engineer.

TESTING DEPTH PERCEPTION

Patients with uncorrected aniseikonia compensate by using monocular clues for space perception and by suppressing binocu-lar vision. Therefore, stereoscopic acuity should be recorded in each case. This is done automatically in the space eikonometer by recording the sensitivity to changes in the image size. Space-eikonometer tests will show defective depth perception in many found normal by other tests in use. If stereopsis is so defective that tests on this instrument are impossible, a few periods of orthoptic training are indicated. Usually, the sensitivity improves remarkably after brief daily tests on the instrument.

Ordinary refraction patients may go for 5 years or more without a change in prescription or even a frame adjustment. Aniseikonic patients soon learn that a change of one millimeter in lens to cornea distance will cause recurrence of symptoms, and are constantly returning for adjustment. It is almost certain that patients who do not return for recheck in 2 years are not suffering from aniseikonia. Of the present series, only 26 returned even once since August, 1944. All 26 were among the improved group. It may be that some patients returned to their ophthalmologist instead of the clinic. At any rate, no other progress notes were found in the records.

SENSITIVITY TO SMALL DIFFERENCES

The sensitivity of the patient to small differences in measuring aniseikonia is very important in evaluating a case, and should be recorded. On the ophthalmo-eikonometer, sensitivity has no relation to stereopsis. However, if the prescription is: O.S., 0.75 percent, and the sensitivity is plus or minus 1.00 percent, the patient will obviously get an imperfect correction. After wearing the rough correction for a month, the sensitivity improves so that a more exact prescription can be made. If it does not improve, the patient must be suppressing, and probably needs orthoptic training.

The sensitivity on the ophthalmo-eikonometer is between 0.50 and 0.25 percent difference in image size of the two ocular

systems. On the space eikonometer it is commonly 0.25 percent on patients, and as high as 0.05 percent in trained observers. The space eikonometer target is so sensitive that it is made asymmetrical by introduction of a −0.12D. cyl. ax. 90° from the trial case before one eye.

Balancing aniseikonia will not overcome mistakes in ordinary refraction. A patient may not have measurable aniseikonia with the proper spectacles, but an incorrect prescription will certainly produce it. It is the experience of all aniseikonic clinics that the majority of referred patients are made comfortable by a quarter diopter change in cylinder, a slight change in axis, introduction of prism, and so forth.

On the other hand, aniseikonia can be balanced in anisometropia by undercorrection. For instance: O.D., +1.0D. sph., O.S., +8.0D. sph., there is likely to be marked aniseikonia with the full correction. However, +1.0D. sph., O.U., may neutralize it. If aniseikonia is thus neutralized, the patient may be relieved—or, more commonly, may suppress. One cannot depend, however, on aniseikonia being proportional to anisometropia.

WEARING OF ANISEIKONIC GLASSES

Patients should not be considered suffering from aniseikonia until it has been demonstrated that they cannot wear their full prescription after a month's continuous trial. Patients should not be permitted to remove the glasses except for sleep. Perhaps medication will be indicated in some patients.

Two patients in this series stated that it required a year to get used to their aniseikonic glasses. This lengthy period is probably due to wearing glasses part time only.

It is known that glasses change the accommodation-convergence ratio, change the habitual accommodation level upon fixing at various distances (one's eyes are seldom optically focused upon the object of fixa-

tion), and also cause varying excursions in the reading and other positions of gaze.

In anisometropia, inducted vertical phoria in the reading position is always found. Since it is known that aniseikonia is an anomaly of binocular vision, and that eye movements are unquestionably involved, the matter of habit must be considered. The patient may be unable to adapt to two sets of conditions for accommodation and ocular movements, when by habit, he could adapt to one.

It is believed unlikely that any patient will get relief of aniseikonia by wearing glasses for reading only, or part time only. Of the 9 patients in this series who used glasses for reading only, only partial relief of symptoms was reported by 6.

When first putting on glasses correcting his aniseikonia, the patient notices space distortion. Table tops tilt, and buildings lean. This is diagnostic of aniseikonia, and should disappear in a few days if the glasses are correct and are worn constantly. Originally, patients were given a partial correction at first to avoid this effect, measured on the leaf room or tilting table. This has been found unnecessary.

OBLIQUE ANISEIKONIA

Case reports in the past cannot be properly evaluated because, with few exceptions,[2] oblique aniseikonia has not been considered. Patients have not even been classified as to the possible influence on the results of the oblique astigmatism present.

If one considers about 2.0D. of astigmatism of axis 15 degrees or more as likely to cause complaint, 8 of the unimproved patients and 15 of the improved had a right to continued complaint. As none of the records show whether astigmatism was measured monocularly or binocularly, it is unknown whether the axes prescribed in any case corresponded to the position of action of the eyes in fusion.

All patients with unequal corneal astigma-

tism have proportional aniseikonia, unless by rare coincidence it is neutralized by the crystalline lens, the shape of the posterior segment, or the dispersion of the retinal elements.[3, 4]

CRITERIA OF CLASSIFICATION

Each of the 100 patients in the present series was classified as to the probability of complaint from aniseikonia, according to the following criteria: anisometropia (particularly astigmatic), symptoms of photophobia, eyestrain on reading, headache or eyestrain on driving a car or riding on a train, apparent benefit from wearing the aniseikonic prescription, returns for retesting or adjustment, visual acuity with glasses, presence of oblique astigmatism, phorias, and prism.

Of the 30 patients reportedly unimproved, 11 probably were suffering from aniseikonia according to the above criteria. Most of the group simply reported the glasses did not help, but 8 were contentious and belligerent. Of the 70 patients reportedly improved, 46 were probably aniseikonic according to the above criteria, and 24 were atypical. Of the atypical cases, 21 were possibly improved due to the change in refraction alone, since no test period without anisekonia was prac-

tical. Among the improved patients were: 4 who received vertical prisms, 1 horizontal, and 1 both. Among the unimproved were 4 who received vertical prisms.

Of the 46 probably aniseikonic patients, 19 made return visits after 1944 for new prescriptions. Of the 24 patients not considered typical, 7 returned for new prescriptions. Of the 46 patients considered aniseikonic, 28 reported complete relief and 18 partial relief. Of the 24 not considered typical, 13 reported complete relief, and 11 partial. Of those not considered typical, 6 used their glasses for reading only; and of those probably aniseikonic 3 used their glasses for reading only.

Of the 70 improved patients, only 12 had no significant refractive change. Of the 12, 4 reported complete relief, and 8 partial relief. Three of the latter were in the group not typically aniseikonic.

SUMMARY

One hundred of the first patients treated by the Washington University aniseikonic clinic are reviewed. Suggestions are made to improve recording of case reports for the purpose of future evaluation of aniseikonia.

610 South Kingshighway (10).

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NOTES, CASES, INSTRUMENTS

A SIMPLIFIED METHOD OF ENUCLEATION WITH A MOTILITY IMPLANT*

Frank W. Newell, M.D., Robert W. Zeller, M.D., and Harry S. Kupersmith, M.D.

Chicago, Illinois

Recently ocular implants, which transmit motility to an artificial eye by means of a connecting bar or peg have been described. Usually the operative procedure involves isolating and individually attaching the rectus muscles to the implant. We wish to report a simple surgical method which has yielded excellent results at Cook County Hospital in both primary and delayed implantation.
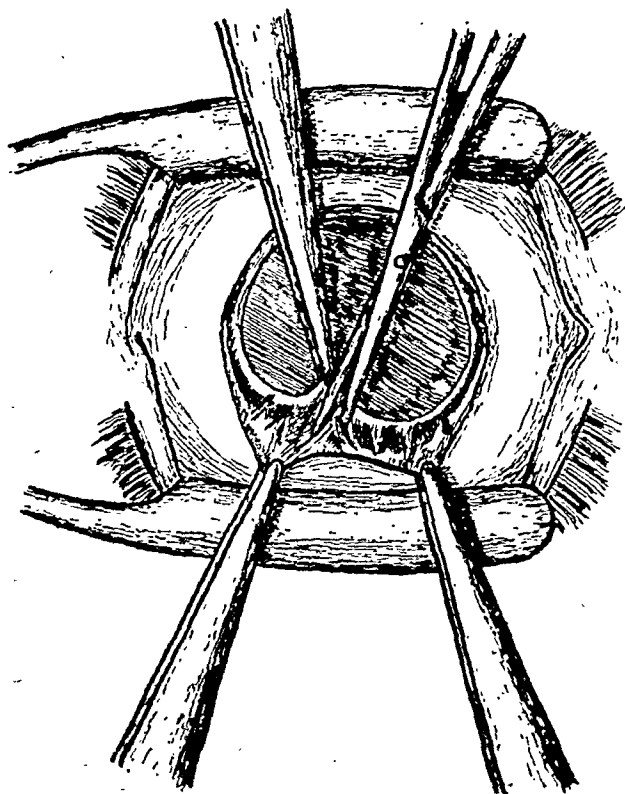
Fig. 1 (Newell, Zeller, and Kupersmith). Dissection of Tenon's capsule from conjunctiva.

Cutler's universal (tantalum mesh) implant is used. Prior to surgery 4-0 chromic catgut sutures are placed in each quadrant of the mesh 3 mm. from the anterior margin.

The conjunctiva is incised at the limbus in the usual manner. Tenon's capsule is bluntly undermined in the oblique quadrants. The rectus muscles are cut from the
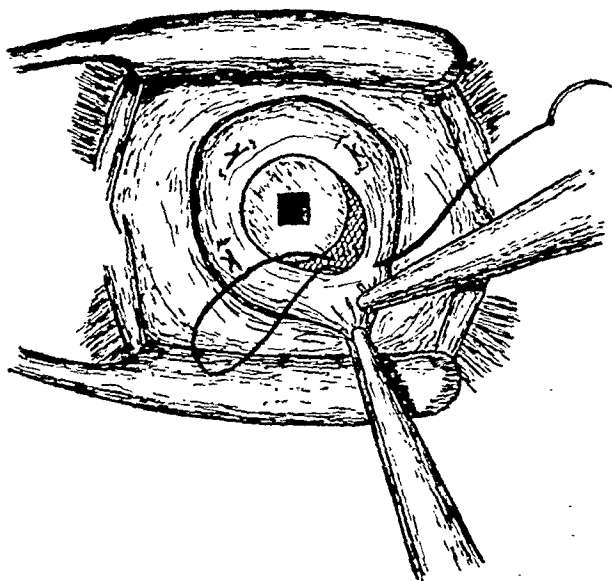
Fig. 2 (Newell, Zeller, and Kupersmith). Preplaced sutures are passed through Tenon's capsule and tied.

globe and allowed to retract. After enucleation Tenon's capsule is separated from the conjunctiva for a distance of 3 mm. (fig. 1).

The implant is then placed within Tenon's capsule and the preplaced sutures are passed through the edge of the capsule and tied (fig. 2). No attempt is made to attach individual muscles and, although they retract, their action is exerted through the capsule. The conjunctiva is attached to the anterior edge of the mesh with six interrupted black silk sutures (fig. 3). A conformer is placed in position immediately and a pressure dressing is applied. Motility is good immediately and improves as the capsule shrinks.

The technique has been equally satisfactory with immediate and delayed implanta-

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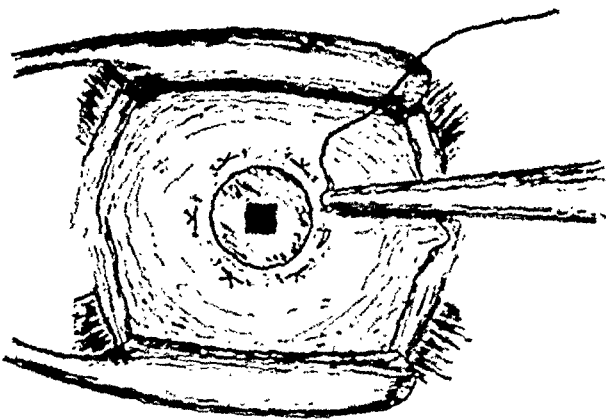
Fig. 3 (Newell, Zeller, and Kupersmith). The conjunctiva is closed with interrupted black silk sutures.

tion. Excursion of the artificial eye is as good, or better, as with the usual operation and the postoperative reaction is minimal.

30 North Michigan Avenue (2).

ALNICO-5 PERMANENT HAND MAGNET*

FOR THE REMOVAL OF MAGNETIC INTRA-OCULAR FOREIGN BODIES

MERRILL LINEBACK, M.D., AND JAMES CRAWFORD, M.D.
Atlanta, Georgia

In November, 1945, Brodsky[†] gave an interesting historical review on the use of magnets in ophthalmology and reported on a new permanent hand magnet which he described as belonging to the "alnico" family of magnetizable alloys. In addition to the magnet he used soft iron caps, some with straight—others with angular—points for slipping on either end. This simplification over the electromagnet with at least three separate parts is still not completely satis-

† Brodsky, B. S.: New permanent hand magnet in the light of present day magnet operation methods. Am. J. Ophth., 28:1245-1251 (Nov.) 1945.

factory because of the ease with which the caps may be lost or misplaced. The addition of soft iron caps to the end of the magnet *results in an increase in the reluctance with an appreciable loss of flux due to the air gap no matter how small it may be between the two metals.*

The desire for a single unit hand magnet of the permanent type suitable for insertion directly into the globe, if need be, led to the design shown in Figure 1, *using the product developed by the General Electric Company about a decade ago known as Alnico-5. This is an alloy of 8 parts aluminum, 14 parts nickel, 24 parts cobalt, 3 parts copper, and the balance iron. This particular magnet material differs from Brodsky's magnet in having the addition of copper and is about twice as strong. It is interesting to note that, of all metals in the alloy, iron is the only one capable of separate magnetization, although cobalt is weakly so under the proper conditions. The maximum induction of Alnico-5 is 15,700 gausses and the coercive force is 575 oersteds. A comparison of Alnico-5, which has a higher external energy than any other alnico or other available permanent magnet material known today, and other magnets is shown in Table 1.*

TABLE 1
COMPARISON OF VARIOUS TYPES OF MAGNETS

Magnet Material	Minimal Residual Induction Br (Gausses)	Minimal Coercive Force H (Oersteds)	Minimal External Energy (BdHd) max.
Carbon steel	8,600	48	180,000
Chromium steel	9,000	63	290,000
36% Cobalt steel	9,000	210	935,000
Alnico 1	7,100	400	1,300,000
Alnico 4	5,200	700	1,200,000
Alnico 5	12,000	575	4,500,000

The first model of the magnet is much *smaller and lighter, weighing approximately 5 gm., than conventional hand magnets and has about 7 times the magnetic energy value. This value per unit weight is over 17 times that of carbon steel. This particular type of alnico is best cast to the shape finally desired*

although the point of the second model of the magnet was satisfactorily ground to shape without loss of flux. Other alnicos of less energy value can be sintered. In the handling of these small cast magnets, care must be taken not to drop or otherwise mishandle them because of the danger of chipping or fracturing. This is because, in the cooling of these magnets, large crystals of the metal orient themselves at the corners or edges.

Once magnetized this magnet will lose only a fraction of 1 percent of its energy per year. It can be remagnetized readily if occasion demands. After the alloy has been removed from the field of the magnetizer, but kept in a closed circuit (soft-iron keeper across its poles), it will have the maximum residual induction it can maintain without outside influence. If the keeper is removed (open-air circuited) the magnet will become partially demagnetized and the value of the magnetic flux density will drop to a lower point on the demagnetization curve. This value will remain constant until the magnet is subjected to further adverse effects such as heat, vibration or impact, stray magnetic fields, or changes in the external magnetic circuit such as an increase in the air gap length.

Electromagnets of various composition, construction, and weight have been in use for many years in the removal of intraocular pieces of steel. While mobilization of the foreign body and delivery to the operative site is comparatively easy using the powerful flux of the electromagnet, the actual removal of the object from the eye with such a force, particularly in the anterior segment, renders the delicate tissues of the iris and ciliary body liable to tearing and even prolapse. It has been observed frequently that the electromagnet would bring the body just to the site only to have it slip back toward its original position when the current was turned off. After several such attempts at removal, the instrument would become too hot to handle with bare hands and the use of a towel or two would make the entire pro-

cedure too cumbersome for practical use. Allowing the instrument to cool is time consuming and serves to unnerve an already anxious patient. Even with the magnet in position and turned on, the use of additional contact instrumental aid does not help matters because of the almost certain blind probing that ensues.

CASE REPORTS

CASE 1

History. Mr. E. L. H., a farmer from middle Georgia, was seen in the office about 6 hours after receiving injury to the right eye on April 10, 1948. He stated that he had been hammering on a nut and bolt attachment of the cultivator to his tractor when suddenly vision in the right eye became very blurred. He experienced no pain but knew that something flew into his eye.

Examination revealed a 2-mm. linear wound perpendicular to the limbus at the 7-o'clock position and extending partly into the cornea. There was a droplet or two of vitreous extruding from the wound, the lips of which were in apposition. The anterior chamber was still formed. Vision was: R.E., fingers at 10 feet; L.E., 20/20. Due to the presence of vitreous floaters the fundus was not observed.

Treatment. The patient denied any past history of immunization of any kind. He was accordingly given 1,500 units of tetanus antitoxin and admitted to the hospital where he received a total of 650,000 units of penicillin G intramuscularly.

The right pupil was dilated with 1-percent atropine sulfate and with the +15 lens of the ophthalmoscope a shiny angular object almost filling the pupil was seen toward the nasal side and was found to move with the observer.

The following day X-ray localization studies, using Sweet's technique, were made showing an opaque foreign body 2 by 1 by 1 mm. located 7 mm. in back of the center of the cornea, 2 mm. to the nasal side of the vertical corneal plane, and 0.5 mm. below

Fig. 1 (Lineback and Crawford). First model of Alnico-5 permanent hand magnet showing the foreign body removed in Case 1 attached to tip.

the horizontal plane. This placed it just behind the lens. By use of the Berman locator the foreign body was found to be magnetic.

Operation. In the office about 42 hours after injury, the patient was prepared for operation. Local anesthesia was 2-percent butyn. The patient coöperated splendidly so that only minimal use of the fixation forceps was necessary.

A conjunctival flap was made from the 6- to the 9-o'clock positions, 3 mm. from the limbus, undermined and laid back over the cornea. A wide-angled keratome was inserted just at the limbus in the site of the original wound and into the anterior chamber about 3 mm. The Lancaster hand electromagnet was then brought up to the incision after the keratome was removed. When the magnet was turned on a tugging and bulging was seen in the lower portion of the iris but, in spite of repeated attempts, the piece of steel could not be delivered. The patient experienced moderate pain at this point.

While waiting for the electromagnet to cool, the slim-nosed hand magnet was inserted 0.5 cm. into the incision and anterior chamber. Upon slow and cautious withdrawal from the globe the foreign body was found attached to the inferior surface (fig. 1).

The conjunctival flap was then reposited in its original position, penicillin ophthalmic ointment was placed in the conjunctival sac, and an eye pad was applied with moderate pressure. When anesthetization was completed the entire procedure took only 5

minutes. After undermining the flap and before the keratome incision is made, it is advisable to place a drop or two of 2-percent butyn on the limbus before proceeding.

Course. The following day the anterior chamber was found reformed and the pupil was dilated to perfect roundness by using the 10-percent emulsion of neosynephrin hydrochloride. A week after the removal of the foreign body, vision was R.E., 20/200, without glasses. He was then put on iodides orally and 2-percent dionin (ethyl morphine) drops to the right eye twice daily. One week later (2 weeks after his accident) vision was: R.E., 20/25—1 with a —1.75D. sph. ⊂ —0.5D. cyl. ax. 180°. One month after the accident vision was: R.E., 20/50 without glasses and with a —1.25D. sph. was 20/20. Four months after his accident vision was: R.E., 20/20, without glasses; L.E., 20/15—.

Comment. After the success with the first model magnet, it was decided to design one still more powerful yet not too large to be used by hand. Alnico-5 is so hard and brittle that it is not readily ground to dimensions, and heating the alloy to grind it destroys most of the magnetic properties; however, it was decided to go ahead anyway with cold grinding and see how it would affect the resulting magnet. This ended with Model 2 as shown in Figure 2. It is 9 mm. in diameter, 11.5 cm. long, and weighs 30 gm. It starts vibrations in an object at 60 mm. At 55 mm. it raises the object and at 53 mm. holds it vertically without vibrations. This model arrived just before Case 2.
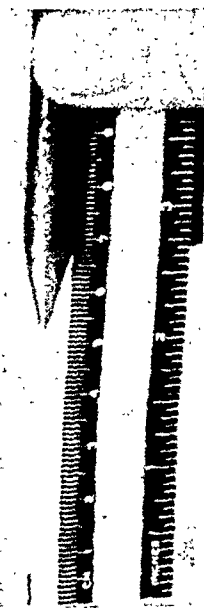
Fig. 2 (Lineback and Crawford). Second model of Alnico-5 magnet showing foreign body removed in Case 2 being held vertically without vibration at 53 mm.

Case 2

History. Mr. E. H. C. was operating a punch drill on May 21, 1948, when the bit shattered and a piece of it entered his right eye, nasally. There was profuse bleeding and much pain. He was seen in the office within one-half hour after his accident.

Examination revealed a large subconjunctival hemorrhage in the inner canthus and a small 0.5-mm. linear wound, 2 mm. out from the limbus at the 3-o'clock position. Nothing was seen in the depths of the wound even with the binocular loop.

An X-ray film was not taken at this time for the desire to try the new magnet was great. It was brought up to the tiny wound after a drop or two of 0.5-percent pontocaine was first placed in the conjunctival sac. Before the point was within an inch of the wound the foreign body appeared, but it was not brought completely out because of a "hook" at the distal end which caught in the conjunctiva (fig. 3.). This was divided and the body was removed easily.

An X-ray film was then taken showing no more opaque bodies. Intramuscular injection of Omnadin* was given, and the right pupil was dilated with 1-percent atropine. Funduscopic examination revealed no lens or vitreous changes or hemorrhages intraocularly.

Five weeks after his injury his vision was: R.E., 20/40, without glasses and with a 0.50D. cyl. ax. 90° was 20/20; L.E., 20/15, without glasses.

Summary

Two cases of magnetic removal of an intraocular foreign body using the new Alnico-5 permanent hand magnet are reported. The advantages of such a magnet are emphasized:

1. Its light weight and small size as compared with the electromagnet result in ease of handling.

2. Its increased magnetic energy over conventional permanent type hand magnets.

3. Its comparative ease of sterilization.

4. Its use to shorten operating time in stubborn cases when the electromagnet fails to deliver the foreign body.

5. The fact that it is in one piece and its portability allows it to be used by the physician anywhere, particularly when no current is available for the large electromagnets.

Fig. 3 (Lineback and Crawford). Showing "hook" on distal end of foreign body removed in Case 2. This "hook" caught in the bulbar conjunctiva preventing the removal of the entire foreign body by the magnet.

Where possible pre- and postoperative X-ray studies should be made; the former to localize accurately the foreign body and to determine the position of the removal incision, and the latter to prove, if a medico-legal question ever came up, that the body actually was removed. It is possible, although not likely, that a patient would get another foreign body in the same eye a few days later and claim that the first one had not been removed completely.

Once localized and a choice of incision having been made, it is essential that all conjunctiva surrounding the operative site be dissected away cleanly so that there is nothing for the body to catch in when it is removed from the depths of the globe.

It is hoped and expected that, with accurate localization of the intraocular foreign body, careful selection of the site of the incision to remove it, and adequate exposure to prevent catching in the conjunctiva, this magnet can be used in place of the more cumbersome electromagnets.

616 Grant Building (3).

* Omnadin—brand of Prolipin, product of Winthrop Chemical Co., Inc.

REFRACTION CLINIC*

DISCUSSION

ALBERT E. SLOANE, M.D.†
Boston, Massachusetts

A 38-year-old housewife, who is complaining of blurred vision and who has recently been given glasses which she cannot wear, appears for examination. She states that she occasionally has headaches, which do not suggest an ocular basis, and, during these periods, she turns to her old glasses which are 15 years old. Her new glasses make her nauseated and she is unable to wear them without discomfort. The patient states that she does not read very much.

Refractive findings. Examination reveals the following: O.D., 20/400 with a −3.5D. sph. ⊃ −3.75D. cyl. ax. 180° = 20/30, slow; O.S., 20/400 with a −3.0D. sph. ⊃ −3.5D. cyl. ax. 180° ≐ 20/30, slow.

Phorias. Distance: 3Δ exophoria; vertical orthophoria. Near: 12Δ exophoria; vertical orthophoria.

Prescription of 15-year-old glasses: O.D., −1.25D. cyl. ax. 180°; O.S., −1.5D. cyl. ax. 180°.

Prescription of recent glasses: O.D., −3.0D. sph. ⊃ −3.75D. cyl. ax. 180°; O.S., −3.0D. sph. ⊃ −3.75D. cyl. ax. 180°.

DISCUSSION

The fact that this patient has gone so many years without changing her glasses, coupled with the fact that she has worn a decided undercorrection, immediately tends to indicate that we are dealing with a person who is not very critical about keenness of vision. Also, the fact that her new glasses which are closer to her refractive error produce symptoms may well be due to several factors.

1. It may be that her accommodation is not

well developed and, therefore, the use of accommodation between infinity and her near point demanded by the full correction of her myopia is the cause of the difficulty.

2. It may be due to the full correction of the "with the rule" astigmatism to which she is not yet adjusted. It is a known fact that people are less tolerant of a full "with the rule" astigmatic correction than of full "against the rule" corrections.

3. The patient may well be one of those persons who have less discomfort when visual acuity is on the blurred side than when it is acute. A fair comparison to this situation may be obtained in considering the fatigue that occurs in looking through opera glasses which improve visual acuity greatly but which may be uncomfortable for prolonged use.

4. Perhaps the most important reason is the fact that this patient has not worn glasses constantly and, for her, a full correction represents a decisive, radical, and probably an extremely different way of using the eyes.

I do not think that the muscle imbalance, in spite of the high normal of 12Δ exophoria for near, is significant in the causation of her symptoms.

MANAGEMENT

The treatment in this case would aim at eventual adequate improvement of vision but the process should be gradual. It is better to undercorrect to a level considerably lower than that tolerated comfortably than to overcorrect above this level of comfort even the slightest degree.

Judgment in this case cannot be perfect, nor are there special criteria for guidance. I would be guided by the correction the patient had worn in the past, and would order a stronger glass, for example: −1.0D. sph. ⊃ −1.75D. cyl. ax. 180°, O.U. This supplies about one half the required cylinder and follows the rule of undercorrection of "with the rule" astigmatism together with undercorrection of sphere so that some ac-

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commodation at near will be unnecessary. The patient will be told to return in a reasonably short period of time (4 months to 1 year), and at that time gradually increase both sphere and cylinder, until full correction may be accepted, if found desirable.

This woman will soon enter the presbyopic period, so it is likely that she will favor an undercorrection of sphere unless her work requires discriminating distant visual acuity. It is much easier to tell the patient that an undercorrection is purposely being given because a full correction would be too much for the patient's comfort and that, as time passes, fuller correction will be ordered.

243 Charles Street (14).

HEMOSTASIS IN TEAR-SAC OPERATIONS*

L. J. ALGER, M.D.
Grand Forks, North Dakota

The tear sac and its overlying tissues are supplied with no less than 5 arteries and 4 veins. It follows that any operation associated with the external approach to the tear sac is an aggravatingly bloody procedure and that the task of ligating the vessels is a difficult one.

The most difficult problem, however, is not the large number of arteries and veins in such a small area. It is the lack of mobility of the tissue. This tissue is, for the most part, held very firmly in place by its attachment to the periosteum and the medial palpebral ligament. As a result of this immobility, the edges of the wound cannot be adequately everted and sponged. This makes tying of the seemingly endless number of blood vessels very difficult indeed.

All of this adds up to a bothersome, time-

taking, and, for that matter, a blood-taking procedure which necessitates the use of a suction apparatus. By the time the operation is over, the suction apparatus usually contains almost a pint of blood and probably that much more blood has been swabbed up with sponges.

BLOOD SUPPLY TO TEAR SAC

After several years of contending with this annoying problem, I have devised a remedy which has been completely effective. Before attempting to describe this method, it would be well to consider the blood supply in detail.

The arterial supply to the region of the sac comes from two sources, the ophthalmic and the external carotid. The best known artery is the angular. This artery is actually
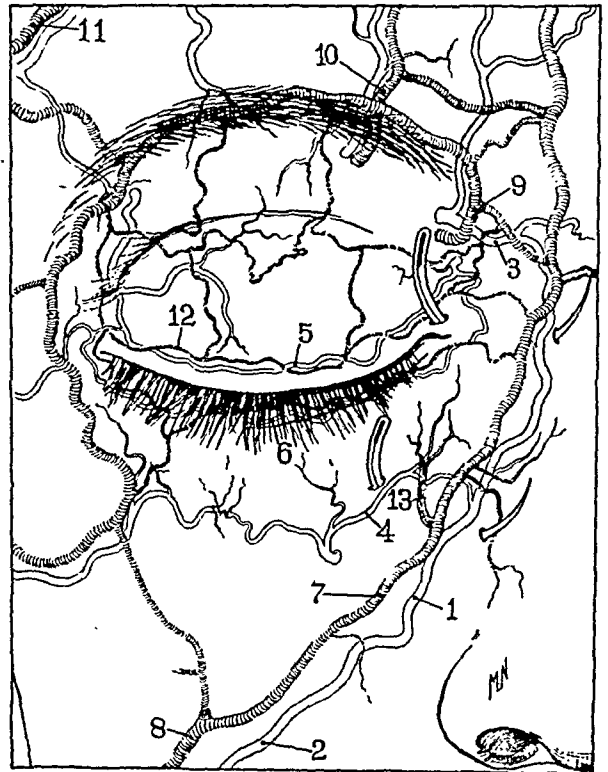
Fig. 1 (Alger). *Blood supply of the tear sac.* (1) Angular artery. (2) Anterior facial artery. (3) Dorsal nasal artery. (4) Infraorbital artery. (5 and 6) Palpebral arteries. (7) Angular vein. (8) Anterior facial vein. (9) Superior ophthalmic vein. (10) Supraorbital vein. (11) Superior temporal vein. (12) Superior palpebral vein. (13) Anastomosis to inferior ophthalmic vein.

a large anastomosis between the dorsal nasal branch of the ophthalmic above and the anterior facial branch of the carotid below. It runs in the angle of the nose and the face, passing about 5 mm. medially to the medial canthus in front of the medial palpebral ligament. It joins the dorsal nasal branch of the ophthalmic artery as it emerges from the orbit about 1.5 cm. above the medial palpebral ligament. There is a lesser blood supply from the infraorbital branch of the internal maxillary branch of the carotid artery and fine branches, called palpebral arteries, come across the lids from the lacrimal and transverse facial arteries.

The veins are somewhat similarly placed. The angular vein runs parallel and just lateral to the angular artery. It joins the anterior facial vein below and the superior ophthalmic and supraorbital veins above. It has a lateral anastomosis by way of the superior palpebral vein to the superior temporal vein. No vein accompanies the infraorbital artery. There is, however, an anastomosis to the inferior ophthalmic vein.

METHOD OF HEMOSTASIS

My method of hemostasis is easily accomplished. It consists of taking two strong sutures, such as No. 2 chromic, and threading one into a needle with a 1-inch diameter, half-circle curve and the other into a needle with a 1.25-inch diameter, half-circle curve. The needles should be of heavy caliber and round. Using a good needle holder, the suture with the smaller needle is placed just above the medial palpebral ligament and a deep bite is taken, commencing at a point 3-mm. above and halfway between the upper punctum lacrimalis and the medial canthus, then extending down close to the lacrimal bone, and emerging at a point on the nose about 1.5 cm. medial to the medial canthus.

Since the second suture should take a broader bite, the needle with the larger curvature is used. The suture should commence at the rim of the orbit where the floor

and the medial wall meet. Staying close to the bone, it should pass across to the nose, emerging on the nose about 1 cm. from the angle.

If the anatomic relation of these sutures is studied, it will be seen that the upper suture blocks off the angular artery and vein before they join the dorsal nasal artery and the ophthalmic vein. The ligature also is below the anastomosis with the superior palpebral artery and vein; therefore, this one suture blocks all blood supply from above.

The lower suture is equally effective. It blocks the lower end of the angular artery and vein, the anastomosis between these vessels, and the infraorbital artery and inferior ophthalmic veins.

The result is a surprisingly effective hemostasis which makes the suction apparatus unnecessary and does away with practically all ligations and sponging. The operator can proceed undisturbed with the operation itself. These ligatures should not be removed until the day following the operation in order to prevent severe bleeding.

SURGICAL TECHNIQUE

The question now presents itself as to how, after placing these two ligations, can the classical incision described in all the texts on ophthalmic surgery be made.

At the American Academy of Ophthalmology meeting in Chicago in 1947, a well edited moving picture by Dr. Michael J. Hogan of San Francisco was presented. His incision for a dacryocystorhinostomy commenced just about at the lower half of the medial palpebral ligament and extended in a straight line downward in the angle of the nose and cheek. I had been making my incision lower than described in the textbooks because of my ligatures but, after seeing his pictures, I commenced to make my incision like his. The results are very gratifying. I now make a lower trephination and get entirely in front and below the middle turbinate. With the incision and trephination in this position, I find that it is no trick at all

to suture both the anterior and posterior lips of the incised sac to the nasal mucous membrane—something I was unable to do when I made the trephination a bit higher up.

Since I could find no mention of this in-

Fig. 2 (Alger). The dotted line shows the technique of incision and trephination formerly employed. The solid line shows the present method of trephination and "Martin-Cordes incision."

cision in the literature, I wrote to Dr. Hogan asking him the history of his method, and whether or not it resulted in less bleeding. He very kindly sent me the following reply:

"The incision has been used by Dr. Robert C. Martin and Dr. Frederick C. Cordes since about 1930. They decided to make the incision lower because they felt that it made the exposure of the sac much easier. They also have told me that, by making it lower, they are able to make it in a straight line. Dr. Martin feels that a straight incision is better than the old curved, or bow-shaped incision, which Mosher and others have recommended. The bow-shaped incision tends to contract and become more curved in time; whereas, a straight incision is parallel with the nose—giving a better cosmetic result. I

do not think they lowered the incision with any idea of avoiding the larger vessels."

It might be well to name this incision the "Martin-Cordes incision" in honor of the inventors.

SUMMARY

A description of the blood vessels in the area of the lacrimal sac is presented.

A method of ligating these blood vessels before making the incision is described. The incision, which I suggest naming the "Martin-Cordes incision," is best suited to this method of ligation.
517 First National Bank Building.

EYELASH BURIED IN CLEAR LENS SUBSTANCE

VICTOR A. BYRNES, M.D.
Randolph Field, Texas

Eyelashes as intraocular foreign bodies are not unique. Sharpe[1] reviewed the literature to 1925 and reported 75 cases in the 100 years preceding. Graff[2] reviewed the English literature in 1931 and added 30 cases. Cowen[3] reported 29 cases in 1942. It is, therefore, not by any means a rare complication of ocular injuries. It is unusual, however, when an eyelash is introduced into an eye during an injury in youth, remains to become incorporated into the growing lens and the lens substance surrounding it remains clear. Such a case is here reported.

Review of the literature reveals only one similar case. It was very briefly reported by von Hippel[4] in 1927. It occurred in a 16-year-old patient whose history of eye injury was not available. A cilium was identified in the clear anterior cortex of the lens by use of the slit lamp. Visual acuity in the involved eye was 0.5.

This present case is considered to be unusual enough to warrant rather complete reporting. An abstract of the clinical record and illustrations to show the appearance of the lens follow.

Lieutenant H. L. R., aged 28 years, was referred for eye examination in April, 1948.

History. This patient had no eye difficulty until 1932, when he was 12 years of age. At that time he fell against a window frame containing a projecting nail. This nail punctured his left eye. He was operated within a few hours by an ophthalmologist. About six weeks after the original operation he was again operated; this time for removal of an

The lens of the left eye showed a thin, traumatic, wedge-shaped cataractous opacification at the level of the anterior surface of the infantile nucleus on the temporal side of the lens. It was covered anteriorly by perfectly clear adult nucleus and cortex. Posteriorly, there was a small dense capsular opacity temporally. On the nasal side of the lens was an unmistakable encysted eyelash lying on the posterior surface of the infantile
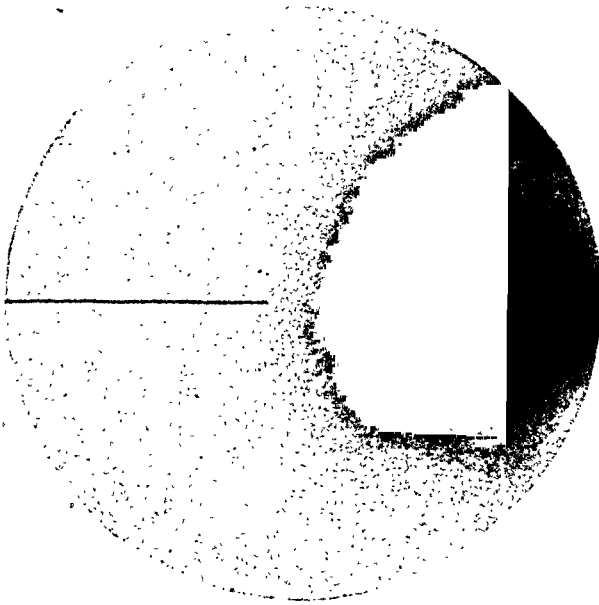
Fig. 1 (Byrnes). Ophthalmoscopic appearance of eyelash buried in clear lens substance. The eyelash can be seen as a thin dark line. Mild traumatic cataractous changes on the opposite side of the lens are due to the original injury 16 years ago.

Fig. 2 (Byrnes). Drawing to illustrate, from above, the location of the eyelash in the lens substance. The locations of the traumatic cataractous changes are also shown.

eyelash from the interior of his eyeball. His eye cleared up and gave him no further trouble. He engaged in athletics and later passed an Air Force examination and learned to fly military aircraft.

Examination. Visual acuity was: O.D., 20/15; O.S., 20/25.

External examination of the left eye showed a small corneal nebula extending from within 1 mm. of the limbus at the 4-o'clock position to within 1.5 mm. of the center of the cornea (result of the old injury).

Cover test revealed a constant convergent, concomitant strabismus of the left eye of about 6 diopters.

nucleus and extending from the equator at the 9-o'clock position almost to the center of the lens. This cilium was entirely surrounded by clear adult nucleus and cortex. It was seen as a thin black line against the red fundus reflex on ophthalmoscopy and was unmistakable under the slitlamp. The eyelash was slightly decolorized and there were gray encysted nodules along its length. Its appearance and location are illustrated in Figures 1 and 2.

This foreign body undoubtedly entered the eye 16 years ago at the time of his accident when he was 12 years of age. The cilium lodged against the posterior surface of his lens where it caused so little irritation that it became encysted and then buried be-

neath the forming adult nucleus and cortex which remained entirely clear. The mild cataractous changes present were on the opposite side of the lens from the cilium and obviously were due to the injury and not to the presence of the cilium.

COMMENT

There is a disagreement as to the reaction of the eye to retained intraocular cilia. Graff[2] states they usually cause no reaction but purulent and plastic inflammation have been reported and he feels it is always advisable to remove them if practicable. Gradle[5] reported a case with a depigmented cilium present for 19 years without reaction. Fox[6] reported two cilia present in a quiet eye for 2 years. McKee[7] reports a case with a cilium present in the anterior chamber for 18 years with no reaction and normal vision. Mattos,[8] Tokuda and Tanaka,[9] and Shagov[10] have all reported similar experiences.

However, Cuvier[11] and von Graefe[12] report sympathetic ophthalmia; Bonnet and Paufique[13] report an iris cyst; and Papogno[14] the formation of posterior synechias following penetration of eyelashes into the anterior chamber. Cowen[3] feels that, like other foreign bodies, a cilium usually produces a severe reaction such as iritis, iridocyclitis, photophobia, lacrimation, synechias, iris cysts, epidermoid tumors, giant-cell development, subsequent cataract, glaucoma, or terminal blindness and often loss of the eye.

Sharpe's[1] case retained the cilia asymptomatically for 33 years at which time the eye became red, irritated, painful, and lost its sight. It was his feeling that apparent early quiescence did not prevent late serious complications of these retained foreign bodies. It would appear, therefore, that removal of cilia is indicated if they are located where such removal can be done without probable damage to the eye. If they are not located where they can be readily removed the risk of leaving the cilia must be balanced against the danger inherent in their surgical removal and decision made on that basis.

In the present case it is believed that the decision made at his operation in 1932, to leave the cilium, was the correct one. Its removal would have jeopardized the patient's sight which at present is excellent. It is unlikely that the foreign body now completely buried in clear lens substance will ever cause any inflammatory reaction in the eye. Whether or not the lens will become cataractous late in life will be a matter of interest.

SUMMARY

A case has been reported in which an eyelash was left in an eye following a perforating eye injury in 1932 when the patient was 12 years of age. This cilium has subsequently become encapsulated and completely buried in the clear lens substance of the adult nucleus and cortex.

Only one similar case has been previously reported in the literature.

School of Aviation Medicine.

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MONOCULAR APHAKIA AND EXOTROPIA CORRECTED BY CONTACT LENSES*

BERNARD C. GETTES,† M.D.
Philadelphia, Pennsylvania

AND

EMILE M. RAVDIN, M.D.
Los Angeles, California

The correction of monocular aphakia by the use of contact lenses is neither a new nor an infrequent procedure. The correction of monocular aphakia with spectacle lenses has two serious disadvantages:

1. There is a difference of about 25 percent in the size of the images of the two eyes with resulting difficulty in fusion and diplopia.

2. The strong convex lenses before the aphakic eye and a plano or weak spherical lens before the phakic eye introduce prismatic effects which, together with the difference in the size of the images, produce diplopia that makes the wearing of the spectacle lenses difficult and in some cases impossible.

It has also been observed that, when one eye becomes amblyopic but the vision in the opposite eye remains good, the amblyopic eye will tend to diverge. This is especially true if the loss in the visual acuity occurs past the age of 12 years.

CASE REPORT

We are presenting a case of monocular aphakia and exotropia which was corrected by the use of contact lenses.

History. Mrs. R. C., a white woman, aged 25 years, first presented herself in the clinic of Dr. J. S. Shipman on October 15, 1946, at which time she complained of the inability to see with the right eye. She first wore glasses at the age of eight years. With glasses, her vision in both eyes was always good until she was struck in the right eye in 1936. Since then, her vision in the right eye had become progressively worse. In 1944, she first became aware that her right eye turned out.

Eye examination. Visual acuity was: O.D., hand movements; not correctible; O.S., 6/60, with correction, 6/9.

External examination revealed no abnormalities of the conjunctiva, cornea, anterior segment, or adnexia of either eye. The right eye diverged 15 degrees as measured by the Hirshberg method.

Ophthalmoscopic examination. The right eye was obscured by a posterior lens opacity. The fundus of the left eye was within normal limits. Slitlamp examination disclosed a typical traumatic cataract of the right eye. Diagnosis was traumatic cataract and monocular exotropia of the right eye.

Operations. On December 20, 1946, a discission was performed with a Ziegler knife needle, and on January 17, 1947, a linear extraction performed. Following this, the pupillary space was filled with a dense capsule. On October 15, 1947, a capsulotomy was performed and a good central opening was obtained.

On November 3, 1947, refraction was: O.D., +11.0D. sph., 6/9; O.S., —3.0D.

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sph., 6/9. At this time the patient was ad-vised to consider contact lenses for both eyes since the myopia of the left eye required her to wear lenses at all times. Moulds were taken of both eyes after the method of Obrig on December 3, 1947. With the finished contact lenses, her vision (December 10) was: O.D., 6/9 + 2; O.S., 6/6.

Muscle tests. By screen and parallax tests, there was a right exotropia of 25 prism diopters and a right hyperphoria of 5 prism diopters. With the contact lenses, the patient complained of diplopia for both distance and near. Nevertheless, she was urged to wear her contact lenses an hour at a time, increasing this amount each day.

It was contemplated at this time that if the diplopia persisted, we would grind vertical prisms in the contact lenses and overcome the divergence by the use of horizontal prisms in a pair of spectacles.

By January 8, 1948, the patient was quite comfortable and could wear her contact lenses from 4½ to 6 hours daily. There was no double vision for distance or for near.

Screen and parallax tests disclosed 5 diopters of exophoria at both 6 meters and 33 cm. With the Maddox rod, there was 4.5 diopters of exophoria present. There was vertical orthophoria as tested by both methods.

The patient stated that her double vision disappeared within the first week of wearing the contact lenses.

On April 13, 1948, the patient could wear her contact lenses for as much as 8 consecutive hours with no discomfort. The muscle tests on this date were essentially the same as at the last examination.

Comment. This case demonstrates (1) The desire for single binocular vision is so great that it permits a divergence of 15 degrees to be overcome in spite of the disuse of the eye for 10 years; (2) the advantage of the use of bilateral contact lenses in a case of monocular aphakia when the existing ametropia in the phakic eye requires spectacle lenses.

SUMMARY

A case of monocular aphakia with a 15-degree monocular exotropia in the same eye and with a myopia of −3.0D. sph. in the opposite eye is presented.

Correction by the use of contact lenses overcame the exotropia of 10 years' duration and gave the patient comfortable single binocular vision.

2028 Pine Street.
4036 Wilshire Boulevard (5).

HISTORICAL MINIATURE

Your eyes must continue very good, since you are able to write so small a hand without spectacles. I cannot distinguish a letter even of large print, but am happy in the invention of double spectacles, which, serving for distant objects as well as near ones, make my eyes as useful to me as ever they were. If all the other defects and infirmities of old age could be as easily and cheaply remedied, it would be worthwhile, my friend, to live a good deal longer. But I look upon death to be as necessary to our constitutions as sleep. We shall rise refreshed in the morning. Adieu, and believe me ever,

Your's most affectionately,
B. Franklin

From Benjamin Franklin, Complete Works, 1806.

SOCIETY PROCEEDINGS

Edited by Donald J. Lyle, M.D.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

Section on Ophthalmology

April 22, 1948

Dr. Perce DeLong, *chairman*

HETEROPLASTIC GRAFTS

Dr. O. A. Capriotti (by invitation) and Dr. Edmund B. Spaeth presented a 15-year-old boy from the service of Dr. Spaeth at Wills Hospital upon whom successful isografts had been performed for ectropion of the four eyelids complicating ichthyosis congenita. He was an only child, and there was no history of abnormalities of the skin in either side of the family. Two weeks after his birth, a red rash appeared over the entire body, and this was soon followed by a generalized scaly condition of the skin. The diagnosis of ichthyosis congenita was established when he was a child, and he was presented by Dr. John Ludy at a dermatologic convention.

Epiphora started at about the age of 8 years, and ectropion of the lids was rather severe by the time he was aged 10 years. About 4 years previously, the patient had been treated for 1½ years for a corneal ulcer of the left eye. Prior to admission, he was treated for 3 months as an outpatient for a corneal ulcer of the left eye, with no benefit.

On general examination, the entire body of the patient was covered with brownish scales. The palms and soles were blackish in color and were deeply fissured. The skin of the fact was taut, and there was severe ectropion of both lower lids with a slight ectropion of both upper lids.

Considerable photophobia and marked epiphora were present. The slitlamp showed the right cornea to be clear while the cornea of the left eye showed some scarring, just below the pupillary area, and an active ulcerative keratitis on the temporal side.

It was obvious that to correct the ectropion, which was the basic cause of the exposure keratitis, a skin graft would be necessary. Since the skin of the whole body was not normal and no members of the family were available, a skin donor was obtained. Patient and donor were of the same blood type and cross matched as to blood type and M, N, and Rh factors.

On January 18, 1948, under Avertin anesthesia, a median tarsorrhaphy was performed on the patient's left eyelids. A linear incision was made parallel to the lid margin, and the skin was freed on either side. A free graft, taken from the donor's thigh, was fitted into the area which had been prepared with thromboplastin solution. The lids were then covered with oiled silk, and a firm pressure bandage was applied. At the first dressing, 10 days later, the isograft was found to be adherent, pink, and free of discharge.

About 20 days later, a similar operation was performed on the right eyelids using the same donor. Ten days later, on first dressing, the graft was found to be adherent, pink, and healthy.

The presence of ectropion in ichthyosis congenita is not a constant feature. According to the cases reviewed from the literature the presence or absence of ectropion depends on the following factors: (1) Whether there is involvement of the face; (2) whether atrophy of the skin occurs; (3) the degree and severity of the skin atrophy.

The skin of the face atrophies, and the skin of the eyelids retracts, thus everting the lid margins. Ectropion of the four lids is extremely rare, occurring only in severe cases and these patients usually die in the first year.

Cases similar to the one presented, and with successful isograft, were reported by Elschnig, in 1912, in the German literature and Shimkin, in 1945, in the *British Journal of Ophthalmology*. In a review of the American literature no previously reported case of this type could be found.

Discussion. Dr. James S. Shipman: This case brings to my mind a case that I saw about 10 years ago which should have had this operation done, and did not. Indeed, it would have been very fortunate for the patient if she could have had this surgery done earlier in life. The patient was a white woman, aged 40 years, who made her living as the "alligator woman" in a carnival. She certainly presented a very marked case of ichthyosis, and there was no mistake about her skin looking like that of an alligator. She had been making a living out of this for many years.

When I saw her, she had hypopyon keratitis with about half of the anterior chamber filled with hypopyon. We did a Saemisch section through the lower third of the cornea and postoperative recovery was fairly satisfactory for about a week. At the end of this time, the patient left the hospital and moved away with the carnival. We saved the eye, but with very little vision. She went down to Richmond and, at my suggestion, reported to Dr. Courtney for a follow-up, but she did not stay with him long. She kept moving on. I cannot help but think that, if she had had such an operation, it would have prevented this serious complication.

I think Dr. Spaeth is to be complimented on this very excellent result. I had the pleasure of seeing this boy at Wills Hospital before and after his operation, and I feel that the result in this case is all that one could ask for. However, if I might be so bold, I would like to suggest to Dr. Spaeth that I would not destroy the beautiful adhesions holding these lids together for at least another six months. The boy is able to see to get around, and I would be too much concerned about these lids turning out again if they are cut too soon. I do not like to disagree with Dr. Spaeth who has had much more experience with these cases than I have, but I do feel that one must wait a long time before cutting these adhesions.

INTRAOCULAR NONMAGNETIC FOREIGN BODIES

Dr. James S. Shipman presented six cases of intraocular copper and described a technique which he uses for the removal of nonmagnetic foreign bodies from the vitreous and the anterior chamber. The first four cases, all with copper in the vitreous, were operated by means of a posterior sclerotomy, through the lips of which a small capsule forceps was inserted. While looking with the ophthalmoscope through the dilated pupil, the operator was able to grasp the foreign body in the vitreous and extract it through the sclerotomy opening. In the first case, the scleral opening was closed with interrupted black silk sutures and no cauterization. In the other three cases, the same method was employed, but the sclera was coagulated around the incision with diathermy before suturing.

The first case made an uneventful recovery, and the vision was normal for 5 weeks following the operation. At the end of this time, a retinal detachment was observed. This became more marked and, approximately 2 months after the original accident, the first retinal detachment operation was done with the Weve needles. This was unsuccessful, and two more retinal detachment operations were performed, Safar pins being employed with the last. These were also unsuccessful. Today, more than 15 years following the patient's injury, the injured eye has no light perception, has a complicated cataract, and is divergent.

The patient in the second case made an uneventful recovery and, in spite of the fact that he has a partial posterior cortical cataract, he has had useful vision, 6/15 with correction, from the time he was first seen until now, almost 15 years after the injury. There was no evidence of any retinal detachment at

any time, and the visual field has remained full.

The third case showed more reaction following operation than the first two cases. The partial cataract which was present before operation became complete shortly after this, and a linear extraction was necessary. Following the cataract extraction, the patient made an uneventful recovery and has had no trouble since. Today, 13 years after the injury, the eye is entirely quiet with normal tension. The vitreous is clear, and the fundus is healthy with no evidence of detachment. The visual field is full, and the visual acuity of the injured left eye is 6/9+ with a +13D. sph.

The fourth case offered a poor prognosis because of the very large foreign body and the massive preretinal hemorrhage which were present when the patient was first seen. A considerable amount of vitreous was lost, and more hemorrhage occurred at the time of the extraction of the foreign body. This hemorrhage persisted, and eventually the eyeball became phthisical. Enucleation of this eye was advised.

The fifth case showed the copper wire to be present in the anterior chamber. This was removed by means of a paracentesis made with a keratome and enlarged with scissors. The foreign body was then grasped with iris forceps and withdrawn. However, the iris became entangled, and had to be replaced through the wound. This resulted in some incarceration but no prolapse of the iris in the paracentesis wound. The pupil was pear-shaped and drawn to the nasal side. A localized opacity still remains on the nasal side of the lens capsule. Otherwise, the media are clear, the fundus is healthy, and both eyes are entirely quiet. The visual acuity without correction today is 6/5, in the right eye, and 6/6, in the left.

The sixth, and last, case reported was one in which the nonmagnetic foreign body was localized in the vitreous. The same procedure, as in the other cases of nonmagnetic foreign bodies in the vitreous, was followed.

However, in this case, we were much more fortunate than in the others due to the fact that after the sclerotomy opening had been made, a bead of vitreous presented with the piece of copper glistening in the center of the bead. This was then extracted with forceps and the necessity for going any deeper into the vitreous was avoided. The scleral wound and conjunctiva were then closed in the same manner as in the other cases. This patient at the present time is still hospitalized, and the outcome is uncertain.

It is now realized that, in the first case, the eye should have been saved. The retinal tear made by the posterior sclerotomy should hav been sealed off, and the detachment could have been cured. Failure to do this was the result of lack of sufficient knowledge about the method for closing retinal tears 16 years ago. In Cases 2, 3, and 5, the results were as satisfactory as one could expect with such drastic surgery. Case 4 was considered very unfavorable when first seen because of the large size of the foreign body and the massive preretinal hemorrhage. However, a larger sclerotomy might have been done earlier. It is realized in retrospect that an an iridectomy should have been done in the fifth case.

I feel that the results obtained in the five reported cases of copper in the vitreous justify the technique followed. However, a special type of forceps, such as a modification of the alligator forceps used by otologists, or a smaller and stronger forceps similar to Thorpe's, might aid in grasping and holding the foreign body. I recognize the fact that if the lens is too opaque for one to see the foreign body, the procedure described cannot be employed. However, since removal of the cataractous lens would be indicated anyway, this could be done first, and then the technique described could be followed through.

Discussion. Dr. George H. Cross: I think that Dr. Shipman has been fortunate in having cases in which the intraocular foreign body could be seen with the ophthalmoscope.

Usually the lens is cataractous or the vitreous is filled with blood or exudate through which it is impossible to see the foreign body. In such a case the foreign body is best removed with the aid of a biplane fluoroscope. By this method the foreign body is accurately located by X rays.

Dr. Shipman was fortunate in that most of the foreign bodies were small ones. He spoke about the use of the endoscope which, to my mind, requires such a large opening in the eyeball.

My experience with nonmagnetic foreign bodies is limited to about 100 cases, 50 of which were operated upon. In many cases the localization was very poor, or the foreign body was outside of the eyeball. In one case it was located in the lower conjunctival cul-de-sac. It is very essential to have a good localization of the foreign body.

If you have a good X-ray report, and cannot see the foreign body and know that it is nonmagnetic, you can try the biplane fluoroscope. I think Dr. Shipman is to be congratulated on the nice results obtained in these cases.

Dr. Edmund B. Spaeth: Dr. Cross has done a tremendous amount of work with the biplane fluoroscope. I know so little about the use of this instrument that it perhaps seems unseemly to discuss its use. In spite of that, I am not at all satisfied or convinced that the biplane fluoroscope is good for the removal of nonmagnetic foreign bodies. The traumatism done to the eye because of the mechanical difficulties connected with the use of the forceps without visualization of the operative field is too extensive for approval.

I do want to speak in greater detail about the use of the endoscope. I have had a fair amount of experience with this, and have found it to be a valuable instrument in cases in which it can be used. Naturally, one cannot use the endoscope when the vitreous is full of hemorrhage.

There are many factors connected with the removal of nonmagnetic metallic foreign bodies from the eye, and many different means of localization and extraction. Each individual case may need an individualized technique. At the best, these cases are frequently difficult problems, and should be studied in detail as to the method most applicable for the situations present.

Dr. Shipman is to be congratulated on his results in these cases. The real tragedies in ophthalmology are those cases in which the foreign body cannot or could not be removed. I believe that, with the exception of zinc and aluminum, every eye with a retained intraocular foreign body will be lost ultimately. In some instances the initial injury, as with lead shot, is so great that the eyes are destroyed irrevocably at the start.

Dr. James S. Shipman: In answer to the remark that it was my good fortune that these foreign bodies could be seen, I do not feel that an opaque lens is a contraindication to this procedure. The lens has to be removed anyway, and, when it is, you can see the foreign body and remove it with the technique as described.

I feel that, in order to see and remove a piece of copper by means of the biplane fluoroscope, the foreign body would have to be quite large. In such a case the eye would be practically destroyed.

I doubt if any of the foreign bodies in the cases we have described could have been seen well enough with the fluoroscope to warrant their removal by that method, since they were all unusually small pieces of copper.

I wish to thank Dr. Cross and Dr. Spaeth for their discussion, and I trust that the report of these cases and the method which we used will stimulate others to try to remove all pieces of copper from the interior of the eye, which can be seen ophthalmoscopically.

CEREBROVASCULAR RESISTANCE AND GRADE OF HYPERTENSIVE RETINAL FINDINGS

DR. IRVING H. LEOPOLD, DR. SEYMOUR S. KETY (by invitation), DR. WILLIAM A. JEFFERS, DR. JOSEPH H. HAFKENSCHIEL

(by invitation), and Dr. HENRY A. SHENKIN discussed 21 hypertensive and 3 nonhypertensive individuals who were studied in an effort to find whether or not there was any correlation between the retinal vascular changes and the cerebrovascular resistance in hypertensive individuals. The cerebral blood flows were determined by the method of Kety and Schmidt, and the retinal vascular changes were evaluated according to the classification of Wagener and his coworkers. (See the AMERICAN JOURNAL OF OPHTHALMOLOGY, volume 32, page 365 (March) 1949.)

It was found that a statistically significant correlation existed between retinal changes and the cerebrovascular resistance. The relationship was a direct one in that, as cerebrovascular resistance increased, the grade of retinopathy also tended to increase.

It is evident that the retinal findings do reflect with some accuracy the state of the cerebral circulation, but the degree of accuracy is not marked in that one cannot predict from the ophthalmoscopic findings the exact extent to which the cerebrovascular resistance has been elevated.

Discussion. Dr. Seymour S. Kety: A few words about the physiologic significance of these studies may not be amiss.

As you know, when the physiologist studies hypertension in man, he is impressed with the fact that practically everything he investigates turns out to be normal. Measurements have been made of the output of the heart, and that is perfectly normal. The blood flow through the kidney is essentially normal except in the very late stages of hypertension. The blood flow through the skin, through the periphery of the body, through muscles, and so forth, has always been found to be physiologic. If one calculates the resistance in the blood vessels of these various organs, one finds that uniformly there is an increase in the peripheral resistance through the body, and in any individual organ. Since the brain has been implicated in numerous theories for the etiology of hypertension, we thought it of great interest to study the cerebral blood flow, and finally a method was developed at the University of Pennsylvania which permitted such a determination. We were interested in finding that, in the hypertensive individual, the blood flow in still another organ is perfectly normal. Just the same amount of blood passes through the hypertensive brain as passes through the brain of a normotensive individual.

The interesting thing, however, was that this occurred in the face of blood pressure which might sometimes be twice the normal level. This must indicate a high degree of resistance in the blood vessels of the brain which keeps back the flow of blood that would otherwise be much above the normal.

Dr. Leopold has discussed the possibility that was presented to him as an ophthalmologist; namely, with a method for calculating the resistance in the brain, one could evaluate the clinical impression of clinicians and ophthalmologists that eyeground changes were a reflection of what was going on in the brain. We were gratified to find that there was a fairly good correlation between the two. It is not at all surprising that the correlation is not better because one must remember that we were measuring the vascular resistance at one time (at the time of observation) and that that resistance was a function of the degree of spasticity of the vessels at that particular moment.

The eyeground changes, according to the classification used, are not only a measure of the degree of spasm in the vessels at that particular moment, but also reflect how long that spasm has been going on, and how severe it is. The eyeground changes are not only those of spasm, but also the changes which may result from spasm over a long period of time. If it were possible to separate the various factors that make up a retinopathy, particularly the degree of hypertonus at the time of observation and the results of the past history of that tonus, one might get an even better correlation than

the quite satisfactory one which Dr. Leopold found.

Dr. Francis Heed Adler: I would like to ask Dr. Leopold whether there is any difference in the cerebrovascular resistance in patients with atherosclerosis as compared with arteriolarsclerosis. Dr. Leopold is evaluating the eyeground changes which are admittedly more severe in cases of arteriolarsclerosis. It is possible that cases with atherosclerosis might have high cerebrovascular resistance, and yet would show no pathologic changes in the fundus. Such cases would upset the true correlation between cerebrovascular resistance and hypertensive retinopathy seen in cases of benign and malignant hypertension.

There are still a great many things we do not know about the retinal circulation. We have always taught that the ocular vessels are end arteries, because we say they are like the cerebral arteries. Until fairly recently, we believed that the cerebral arteries were end arteries in the sense of Cohnheim. Lorente deNo states that the cerebral arteries are in no sense end arteries, and that blood cells in the capillaries can pass freely from one end of the cerebral cortex to the other. It may be time that we reinvestigated the retinal circulation to determine more exactly whether there are anastomoses between the various branches of the retinal arterial tree.

Dr. I. S. Tassman: It is difficult to hear a presentation of this kind and be able to digest it and interpret it properly in such a short period of time. It occurred to me to ask a question, especially with reference to the point that Dr. Adler introduced, "Is it possible to correlate the findings of this kind for practical purposes?" The vascular bed in the two organs are of a different nature. There are differences in these structures, as well as possible differences in the arterioles of the brain and those of the retina.

The origin, course, and number of cerebral vessels with their ramifications are quite different from those of the retinal vessels, so that a difference in the vascular resistance of the two sets of vessels might be expected for this reason. Is it therefore possible to correlate satisfactorily the resistance of the one with the pathologic changes in the other?

Dr. Irving H. Leopold: The normal cerebral blood flows are based mostly on values found in young individuals between 20 and 30 years of age. The hypertensive patients studied here were also in a young age group, approximately 20 to 45 years for the most part. In this group, senile atherosclerosis would probably have a low incidence. The same cannot be said for local atherosclerosis. To date no study has been made to correlate atherosclerotic retinal change with cerebrovascular resistance.

The retinal and cerebral vessels certainly differ in many ways. There is, for example, no cerebral counterpart of the retinal-vessel crossing phenomenon. Nevertheless, there has been evidence presented in the past suggesting that both systems of vessels show similar changes, and this study also demonstrates a significant relationship in the presence of hypertension.

<div style="text-align: right">M. Luther Kauffman,
<i>Clerk.</i></div>

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LOS ANGELES OPHTHALMOLOGICAL SOCIETY

May 6, 1948

Dr. Orwyn H. Ellis, <i>chairman</i>

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EXOPHTHALMOS AND ITS SURGICAL TREATMENT

Dr. Howard Naffziger of San Francisco (by invitation) discussed bilateral exophthalmos related to thyroid disease. Since the etiology is not well understood, the literature reflects a wide divergence of opinion. An enormous amount of laboratory work has resulted. Recent investigations have revealed that sympathetic stimulation in man does not produce protrusion of the eye, nor

does paralysis produce measurable retraction, in spite of appearances to the contrary. Late contributions to the literature have avoided this pitfall in interpretation. Statistics show a wide range of variation of the position of the globe with reference to the orbital margin. In thyroid disease a slight exophthalmos is usually present, and following thyroidectomy there is a slight further increase in 40 percent of cases.

In pathologic studies, lymphorrhages were found not only in intrinsic eye muscles, but in the heart, deltoid, rectus, and biceps muscles. The eye muscles were the ones most severely affected. In the orbital tissues there was quantitatively an increase in orbital bulk, relatively greatest in the eye muscles, of which the fat content was doubled. The changes were most marked in the levator superioris, which is responsible for lid retraction. Similar changes have been produced in laboratory animals. Certain chemicals are known to have a marked affinity for orbital tissues, and may produce orbital edema and proptosis.

Clinically the thyroid bears a common but variable relationship to progressive exophthalmos and eye-muscle dysfunction. The thyrotropic fraction of the anterior pituitary body in producing experimental exophthalmos is well known. Thus patients can be divided into two groups, the thyrotoxic and the thyrotropic, the latter being the ones in whom eye signs predominate and evidences of toxicity are relatively insignificant or absent. The degree of exophthalmos and the disturbances of eye-muscle movements do not necessarily run parallel.

Proptosis usually begins months after an otherwise satisfactory thyroidectomy. The extreme cases progress to intracranial infection and death. In its development are seen increasing protrusion, lacrimation, burning, injected and irritated conjunctiva, puffy lids, and limited eye movements. Scleral irritation is a prominent feature. Of the eye movements, the upward movements are the most frequent and the earliest to be restricted, next the lateral movements and least often the downward excursions. Frequently poor vision will be present without evident change in ophthalmoscopic or other findings. Retrobulbar resistance is palpably increased. In the final stages, lack of lid protection because of incomplete closure, protrusion, and edematous conjunctocorneal ulceration are present.

Dr. Naffziger uses orbital decompression to treat these cases. The results of the operation depend greatly on whether or not the muscles show a minimal or marked fibrosis to hyaline change. The surgical treatment consists of enlarging the orbital space to accommodate the increased orbital contents. If the muscles are enlarged with relatively little fluid content, then the recession is immediate. On the other hand if the predominating feature is edema, then the same factors may persist after the operation and additional fluid is taken up until the preoperative balance is reached. These edematous muscles show little infiltration or degenerative change. The use of thyroid with or without iodine in some cases may promote water excretion and thereby lessen the edema. Occasionally unilateral decompressions have been performed due to the predominance of the protrusion on one side. Other methods of surgical treatment have proven of little or no value. Orbital decompression, although carrying little risk, is a procedure of such magnitude that it must be reserved for cases of considerable gravity. Efforts at reducing pituitary function by X-ray therapy have produced no more convincing results than have other general or local forms of therapy.

Daniel B. Esterly,
Recorder.

AMERICAN JOURNAL OF OPHTHALMOLOGY

Published Monthly by the Ophthalmic Publishing Company

SUPPLEMENTS

Accompanying this number of the JOURNAL is a beautiful supplement that is presented to every subscriber. It is officially the *Proceedings* of the Association for Research in Ophthalmology for 1948, and is dedicated to Jonas S. Friedenwald, the first winner of the Proctor Medal for ophthalmic research. It should be highly valued and, in time, will become no doubt a collector's item.

In the past years the *Proceedings* of the Association for Research were collected reprints of the papers read before the association and printed in the JOURNAL a few at a

time. Thus, a copy of the *Proceedings* was not available until all the papers had been published. The method employed was simple and relatively cheap so that the expense to the association was trivial. In return for this privilege, the association granted the exclusive right to the JOURNAL to publish the papers read before that society.

In the past, when there was but a single meeting of the association and only 10 or, at most, 12 papers were presented before it, the agreement was most satisfactory to both parties.

Now, however, with the growth of oph-

thalmic research in this country and the many excellent contributions waiting to be read before the association, it was found necessary, beginning last year, for it to hold its meetings for two days. This healthy and important growth of the association is most valuable to ophthalmology, and is highly significant of our maturity.

The great increase in the number of contributions has created a problem for the JOURNAL and for the association. The problem is solved for the time being by bringing out this Supplement. However, this is very expensive business, especially in these days of inflated costs of printing, and some solution on a more permanent basis must be had for the future.

The trustees of the association are working on the problem which is, of course, a matter of finance, and it is sincerely hoped that the policy of printing the *Proceedings* as a supplement to the JOURNAL will continue, for in this way all the subscribers to the JOURNAL, and this includes most if not all the members of the association, will be assured a copy of the *Proceedings* and the authors a worldwide audience.

The JOURNAL has always been proud of its practical nature. Emphasis has been placed, as an editorial policy, on clinical papers that will be of assistance to those who are on the firing line. Ophthalmic research, however, is playing an increasingly significant role, and papers of this nature should not be buried somewhere and inaccessible to the clinician, for often he can seize upon an idea from the laboratory and apply it with benefit in the clinic.

Thus, a well-balanced ophthalmic journal must have all kinds of contributions if it is to fulfill its important function of bringing new and useful facts to its subscribers. If it is top-heavy on one side or the other, it will alienate groups of readers with loss to all parties.

For this reason the JOURNAL is planning to have a quarterly section, under the editorship of Phillips Thygeson, devoted to some phases of ophthalmic research in the form of preliminary reports and other items of interest. It is also the policy to publish, as usual, papers of research nature as they come over the editor's desk that, in his opinion, warrant publication.

The JOURNAL is happy to present this historic Supplement. It represents a great deal of work and effort on the part of officers of the association and a pleasurable task for the JOURNAL.   Derrick Vail.

NIGHT DRIVING

Motor vehicle fatalities have increased steadily with the travel mileage, the present toll being over 32,000 deaths annually. Night accidents are twice as likely to be fatal as those of the day, the deaths per accident being respectively 1 to 26 and 1 to 49. The fatal accident rate per mile at night is three times that of the day. Although only one third of the driving is done at night, two thirds of the traffic deaths then occur. Motor vehicles cause more loss of life among other road users than among their own occupants. Of the pedestrians, 70 percent were killed at night.

The three most important visual factors involved in night driving are: (1) discrimination under conditions of poor illumination, (2) ability to see against glare, (3) recovery from glare. Tests designed to test these faculties should be simplified and adapted for the driver's examination. Glare resistance measures the ability to distinguish a dimly illuminated object when bright lights are shining in the eyes at various angles. To test glare recovery the adapted eyes are first checked for discernment of a dimly illuminated object, then exposed to a glaring light for 30 seconds, after which the interval is noted before the dimly illuminated object can again be perceived.

Signals composed of reflector buttons, five-eighths inch in diameter, are visible at 1,000 feet. The return beam from the headlight does not exceed 0.000,001 foot-candles

at this distance. At a driver's eye level the high beam of an oncoming car gives 1.0 foot-candle. The pupils contract within one second, but require seven seconds to fully redilate, and adequate readaptation takes one minute. The effect of glare in reducing peripheral vision depends on how greatly the glare light contrasts in intensity with the general illumination and its angle of incidence. The effect at one degree from the line of vision is over three times that produced at five degrees. Hence shifting the gaze down to the right edge of the road materially reduces the glare effect. Likewise, when the opposing headlight beam is depressed, the light seen is reduced from 1 foot-candle to 0.2 foot-candle, and the glare effect is proportionately less.

The prime reason for the excess of night accidents is inadequate vision. A shorter sight distance results and, because of unreliable visual clues, errors in the judgment of distance and speed occur. As the illumination lessens, the field of vision decreases, especially so when fatigue develops. About 75 percent of accidents have involved objects in the peripheral field.

As a visual deficiency in daylight is even more significant at night, the one-eyed person and those with corrected acuity below 20/40 should be cautioned especially against night driving. Motorists with only one efficient eye, which includes 1 to 2 percent of all drivers, are much inferior to the binocular sighted in night vision, glare resistance, and recovery from glare. A similar deterioration, though without loss of acuity, often affects the aged due to the rigid iris not dilating adequately or to the media being less transparent to the rays most sensitive to the dark-adapted retina. Fatigue from night driving prolongs the glare recovery time, and the accident-prone drivers often show a significant deficiency in dark adaptation.

The hazards of night driving can be reduced by improved highway lighting. This has been feasible only in congested areas, but two thirds of all accidents happen in the country. Accidents have occurred at speeds below 20 miles per hour so that it seems hardly possible to get the speed of vehicles down to a safety level. Polarized light to reduce glare is impracticable as the headlights would then require over four times the present power and dust on the screens would modify the filtering effect.

But various simple measures are worth while. Light objects are discerned with only one fourth as much light as dark objects. When a light road surface in the environs of Philadelphia was changed to dark a marked increase in night accidents followed. Pedestrians should not only face the traffic in walking but at night should wear something white if only a handkerchief around the neck or arm.

Spectacles, although necessary, cause a loss in light transmission. Tint aggravates the absorptive light loss and so any kind of tinted glass should be taboo after nightfall. In clear crown glass of 1.5-mm. center thickness only 0.6 percent of light is absorbed. However, the loss from surface reflections is significant—4 percent from each surface in crown glass, 6 percent in flint glass. Moreover the reflections cause secondary images with consequent haze and reduction of image quality. The magnesium fluoride coating cancels almost completely the reflected light in flint glasses and lessens considerably the loss in crown glasses. On changing to thinlite coated lenses, the appearance of myopes is remarkably enhanced and a subjective improvement in vision is experienced, especially at night.

Glasses have been constructed that effectively lessen the disturbance from headlight glare. For the past year the Night Driving Lens Company of New Haven, Connecticut, have been making up the driver's distance prescription in a clear glass on which has been placed a small mirror shield just to the left of the pupillary margin in each eye. The shield is a thin front-surface mirror that permits clear vision through it. It is probably made of inconnel (an alloy of chrome, iron,

and nickel) and is guaranteed to be harder and more resistant to wear than the glass itself. The mirror reflects the headlight glare and, at the same time, casts a protecting shadow across the pupil. Dr. W. J. Holmes of Honolulu, who has been much concerned about the problems of night vision, and I have given these glasses a trial for the past six months and can confirm their value. The coated lens mitigates a different disturbance of night vision from the "silvo-flect" shield, but the two cannot be combined, as the magnesium fluoride coating cannot be successfully applied to the latter.

In prescribing special glasses for night driving, the oculist should recall that the greatest luminosity of the spectrum shifts from 555 millimicrons (yellow-green) in day vision to 510 millimicrons (green-blue) at night. The focus of the eyes changes accordingly so that the eye is functionally about 0.5D. more myopic in night vision. Consequently, to obtain the clearest vision at night a −0.5D. should be added algebraically to the regular distance prescription to compensate for the night myopia.

James E. Lebensohn.

THE AMERICAN BOARD OF OPHTHALMOLOGY EXAMINATIONS

If the results of the American Board of Ophthalmology examinations can be taken as an index of the general level of ophthalmic education throughout the country, the prospect is pleasing. Some years ago 25 to 30 percent of the candidates taking the written test failed and were not admitted to the practical. At the recent written examination held in January, 1949, only 11 percent failed.

This definite improvement may be interpreted in several ways—the questions asked are easier, the examiners are becoming more liberal in their grading, or the candidates are better prepared. A study of the situation reveals the last interpretation to be the most likely. We are now seeing the first crop of postwar trained men who have completed three years in ophthalmology. There is no doubt that the laudable efforts made by the universities and by the Ophthalmological Study Council in giving basic courses are bearing fruit.

The fact that many more men are now being prepared to take the examination has contributed greatly to the work of the board. Last January, 256 candidates, a record number, took the two-day written examination in 34 cities throughout the country with the result that it has been necessary to schedule three practical examinations during the remainder of the year. The board appreciates the coöperation of ophthalmologists who have given their services in proctoring the written examinations and who have acted as associate examiners in the practical. Without them it would be impossible to examine such large numbers of candidates.

It is the feeling of the board that the written examination should be held only at medical schools and hospitals and that the local head of the department of ophthalmology should be responsible for conducting the examination, either proctoring it himself or delegating this important function to a member of his visiting staff. Efficient proctoring by an ophthalmologist is essential even though it entails some sacrifice of time and money once a year. Since the board members themselves serve without pay, it is not too much to ask the proctors to do likewise. In this way they can help make their contribution to ophthalmic education.

Edwin B. Dunphy.

OBITUARIES

JOHN GREEN
(1873-1949)

To understand John Green, a knowledge of his background is necessary. If all of the readers of his obituary were of the older generation, no description of his father

JOHN GREEN

would be necessary, but for the younger ones something must be written.

John Green, Senior, was one of the most eminent ophthalmologists of America and a dominant and dominating factor in the early history of the specialty. For many years he was chairman of the powerful membership committee of the American Ophthalmological Society and, when it was voted to elect this officer annually, Dr. Green withdrew from activity in the society. He was famous for his originality of thought and his brilliant mind. Being so constituted, it was natural that he thought that St. Louis schools were not good enough for his son, John Junior, and so had him taught privately until time for him to go to college. This made adjustments hard at Harvard for the boy who had never learned to play with his fellows. He had the further handicap of being very young, only 16 years old, when he matriculated. Hence the young boy, with very limited experience in making acquaintances, probably did not get as much from his university association as others who were more mature.

Of splendid mentality and the son of such a distinguished father, Dr. John Green was certain to become an outstanding figure in ophthalmology. But, because of his heritage and training, there was always about him some shyness and sensitivity, and, well liked as he was by his associates, because of this he was at times somewhat reticent.

He studied to be well informed on everything pertaining to medicine and kept himself young by his eagerness to learn and his active association with ophthalmological societies, national and local.

His written contributions were largely clinical because the practice rather than the theory of medicine intrigued him, as one might expect from a man who was always busy with patients and spent little time in laboratories.

When he returned to St. Louis from Cambridge, in 1894, he studied medicine in Washington University Medical School from which he was graduated in 1898. He was then associated for a brief period with a well-known general surgeon, but soon took up the study of ophthalmology in his father's office. For a number of years he practiced with him, but the two very positive natures struck sparks so often that the younger man opened an office for himself and formed an association with Dr. William F. Hardy which was continued for many years.

In 1902, Dr. Green married Lucretia Hall

Sturgeon and of this union six children were born. They were: Helen C. (Mrs. Leonard Lee Bacon), Harmon, John, Nathaniel Pope, Lucretia H. (Mrs. William C. Lindsley), and Elizabeth. His wife and children all survive him.

Never deeply interested in athletics, Dr. Green did, however, devote some time to tennis and in his early days could often be seen on the courts of the St. Louis Amateur Athletic Association.

He became a member of the staff of the ophthalmological department of Washington University Medical School at the time of its reorganization in 1910. He worked in the clinic there for a few years and then transferred to St. Louis University where he rose rapidly to the rank of professor.

His chief interest outside of his family was his profession. An avid student, he was a regular attendant at the St. Louis Ophthalmic Society meetings to which he contributed many interesting papers and discussions. In the early days, this organization was confined to 12 members and was of a very informal nature where participation in the discussions was general. Dr. Green invariably contributed something of value. An interesting feature was the annual calamity meeting at which each member described his most distressing case of the year. This served the double purpose of getting expert advice, a sort of curbstone consultation, and of raising the morale of each member when he heard of the awful things that happened to others! Unfortunately as new members were added, expediency occasioned the discontinuance of this meeting. There are now 45 members of this society, and it would take a long time to listen to all of the sad tales and there would be no tears left to shed for the last raconteur!

Dr. Green was naturally one of the early presidents of this society. He was always interested in its activities and was one who insisted on maintaining a high ethical standard and good quality for the papers presented. To him and to men like him can

the society turn in appreciation for the excellent quality of the programs delivered at its meetings and the great esteem with which ophthalmologists are held in St. Louis.

Dr. Green was truly civic minded. He was a member of the Board of Education, University City, from 1910 to 1920 and a member of the Board of Health from 1921 to 1926. From 1906 to 1910 he was secretary of the Joint Medical Council, an organization to change the plan of administration and control of public hospitals in St. Louis.

Of his many honors and achievements only three can be here detailed. First, and very dear to his heart, was his secretaryship of the American Board of Ophthalmology. He held this office from 1933 to 1943 and, during his final year on the board, was its chairman. The second honor was the chairmanship of the Section of the American Medical Association in 1936, and third, and perhaps most highly prized, was his election to the presidency of the American Ophthalmological Society in 1944.

John Green was a jolly fellow, always ready for a laugh, a fine companion. He loved the Racquet Club, a man's club, where he often foregathered of an evening with his friends. His was a happy life, a long life, full of achievements. He never did live to get old. The remark oftenest to be heard from his colleagues in the days after his death was, "I didn't realize that John was 75." When he died, the world lost a fine doctor and his confreres a loyal friend.

Lawrence T. Post.

LOUIS BOTHMAN
(1893-1949)

Dr. Louis Bothman was born on November 16, 1893, at Saint Louis, Missouri. He died of coronary disease on January 19, 1949, at Chicago. After finishing high school at Murphysboro, Illinois, he entered the University of Chicago from which he received his B.S. degree in 1913. In 1917, he received his M.D. degree at Rush Medical College.

Deciding to specialize in ophthalmology, Dr. Bothman worked for five years on half-time at the University of Illinois College of Medicine. He spent a short period at the Illinois Eye and Ear Infirmary and six months' study in Vienna in 1926. In 1932, he went to India for intensive study of cataract surgery. He also did considerable graduate work in physiology at the University of Chicago.

From 1926 to 1941, Dr. Bothman was first assistant and associate clinical professor of ophthalmology at Billings Hospital, University of Chicago. He was attending ophthalmologist at St. Luke's Hospital, being senior attending ophthalmologist at the time of his death. From 1941, he was clinical professor of ophthalmology at the University of Illinois College of Medicine.

Dr. Bothman had a fine, precise mind, was a careful observer and reporter and an enthusiastic, devoted teacher. In particular he was a close student of ophthalmic literature and was leader of the Eye Journal Club, a group of 40 to 50 men who met monthly

LOUIS BOTHMAN

for 10 or 12 years in an assigned study of the most recent ophthalmic literature. From 1932 to 1949, he edited the eye section of the Eye, Ear, Nose, and Throat Yearbook, a work that has been highly praised by Dr. Arnold Knapp. In addition, Dr. Bothman made many contributions to ophthalmic literature. Many of his papers were concerned with eye surgery in which he was deeply interested and very proficient.

For many years—17, in fact—Louis Both-

man and I were closely associated in the care of patients, in study, writing, and teaching. I found him to be an even-tempered, considerate man, keen and thoughtful, with whom it was a pleasure and satisfaction to work. During all those years, I am proud to say, neither of us ever had a cross word for the other.

Any man who has lived and felt as intensely as did Louis Bothman—and he did feel intensely about many things and persons—and still be as wisely tolerant as he, commands profound respect and admiration. We deeply mourn his passing.

E. V. L. Brown.

CORRESPONDENCE

NOTICE OF MEETINGS

Editor,
American Journal of Ophthalmology:

This is simply a note to let you know that I appreciate reading the "News Items" for the scheduled meetings in the JOURNAL. However, I would like to add that there is so little time between the dates of the meetings and the time when the JOURNAL is received, that it is practically impossible to plan to attend one on such short notice.

It would be greatly appreciated if more time, either through a separate "News Items" sheet announcing these dates could be received, or more advanced notice made possible in the JOURNAL.

(Signed) Bernard B. Friedman,
Corpus Christi, Texas.

EDITOR'S NOTE

The matter of getting advance notices of meetings, graduate courses, and so forth has given the JOURNAL considerable concern. In order to give advance notice of these meetings, it is necessary that information concerning them be received by the JOURNAL three months prior to the meeting.

USE OF AIR TUBE DURING LOCAL ANESTHESIA

Editor,
American Journal of Ophthalmology:

On patients undergoing surgery of the eye it is necessary to cover the face with drapes which frequently cause anxiety to the patient, and this is often manifested by air hunger. Such anxiety may result in restlessness and tenseness, thereby making the operative procedure more difficult and more hazardous.

During the past two years at the Eye Institute, all patients under local anesthesia have had an air tube placed under the drapes in an effort to relieve these unpleasant symptoms. A long rubber tube is attached to the air jet in the operating room and pinned to the drapes near the base of the neck before the sterile part of the drapes has been applied. The air is turned on so that there is a gentle flow coursing up over the face. There is a remarkable quieting effect on the patient when the air is turned on and the patient is visibly relaxed.

Not infrequently, elderly patients may become disoriented shortly after operation. This condition, seen in those who have had preoperative sedation in the form of barbiturates or other sedatives, is thought to be due to a cerebral anoxia in a person with poor circulation who is further embarrassed by the sedation and heavy drapes about the face. Since the air tube has been used, this postoperative disorientation has not been a serious problem. In some patients in whom the circulation is extremely poor and the vital capacity is very low, oxygen has been substituted for the air with very gratifying results.

(Signed) Joseph A. C. Wadsworth,
New York.

BOOK REVIEWS

An Introduction to Clinical Orbito-
nometry. By A. C. Copper, M.D. Leiden,
Stenfert Kroese, 1948. 117 pages, illustra-
tions, diagrams, and bibliography. Price:
Clothbound, $3.00; paperbound, $2.25.

There has long been a need for a simple
instrument, comparable to the tonometer,
that would give some degree of accurate
estimation of the orbital tension, especially in
those conditions that cause an increase in the
intraorbital pressure. The clinician in the
past has had to be satisfied with the sense
of resistance to digital palpation on pushing
the eye back into the orbit. Dr. Copper re-
views the efforts of scientists to devise an
instrument that would give a reliable index
of orbital tension. He points out that Lang-
enhan was the first to describe such an
apparatus in 1910. Since then, there have
been several attempts to improve on the idea
and to devise new instruments. Gutmann,
in 1914, presented an instrument similar to
the Schiøtz tonometer, by which he applied
increasing amounts of pressure directly on
the cornea. He named his apparatus the
"piezometer." There were many disadvan-
tages to this instrument and the clinical
use of it was disappointing.

Copper has invented an instrument that
may turn out to be of great use to the in-
ternist and to the ophthalmologist. By it one
can apparently measure the variation of the
orbital tension from the normal, and con-
struct curves that yield information as to the
character of the lesion behind the eyeball,
that is to say whether it is of solid or fluid
nature. This should be particularly useful, as
the author points out, in helping to decide
whether the proptosis is of the thyrotoxic or
thyrotropic type, and may be a very impor-
tant factor in determining whether or not
thyroidectomy is indicated.

He also presents some evidence that with
it one can get some help in determining
whether a solid growth is in the temporal

or nasal side of the orbit. Tumors can be
diagnosed even in the absence of proptosis.
It will not reveal the nature of the new
growth, of course. It is only capable of dis-
closing the presence of abnormal density in
the orbit and of deciding whether the process
is stationary or progressive.

Copper's instrument consists of a bridge,
not unlike that of the Hertel exophthalmom-
eter, resting on each outer orbital rim and
the nose. The patient lies down and this
bridge is adjusted and held in place by a
headband. The eyes are directed forward in
the primary position. A plastic contact glass,
on the apex of which is fitted a small cylin-
drical projection, is applied to the cornea.
A dynamometer similar in principle to that
of Bailliart and calibrated to represent pres-
sures up to 400 gm. is passed through a slit
in the bridge, and the plunger of the instru-
ment is lightly inserted into the cup on the
apex of the contact glass. The eye is then
displaced backward into the orbit by steadily
increasing the pressure of the plunger. Vari-
ous readings up to 400 gm. of pressure are
taken and a curve of values is constructed.

The author concludes that (1) Orbitonom-
etry is a valuable diagnostic aid in patho-
logic intraorbital conditions, and (2) orbito-
nometry assists in approaching the patho-
physiology of certain endocrinal diseases,
especially those in which the pituitary and
thyroid glands are concerned.

The book is well and clearly written. It
opens up a field of investigation which is
so important that every ophthalmologist
should be acquainted with the subject.

Derrick Vail.

Manual de Oftalmología Clínica y
Teórica (Manual of Clinical and Theo-
retical Ophthalmology). By Dr. Manuel
Márquez, ex-professor of ophthalmology
of the University of Madrid, professor
of ophthalmology of the School of Rural
Ophthalmology of the National Polytech-
nic of Mexico. Book 1, General Clinical

Ophthalmology and Defects of Refraction of the Eye. 274 pages, with 311 figures, and 7 plates, of which 6 are in color. Mexico, D. F., 1949. Imprenta "Grafos."

Spain's political upheavals have scattered some of its prominent citizens to other parts of the world. Manuel Márquez is one of these distinguished former citizens, now active in the city of Mexico. The publication of the present volume is credited by the author in part to the desire of his Mexican students for reproduction of his ophthalmological lectures and partly to the fact that the first two editions of his original manual, published in Europe, have been exhausted.

Dr. Márquez's fame as a teacher of ophthalmology is universal throughout the Spanish-speaking world. This new volume is well printed on excellent paper. It contains a good many new illustrations, a number of them by Dr. Márquez's companion in exile, Dr. Rivas Chérif of Mexico City. The volume deals with ocular anatomy, physiology, and pathology; defects of refraction and accommodation, and their diagnosis by subjective and objective methods; diagnosis of fundus diseases and diseases of the anterior segment; and therapy of the eye and of the general system in relation to the eye. Characteristic of the author's high professional standards is the devotion of a special chapter to "Ophthalmologic Deontology," the science of professional duties and etiquette.

W. H. Crisp.

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MALATTIE CUTANEE E VENEREE ED ALTERAZIONE OCULARI. By G. Sala and P. Noto. With a foreword by Prof. A. Crosti and Prof. B. Alajmo. Palermo, Italy, S. F. Flaccovio, 1948. 410 pages, bibliography. Price, $3.00.

A very important Italian publication is this volume by an ophthalmologist and a dermatologist, showing the close relation of these two branches of medicine. The authors did not limit their observations to the dis-

cases of the skin surrounding the eye, which can be found in any textbook, but made a complete clinical and pathologic study of generalized diseases of the skin affecting the inner eye.

The volume of 410 pages is divided into 16 chapters, which include: Epithelial dystrophies, allergic dermatosis, dermatosis from parasites, from infection, from avitaminosis, precancerous lesions, hemorrhagic syndrome, venereal diseases, and so forth.

A large bibliography completes this interesting and well-written book, for which the authors deserve enormous credit.

Vito La Rocca.

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REFRACTION OF THE EYE. By Alfred Cowan, M.D. Philadelphia, Lea & Febiger, 1948. Edition 3, thoroughly revised. 287 pages, 187 illustrations, 3 colored plates, bibliography, index. Price, $5.50.

The appearance of the third edition of this justly popular book is a testament of its value to teacher, student, and practitioner. The author, who is professor of ophthalmology, Graduate School of Medicine, University of Pennsylvania, has devoted his professional career chiefly to the study and the teaching of refraction. The integrity of his work illuminates every page. His common sense in the handling of this assignment is in refreshing contrast to many other books on the same subject.

Those who possess the earlier editions will want this one to bring them up to date. Those who have not seen or owned an edition have an ophthalmic treat ahead of them. It is highly recommended.

Derrick Vail.

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TRANSACTIONS OF THE OPHTHALMOLOGICAL SOCIETY OF NEW ZEALAND, Supplement to the New Zealand Medical Journal, 1948.

The transactions begin with the presidential address of Rowland P. Wilson which is a scholarly treatment of various facts of

etiology, pathology, and diagnosis of certain bacterial and allergic diseases of the conjunctiva.

Bruce Hamilton discusses choroidal sarcoma. It is 8 times as common in Tasmania as in England; 11 cases were followed 10 years and, in this small number, the mortality was 27 percent, as against 55 percent in England and 66 percent in the United States. The depth of pigmentation seemed to have a definite relation to the mortality rate. The author presents a family tree of five generations, two members of which, a woman and her niece, died early of choroidal sarcoma.

Fairclough calls attention to cataract in myotonic dystrophy. His report is illustrated with drawings of the lens and photographs of each of six patients. There are shorter discussions of pterygium, herpes, and varicella, retinal detachment, prevention of industrial accidents, penetrating wounds, contact lenses, and dislocation of the lens.

F. H. Haessler.

TRANSACTIONS OF THE OPHTHALMOLOGICAL SOCIETY OF PARIS (and of the Ophthalmological Societies of the East, of Lyon, and of the West). Meeting of April, 1948, pp. 105-245.

Hudelos demonstrated a new instrument, the retinal esthesiometer, and discussed the technique of its use and the importance of this more refined test in the prognosis of cataract extraction, organized pupillary exudate, and detachment of the retina. It is of value in detecting field defects in mentally disoriented patients.

A. M. Larmande described a case of craniofacial dysostosis in which a decompression of the orbit and the optic canal caused a regression of the exophthalmos and improvement of vision. Armand de Gramont demonstrated his new instrument for retinal photography.

Velter reviewed his 40 years of experience with sclerecto-iridectomy in the treatment of glaucoma, and Mercier reported surprising success from the subconjunctival implantation of autoclaved placenta in three cases of intractable iridocyclitis.

Legrand recommended iridectomy and tarsorraphy in severe tuberculosis of the anterior part of the eyeball. It gave him better results than any other specific or nonspecific treatment.

In his lecture on periodic and local variations of certain ocular diseases, Professor Brückner pointed out that pterygium, rare in central Europe, is very frequent in Central and South America and in Africa. Koch-Weeks conjunctivitis, which is very rare in Europe, is common during the summer months in Africa and Asia Minor. He also noted differences in the occurrence of diseases associated with inclusion bodies, gonoblennorrhea, phlyctenular conjunctivitis, tuberculous, herpetic, and syphilitic diseases of the eye, and serpiginous ulcers, as well as nutritional and metabolic disturbances. There is also an extensive analysis of the variations of glaucoma and vascular diseases, many charts and statistics, and a bibliography.

Jean Nordman discussed the congenitally luxated lens as a malformation of the eye only, distinguishing it from those associated systemic congenital anomalies. Thomas and Muller reported a case of orbital Schwannoma without any manifestations of Recklinghausen's disease. Gallois recommended diascleral transillumination for localization of intraocular foreign bodies close to the ciliary region.

Brückner and Jazbasic read a paper on the experimental hypertensive retinopathy in dogs and the possible value of the findings in the surgical treatment of hypertension. Cordier and Pissavin analyzed the occurrence of the Argyll-Robertson sign in herpes zoster ophthalmicus.

Alice R. Deutsch.

ABSTRACT DEPARTMENT

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

11

RETINA AND VITREOUS

Maione, Mario. Contribution to the pathogenesis of senile macular degenerations. Ann. di ottal. e clin. ocul. 73:321-331, June, 1947.

Maione presents two cases of disciform degeneration of the macula, one, bilateral, in a 39-year-old woman and the other, unilateral, in a 78-year-old man. Both patients had diffuse arteriosclerosis. In the second patient the unaffected eye showed pigmentary dystrophy in the macular region. It is probable that the pigment epithelium participates in the evolution of the disease and undergoes dystrophy because of circulatory disturbances. (4 figures, references.)

Harry K. Messenger.

Moeschlin-Sandoz, Y. Senile pseudotumor of the macula with multiple lesions. Ophthalmologica 116:272-276. Oct.-Nov., 1948.

A case of senile disciform degeneration of the macula was followed for 18 years. Through the patient's death the eyes became available for histological examination. There is no difference in principle between the markedly elevated and the flat forms of disciform degeneration of the macula. Peter C. Kronfeld.

Neame, H. Angiomatosis retinae, with report of pathological examination. Brit. J. Ophth. 32:677-689, Sept., 1948.

Three cases of angiomatosis of the retina are presented in detail. One of the eyes was enucleated and was studied histologically. There are two distinct clinical types of this disease, a pale pink swelling associated with swollen retinal vessels and enclosed in a capsule or sheath; and a blue venous swelling. Unless treated, eyes with tumors of the first type become blind. Radium, radon, X ray, electrolysis and perforating diathermy were used but vitreous hemorrhages, retinal cystic degeneration, retinal separation and cataract may follow. The cause of the detachment without subretinal exudate or tears is not known. (9 figures.) Morris Kaplan.

Peck, F. B., and Mann, M. Effect of hesperidin methyl chalcone (vitamin P) on diabetic retinopathy. Am. J. M. Sc. 217:277-282, March, 1949.

A group of diabetic patients was studied

to determine the effect of vitamin P on diabetic retinopathy. Prothrombin and capillary fragility were measured; the level of plasma proteins was also determined.

The authors present the following conclusions. There was no significant alteration in the plasma albumin or globulin of 23 diabetics, twenty had evidence of diabetic retinal changes. The prothrombin time and retinal changes were greater in patients who had diabetes more than 10 years. The relationship, if any, between prothrombin time and diabetic retinopathy deserves further study. One half of the patients with retinopathy had increased capillary permeability, but this manifestation was not correlated with prothrombin time. In many cases, the petechial index improves with administration of vitamin P, suggesting that this vitamin has some effect on capillaries but the retinal hemorrhages do not change. Retinal hemorrhages are seen in diabetics, who do not show increased capillary fragility. Vitamin P did not alter the course of diabetic retinopathy in a majority of these patients. Theodore M. Shapira.

Philips, Seymour. **Scleral resection in the treatment of retinal detachment.** (A preliminary report.) Brit. J. Ophth. 32: 811-818, Nov., 1948.

Causes of failure in the usual diathermy repair of retinal detachment are failure to see and then seal off the tear, retraction of the vitreous and shrinkage of the retina so that it is too small and does not fit the globe. When the retinal tear can be seen, then diathermy remains the procedure of choice; however there are very definite indications for the employment of scleral resection. These are multiple tears in a thin atrophic retina where diathermy has failed, detachment in which no tear can be found, long standing detachment of a shrunken retina that no longer fits the globe, and high myopia. In the latter vitreous retraction and atrophic retina give little hope of success with diathermy.

Scleral resection shortens the globe and allows the shunken vitreous and retina to fit. It may encircle the whole globe or be limited to any part of it. In local anesthesia a slice of sclera about 4 mm. wide is removed with scissors. At the same time interrupted white silk mattress sutures are placed in the area from which tissue is being removed. Postoperative treatment is the same as for diathermy repair. Two successful cases are reported. (5 figures.) Morris Kaplan.

Philips, Seymour. **Retinal venous changes in diabetes.** Tr. Ophth. Soc. U. Kingdom 66:231-239, 1946.

Ballantyne, in 1943, described the changes found in the larger retinal veins in diabetes and concluded that the venous anomalies may occur in the absence of hemorrhage and exudate. He had not observed their development from an earlier phase and found that they usually occurred in mild as well as in controlled diabetes. He describes a patient, 51 years of age, whose diabetes had been controlled by insulin for four years and whose vision had become blurred four years before. He ascribed the lesions to phlebosclerosis associated with arteriocapillary fibrosis in the islands of Langerhans. Similar retinal findings in a patient with advanced phlebosclerosis from fibrosis of the lungs and an undoubtedly increased venous pressure suggest that the retinal venous changes may have a mechanical origin. The vitreous pressure may vary through a wide range in those taking insulin. An increase in blood sugar produces a diminished intraocular pressure. Constant changes in vitreous pressure for a long time might lead to phlebosclerosis. (5 figures.)

Beulah Cushman.

Radnót M. **Formation of new blood vessels in diabetic retinitis.** Klin. Monatsbl. f. Augenh. 113:137-140, 1948.

The formation of new blood vessels is an important finding in diabetic retinitis of severe character. Vascular hypertension and damaged kidneys are often found in conjunction with diabetes and diabetic retinitis. The author feels, however, that the formation of new blood vessels is solely due to diabetic changes. It corresponds to the pathological finding of rubeosis iridis, also found in diabetes. The literature concerning retinal hemorrhages in diabetes is briefly reviewed. A clinical case of diabetic retinitis and the histologic findings in another in which there were newly formed retinal vessels, are described. (1 color plate, 2 figures, references.)   Max Hirschfelder.

Saebø, Johan. **Atrophia gyrata choroideae et retinae.** Brit. J. Ophth. 32:824-847, Nov., 1948.

Much confusion in the literature exists concerning the clinical aspects of atrophia gyrata choroideae et retinae and especially as to the possible relationships between this disease and choroideremia. Two divergent conceptions concerning this relationship have persisted; in one the two diseases are the same disease of which choroideremia is the ultimate stage and in the other choroideremia is a defect or malformation whereas atrophia gyrata is an acquired progressive degeneration. To complicate things further, both have often been confused with retinitis pigmentosa; and indeed, the main features of atrophia gyrata are often found in pigmentosa, namely familial occurrence with frequent history of consanguinity, night-blindness, reduction of central vision, defect of the visual field and an area of atrophy of the central part of the fundus from which the immediate macular area is spared.

Case reports of four brothers, aged 27, 38, 44, and 46 years, with typical clinical pictures are presented and paintings of the fundus are included. All four had had night-blindness since childhood and progressive loss of vision. The older the patient, the more advanced was this loss of vision and the more complete was the retinal and choroidal atrophy. The author believes that this progression of the disease with age is a progression toward the typical picture of choroideremia and that actually these two diseases are the same.

Morris Kaplan.

Schulte, D. **Venous pulsations in the retina.** Klin. Monatsbl. f. Augenh. 113: 220-230, 1948.

Various existing theories concerning the cause of the venous pulsations in the eye disregard the fact that these pulsations appear as a rule only at the disc, but not in the periphery. Thin glial tissue alone covers the vessels in the disc and slight changes in pressure can, therefore, easily lead to pulsation. In the retina the nerve fibers prevent pulsation mechanically. Similarly, pulsation may be prevented whenever inflammation and edema lead to an increase of tissue within the disc. Anatomic structure and the level of the vascular bed determine the appearance of the venous pulse. Among 100 patients 36 percent had venous pulsation spontaneously and 31 percent after compression. Pulsation was lacking in 33 percent. In 33 patients there was a simultaneous arterial and venous pulse after compression. In one half of them the vein collapsed during the expansion of the artery and in the other half the movements were synchronous. Synchronous and alternating pulsation in the same eye in different venous branches was observed in three patients. Arteries and veins have a common sheath of tissue in the disc.   Max Hirschfelder.

Shelburne, S. A. Retinal arteriovenous nicking: II A long term study of the development of arteriovenous nicking in patients with hypertension. J. Lab. and Cl. Med. 33:1486-1487, Nov., 1948.

In 1939 the author's group reported their studies on the significance of various stages of retinal arteriovenous nicking in patients with hypertension before the Central Society for Clinical Research. They have now (1948) restudied some of the same patients after 8 to 10-year intervals and followed for the first time the development of this phenomenon from the first stage to the last. It was shown that the early lesion develops into the late lesion. Emphasis was placed on the importance of distinguishing these lesions, one from the other. Clear color drawings showing the various types of arteriovenous nicking and other retinal changes found in hypertensive patients accompanied the lecture. F. M. Crage.

Sorsby, A., and Joll Mason, M. E. A fundus dystrophy with unusual features. Brit. J. Ophth. 33:67-97, Feb., 1949.

The authors record a study of five families in the members of which a genetic affection becomes manifest at about the age of 40 years. In the early stages there is edema and a hemorrhagic-exudative reaction in the central area of the retina which progresses to central atrophy with parietal sclerosis and heavy pigmentation. Ultimately the whole of the fundus becomes atrophic. The affection is inherited as a simple autosomal dominant. The study establishes the existence of a hemorrhagic type of macular dystrophy and confirms the view that dystrophies cannot always be regarded as localized lesions but are occasionally and possibly frequently merely the starting point of a diffuse retinal or choroidal disturbance. Gross pigmental disturbances are not always of infectious or toxic origin. The

earliest changes in a genetic affection may be hemorrhages and exudates identical in appearance with the lesions commonly observed in arteriosclerosis and metabolic disturbances. It cannot be definitely stated that cases of Doyne's choroiditis should not be included in this group. (51 figures, 24 in color.)
Orwyn H. Ellis.

Sorsby, A., and Ungar, J. Intravitreal injection of penicillin: study on the levels of concentration reached and therapeutic efficacy. Brit. J. Ophth. 32:857-864, Dec., 1948.

Since adequate therapeutic levels in the vitreous can now be obtained by subconjunctival injection, direct intravitreal injection of penicillin has become largely an academic question. In the experimental work it was found that adequate antibacterial levels persist in the vitreous for 36 and possibly 48 hours after direct intravitreal injection of 5,000 units of crystalline penicillin in water. In order to control infection it was necessary to start the treatment three hours or less after staphylococcos was introduced into the vitreous. Orwyn H. Ellis.

Sorsby, A., and Ungar, J. The control of experimental infections of the anterior chamber and of the vitreous by subconjunctival and retrobulbar injections of crystalline penicillin in doses of 1,000,000 units. Brit. J. Ophth. 32:873-878, Dec., 1948.

Infections of the anterior chamber can be controlled, even after 24 hours, by subconjunctival injections of penicillin. Retrobulbar injections were less efficacious. The animals which were given penicillin 4 hours after the intravitreal injection of staphylococcus did well, whereas rabbits first treated 24 hours after infection did badly. In the vitreous infections the route of administration was of much

less importance than the time interval between the infection and the instigation of treatment.   Orwyn H. Ellis.

Vila Ortiz, J. M. Intraocular pressure in cases of hemorrhage of the retina. Arch. Ophth. 39:661-664, May, 1948.

The incidence of low ocular tension, both physiologic and pathologic, is significantly greater in patients with hemorrhage of the retina than without. Low tonometric readings can be related to predominance of arteriosclerosis and high readings to predominance of phlebosclerosis.   Ralph W. Danielson.

Waldman, J. and Shannon, C. E. G. Retinoblastoma (retinal glioma) cured by radon seeds. Arch. Ophth. 41:32-41, Jan., 1949.

This method was devised to overcome the difficulties that may occasionally be encountered in inserting radon seeds directly into the tumor or in applying them, embedded in dental stent, to the overlying sclera of the posterior part of the globe, as described by Stallard. Briefly, the method consists in the application of a thin, semipliable chromium-plated or rhodium-plated silver band applicator containing depressions in the distal end into which the required number of radon seeds fit. The length of the band depends on the location of the tumor as measured from a fixed point on the eyeball. This applicator follows the contour of the eyeball and is "buried" under Tenon's capsule and the conjunctiva. A patient with retinoblastoma in the remaining eye has been treated and observed for twelve years. She has been cured for nine years. The total of 3,104 r given was far below the dose advised by the fractionated method of Martin and Reese. The local use of radon by the method described is recommended as another form of treatment of this malignant disease, particularly when the exact and careful technic

of fractionated roentgenotherapy described by Martin and Reese is not available.   Ralph W. Danielson.

Weiss, C., Perry, I. H., and Shevky, M. C. Infection of the human eye with cryptococcus neoformans (Torula histolytica; cryptococcus hominis). Arch. Ophth. 39: 739-751, June, 1948.

A case of infection of the human eye with cryptococcus neoformans is reported. The clinical diagnosis was "possible cyst of the retina with retinal detachment and uveitis." The sclera was trephined, and material obtained for culture showed the presence of this yeastlike organism. Injection of the culture into the anterior chamber of the rabbit produced visible pathologic changes as early as the fifth day. Histologic changes in the rabbit eyes are described. Characteristic was the formation of rosettes along the anterior surface of the iris and posterior surface of the cornea. The rosettes were composed of a central cryptococcus surrounded by a single row of polymorphonuclear cells and monocytes. The technique of culturing the organism in the anterior chamber of the rabbit may contribute to the earlier diagnosis of this fatal disease.
                              John C. Long.

Winkler, G. Fundus changes in hunger patients. Klin. Monatsbl. f. Augenh. 113: 231-234, 1948.

In two prisoners of war hunger induced disease characterized by debility and widespread edema. Visual disturbances developed and led to total amaurosis in one. Small, yellowish-white, sharply circumscribed spots were observed in the macular region similar to the spots in retinitis punctata albescens. (2 figures.)
                              Max Hirschfelder.

Witmer, R. Retinal periphlebitis due to sarcoidosis. Ophthalmologica 116:288-290, Oct.-Nov., 1948.

After an unsuccessful cataract operation one eye of a patient with bilateral chronic uveitis had to be enucleated. The histologic changes in the anterior segment were probably related to the cataract operation and its sequelae. The retina contained tubercles of varying size, without caseation or hyaline degeneration. Without giving any other (clinical) evidence, the author considers these tubercles as a manifestation of Boeck's sarcoid.

Peter C. Kronfeld.

12

OPTIC NERVE AND CHIASM

Angius, T. **Papilledema following a thoracoplasty.** Rassegna ital. d'ottal., 17: 342-354, Sept.-Oct., 1948.

Thoracoplasty was performed on a 24-year-old woman who developed a pulmonary tuberculosis after an acute influenzal infection. Ten days after the operation she noted severe headache, photophobia, and head sweating. Edema of the nervehead that produced a swelling of 3 D. in one eye and 2 D. in the other, retinal edema and numerous hemorrhages appeared. After a year, the fundi were entirely clear and the vision normal. The intracranial pressure was not elevated at any time. Eugene M. Blake.

Duggan, W. F. **Use of vasodilators in syphilitic atrophy of the optic nerves.** Arch. Ophth. 39:645-656, May, 1948.

All of five patients with syphilitic optic nerve atrophy improved under intensive vasodilator therapy. None became worse. The improvement corroborates Kennedy's hypothesis that in syphilis angiospasm occurs in the arterioles of the central nervous system.

Ralph W. Danielson.

Eissler, Rolf. **Atrophy of the optic nerve due to malnutrition.** Arch. Ophth. 39:465-470, April, 1948.

The literature on the relation between vitamin deficiencies and optic nerve atrophy is briefly reviewed and two cases of visual disturbances in white men who were prisoners of the Japanese are reported in considerable detail. The visual difficulties were concurrent with other symptoms of vitamin deficiency and improved with an improvement in the diet.

John C. Long.

Fuchs, A. **Malignant retrobulbar neuritis.** Arch. Ophth. 41:60-64, Jan., 1949.

In three patients loss of vision and the light reflex, binocular in two, developed in two or three days, while the fundi remained normal. Later, primary atrophy of the papilla occurred, and, in spite of energetic treatment, there was not the slightest restoration of vision. For these reasons, this condition is termed "malignant retrobulbar neuritis."

Ralph W. Danielson.

Gát, L. **Toxic papilloretinitis as a typical ocular symptom in tuberculous individuals.** Ophthalmologica 117:43-50, Jan., 1949.

Among 10 to 15 per cent of the patients at the State Tuberculosis Hospital, the author discovered a characteristic form of neuroretinitis which he ascribes to tubercle bacillus toxin. The disease is mild and heals in 6 to 8 weeks. The ophthalmoscopic finding of a neuroretinitis was confirmed by corresponding histologic findings in three patients who died of pulmonary tuberculosis during the period of ophthalmologic observation.

Peter C. Kronfeld.

Jerome, B., and Forster, H. W., Jr. **Congenital hypoplasia (partial aplasia) of the optic nerve.** Arch. Ophth. 39:669-672, May, 1948.

Two cases of bilateral congenital hypoplasia of the optic nerve in otherwise normal eyes are reported. This anomaly

is ascribed to partial failure of development of the ganglion cell layer of the retina and a consequent deficiency of neural elements in the optic nerve. It must be differentiated from atrophy.

Ralph W. Danielson.

Kurz, O. **Papillitis arteriosclerotica.** Ophthalmologica 116:281-285, Oct.-Nov., 1948.

The author describes two cases of a bilateral arteriosclerotic optic nerve disease characterized by sudden onset, papilledema of varying extent, abnormal circulatory and pulsatory phenomena in the retinal vessels, very low blood pressure in the retinal vessels (as revealed by dynamometry), marked ocular hypotony and rapid loss of vision. The outcome is bilateral optic atrophy of the primary type with atrophic excavation, narrowed and partly obliterated arteries, and amaurosis. These ocular findings are associated with severe arteriosclerotic, cardiac and cerebral changes. A few similar cases have been reported before.

Peter C. Kronfeld.

Moginier-Forel, A. **The treatment of optic neuritis with nicotinic acid.** Ophthalmologica 116:304-306, Oct.-Nov., 1948.

The author does not consider the use of nicotinic acid the classical treatment for optic neuritis, but is glad to have it for those cases in which the usual treatment fails. - Peter C. Kronfeld.

Northington, P., and Rouen, R. L. **Optic neuritis and sinusitis.** U. S. Nav. M. Bull. 49:101-103, Jan., 1949.

After recovery from the sinusitis with acute optic neuritis the visual fields, vision and optic nerve returned to normal.

Orwyn H. Ellis.

Reese, A. B. **Invasion of the optic nerve by retinoblastoma.** Arch. Ophth. 40: 553-557, Nov., 1948.

This study is based on the author's experience during the last 13 years. It is rare for the tumor to extend into the optic nerve beyond the lamina cribrosa for more than a few millimeters, and extremely rare for it to extend as far as 8 to 10 mm. The invasion begins in the cup around the central vessels. Extension into the nerve does not depend on the size of the tumor in the globe. When the tumor reaches the subarachnoid space, it spreads rapidly to the chiasm and the brain. In approximately 10 percent of the cases the tumor traversed the sclera and in 25 percent invaded the choroid where the cancer cells may enter the blood stream. On the basis of the arguments presented in this paper, there is no justification for the combined intracranial and orbital operation for retinoblastoma.

Ralph W. Danielson.

Salvi, G. L. **Retrobulbar optic neuritis from nutritional deficiency, a contribution to the war pathology of the eye.** Boll. d'ocul. 27:654-665, Oct., 1948.

Four well observed cases of retrobulbar neuritis in repatriated war prisoners confirm the etiologic role of vitamin B_1 deficiency in these patients.

K. W. Ascher.

13

NEURO-OPHTHALMOLOGY

Cogan, D. G., and Loeb, D. R. **Optokinetic response and intracranial lesions.** Arch. Neurol and Psychiat. 61:183-185, Feb., 1949.

In a series of 90 patients with cerebral disease the optokinetic response was abnormal in 58. With one exception, the optokinetic response was defective on rotation of the drum to the side of the lesion. It was the only ocularmotor abnormality in 26 patients and the only abnormality in the ocularmotor or ocular sensory system in 9 patients. Abnormality in the optokinetic response was most fre-

quent with lesions in the posterior or middle portion of the cerebrum, but was also found on occasion with lesions in the anterior portion. It was not dependent on involvement of the visual pathways. It was found associated with other signs in the following order: homonymous field defect, hemiparesis, nystagmus, deviation of eyes with closure of lids, alexia, motor aphasia and asterognosis. An abnormality in the optokinetic response is a frequent and valuable sign in the localization of cerebral disease but has no constant relation to the lateral lesions in the brain stem, cerebellum, or cerebellopontine angle. Theodore M. Shapiro.

Cohen, R., and Burnip, R. **Nevoid amentia.** Ann. West. Med. and Surg. 3: 47-49, Feb., 1949.

The author reports an interesting case of a child with a large wine-colored hemangioma over the left half of the forehead and the entire region of distribution of the ophthalmic branch of the trigeminal nerve. A bilateral temporal pallor of the optic discs and esotropia, most marked on the right, were present. X-ray studies of the skull disclosed calcification which outlined the cerebral markings on the left side. Right hemiplegia, convulsions and a speech defect were also present. Orwyn H. Ellis.

Collins, R., and Bassenge, W. L. **The participation of the eye in infantile paralysis.** Klin. Monatsbl. f. Augenh. 113: 255-260, 1948.

The authors examined 150 infantile paralysis patients during the Berlin epidemic of 1947. Eleven of the patients had a facial paresis, which was supranuclear in five of them. The prognosis of this facial palsy is relatively good. In two patients the seventh nerve was the only paresis evident in spite of typical findings in the spinal fluid. Other patients had ptosis, nine had abducens paralysis and five internal rectus paresis, some with facial palsy. Nystagmus and pupillary disturbances may be found in the cerebral cases. Papilledema and dilation of the retinal vessels is frequently found in the high-spinal and bulbar-pontine group. Four fifths of the "iron lung patients" showed these dilated vessels and half of them had edema of the papilla. The vision stays normal, the visual field is not contracted and the fundus findings regress after a few weeks. True optic neuritis was not observed, but is mentioned in the literature. Max Hirschfelder.

Crow, John. **A note on certain ocular phenomena of post-encephalitic Parkinsonism.** Glasgow M. J. 30:29-34, Jan., 1949.

In 80 cases nystagmus was usually coarse and either horizontal or vertical. Diplopia was common and was usually associated with the nystagmus. Most of the patients had difficulty in opening or closing the eyes and attacks of rapid blinking. Unilateral or bilateral exophthalmus without hyperthyroidism was occasional. Horner's syndrome was never found. Oculogyric crises were present in 85 percent. One patient turned in a circle in oculogyric crises and the caloric test induced oculogyric crises in him.

F. M. Crage.

Fanta, H. **Opticochiasmatic arachnoiditis.** Klin. Monatsbl. f. Augenh. 113: 246-255, 1948.

Two cases of arachnoiditis are described. One followed typhus and the other injury. In both there was reduction of vision and of the visual field, bilateral central scotoma, negative X-ray studies and meager neurological findings. Fever therapy which improves similar symptoms in retrobulbar neuritis did not influence the clinical picture. Headache is an important symptom. The optic nerve head may look normal or may show a

mild papilledema. Both patients improved temporarily after surgery. The literature of arachnoiditis in ophthalmology is surveyed and critically discussed.

Max Hirschfelder.

François, J. **The ocular manifestations of von Recklinghausen's disease.** Ann. d'ocul. 181:753-791, Dec., 1948.

The basic symptoms include slowly progressive, multiple bodily subcutaneous and nerve tumors and pigmented areas, café au lait spots. Degenerative diseases in the nervous, osseous, and endocrine systems are frequently associated. The nerve tumors most frequently arise from the sheath of Schwann. Centrally, the most frequently involved areas are the acoustic nerve and the pituitary gland. Von Recklinghausen's disease is essentially a constitutional hyperplasia of undifferentiated ecto- and meso-dermal cells throughout the body. These foreign cells called "phakos" by Van der Hoeve are involved in several neuro-ophthalmo-cutaneous syndromes, including those of Bourneville, Hippel-Lindau, and Sturge-Weber-Krabbe. Every part of the eye and orbit may be involved in von Recklinghausen's disease except the lens and the lacrimal apparatus. The lids, orbit, and optic nerve are most frequently affected, and the conjunctiva and sclerocornea least frequently. In the lid the chord-like feel of the nerves is of some diagnostic importance. Extirpation of the tumors is not without danger because of hemorrhage. Optic nerve tumors may take the form of meningoblastomas, gliomas, and mixed tumors. Three cases are reported. In the first case which was clinically diagnosed as a uveal melanosarcoma, a Schwannoma of the ciliary body and sclera was seen in sections. The only other clinical sign was café au lait spots. In the second case progressive exophthalmus resulted from an orbital Schwannoma and in the third a Schwannoma of the conjunctiva coexisted with large numbers of characteristic subcutaneous tumors and café au lait spots. (16 figures, 361 references.)

Chas. A. Bahn.

McKinney, J. McD., Mitchell, W., and Lisa, J. R. **Diplopia due to divergence insufficiency.** J. Nerv. and Ment. Dis. 108: 507-510, Dec., 1948.

A metastatic carcinoma at the right cerebellopontine angle caused homonymous diplopia for distance but not for near, dizziness, headache, unsteadiness of gait, and nausea. The eyegrounds, visual fields, and extraocular movements were normal. Nine months later slight papilledema was noted. Necropsy revealed a hard white mass in the meninges that caused a marked pressure deformity of the pons and a large cystic cavity in the cerebellum. There were no demonstrable lesions in the region of the sixth nerve nuclei. Although no center of divergence is known, divergence insufficiency or paralysis is associated with a lesion of the posterior fossa.   R. Grunfeld.

Morone, G. **Pupillography in glare.** Boll. d'ocul. 27:639-653, Oct., 1948.

Nine normal individuals were exposed to the light of a nonfrosted 500 Watt bulb yielding about 2820 lux at 1 meter. They had to fixate the light with one eye for 10 minutes to 1 hour while the fellow eye was bandaged. In some subjects, the eye to be exposed was covered for a preliminary period of between five and 20 days. Signs of fatigue of the iris were found both in the eye exposed to glare and in the covered fellow eye; in the latter it is explained by the consensual pupillary reaction. (9 pupillographic graphs, references.)   K. W. Ascher.

Morsier, G. de, and Balavoine, C. **Spasm of convergence.** Ophthalmologica 116: 248-253, Oct.-Nov., 1948.

Eight cases of spasm of convergence associated with other neurologic disturb-

ances are reported jointly by an ophthalmologist and a neurologist. In seven of the cases head trauma was the cause, in the eighth an acute throat infection with ear complications. Four of the patients first showed ocular palsies of supra or infranuclear type and during the more or less complete recovery from the palsies the spasm of convergence developed. In all the patients the spasm of convergence could be brought on by movements of gaze, attempted or actually performed, in one specific direction. The spasm of convergence nearly always was a spasm of the near reflex, that is, accommodation and pupil were equally involved. There were neurologic sensory and motor signs of a unilateral cerebral lesion and turning the eyes toward the side of the lesion usually elicited a spell of convergence spasm. There was vestibular hyperexcitability of the central type. The authors are inclined to explain the convergence spasm as a "substitution phenomenon," that is a motor reaction executed by a supranuclear apparatus rather than a defective intentional motor reaction. Peter C. Kronfeld.

Paufique, L., and Etienne, R. **Glioma and pseudoglioma of the chiasm.** Ophthalmologica 117:90-103, Feb., 1949.

In two of three cases of glioma of the chiasm which was suspected on the basis of clinical and roentgenologic findings the diagnosis was verified by surgical exploration. In one an autopsy revealed an astrocytoma. In the third case the findings at the surgical exploration were inconclusive. The authors assume a chronic inflammatory disease on the order of an arachnoiditis, possibly associated with an encephalitis. Peter C. Kronfeld.

14

EYEBALL, ORBIT, SINUSES

Cox, R. A. **Proptosis due to neuroblastoma of the adrenal cortex** (Hutchinson's syndrome). Arch. Ophth. 39:731-738, June, 1948.

Neuroblastoma of the adrenal gland with its subsequent metastases occurs almost entirely in children. It is of great interest to ophthalmologists because of its metastasis to the orbit, with resultant proptosis, discoloration of the lids and loss of vision. The orbit is invariably involved in the metastases, and frequently it is the eye which gives the first noticeable indication of the disease. The condition is highly malignant, and death usually occurs within three months after appearance of the first sign. A case of neuroblastoma is reported with autopsy findings in a 15-months-old-boy.

John C. Long.

DeVoe, A. G. **Fractures of the orbital floor.** Arch. Ophth. 39:595-622, May, 1948.

Lukens, reviewing the literature forty years ago, found 78 cases of traumatic enophthalmos and some nineteen hypotheses to explain its mechanism. It is now felt by most observers that of the factors enumerated only the direct and indirect fractures of the orbital wall are significant. Observation of 34 cases of fracture of the orbital floor suggest that the immediate care of such fractures will rarely be an ophthalmologic problem because of the multiplicity of accompanying injuries, often of a vital nature. A review of the literature reveals the measures most frequently used in immediate treatment. When weeks or months have elapsed the ophthalmologist is the one best fitted to carry out reparative work. Such repair may take the form of operation on the extraocular muscles or may require substitution of inert material in the orbital floor in order to restore orbital volume or to elevate the globe. In anophthalmos the appearance can often be improved by restoration of the orbital floor.

Ralph W. Danielson.

Neudörfer, A. **A rare case of injury to the orbit.** Wien. Klin. Wchnschr. 61:76, Feb. 4, 1949.

Splinters of wood, which for over three years had caused a profusely discharging fistula of the right eye and whose removal had previously been attempted unsuccessfully at four different operations, were finally located and removed through a Krönlein orbitotomy. This operation had to be performed twice as only one piece of wood was taken at the first operation and a second fistula with one layer of many small splinters remained. There was no injury to the eyeball, muscles or nerves.   B. T. Haessler.

Rupprecht, Hermann. **Albucid treatment of cellulitis of the orbit.** Klin. Monatsbl. f. Augenh. 110:310-313, May-June, 1944.

Three patients with cellulitis of the orbit were given Albucid intravenously or intramuscularly. Prompt improvement and complete recovery followed in two patients; in the third abscess formation made an incision through the upper lid necessary. This patient too recovered, but was left with ptosis.   George Brown.

15

EYELIDS, LACRIMAL APPARATUS

Cassady, J. V. **Dacryocystitis of infancy.** Arch. Ophth. 39:491-507, April, 1948.

The author reviews 100 cases of dacryocystitis in infancy and reviews the literature in detail. He advocates probing of the nasolacrimal duct and irrigation of the sac and duct. Prolonged conservative treatment is a nuisance to both parents and the child, and is likely to result in permanent injury to the lacrimal passages. He works without anesthesia and uses a lacrimal cannula attached to a syringe instead of a probe.
                    John C. Long.

Firestone, Charles. **Prevention and relief of stenosis of lacrimal duct.** Northwest Med. 48:111-112, Feb., 1949.

Early repair in post-traumatic epiphora is important for good function and a good cosmetic result. The author describes in detail a method which is always effective. A no. 3 lacrimal probe is inserted into the punctum, is pushed out through the duct opening of the duct on the lacerated surface of the lid, and then through the nasal portion of the duct into the sac. It is held in place by adhesive strips and is removed after seven days.
                    H. C. Weinberg.

Clarkson, Patrick. **Eyebrow repairs by thin deep grafts.** Guy's Hosp. Gaz. 67: 256-258, Sept. 25, 1948.

Three methods are suggested. 1. A graft is cut from the temporal scalp. It is thin and takes evenly. 2. An area of upper temporal scalp is cut to eyebrow shape and size and the artery which enters its lower pole is dissected down to the ear, leaving a graft attached to a long arterial pedicle. A skin defect is established in the position of the missing eyebrow and the graft is tunneled into this position and sutured into place. 3. The use of a flap of hair-bearing scalp carried on a temporal or other pedicle. The pedicle is later returned leaving a flap of hair-bearing skin in the eyebrow region. A full thickness skin graft does not have to be rendered entirely free from subcutaneous fat to take well. Details of the technique of a thin deep free graft of hair-bearing scalp from the temporal area are presented.
                    Alston Callahan.

Fox, S. A. **Crescentic deformities of the lid margin.** Arch. Ophth. 39:542-544, April, 1948.

A surgical method for the repair of crescentic deformities of the upper lid margin is presented. The involved portion of the lid, and the adjacent area of

the other lid are split. The tarsoconjunctival layers of both lids are then sutured together and a full thickness skin graft with hair from the region of the brow is sutured into the defect. The brow hair take the place of cilia. After a month the lids are separated.   John C. Long.

Kettesy, A. **Entropion in infancy caused by folding of the tarsus.** Arch. Ophth. 39:640-642, May, 1948.

A case is reported.
          Ralph W. Danielson.

La Rocca, Vito. **Implant of "Vitallium" tube in treatment of stenosis of the lacrimal duct.** Arch. Ophth. 39:657-660, May, 1948.

The use of an implant is simpler and more effective than dacryocystorhinostomy. The technique is described.
          Ralph W. Danielson.

Mildenberger. **Dacryoadenitis after dysentery.** Klin. Monatsbl. f. Augenh. 113:268, 1948.

The author observed three cases of dacryoadenitis caused by dysentery. The course was favorable.
          Max Hirschfelder.

Murphey, P. J., Newton, F. H., Stell, C., and Hawk, P. P. **Esthetic correction of unilateral anophthalmos by ophthalmoprosthesis.** Arch. Ophth. 40:497-508, Nov., 1948.

From the results obtained in the esthetic correction of anophthalmos by the ophthalmoprosthetic technique in the cases reported, it is evident that growth of the cul-de-sac and the orbital area of the face may be stimulated, in a manner similar to the growth of muscle and bone associated with facial changes produced by orthodontic correction. Infants and children do not seem to experience any pain or discomfort during the period of

construction and wear the prosthesis without being aware of its presence in the orbital socket.   Ralph W. Danielson.

Papolczy, F. **Purulent inflammation of the lacrimal canal caused by an accumulation of stony concretions.** Klin. Monastbl. f. Augenh. 113:269-271, 1948.

After an unsuccessful tear sac extirpation purulent discharge persisted and was caused by ten stony concretions in the lacrimal canal, which had been overlooked. Single lacrimal stones are rare and multiple ones have not been described. Stones appear only in the lacrimal canal, never in the tear sac itself.
          Max Hirschfelder.

Rössler, F. **A suture for entropion.** Klin. Monatsbl. f. Augenh. 110:377-380, May-June, 1944.

Both needles of a double-armed suture with a glass head are inserted half way between the lid margin and lower orbital margin and between middle and temporal third of the lid, parallel to the lid margin and behind the orbicularis and brought out at the temporal orbital margin. Here the suture is tied over another glass bead. The suture is removed after eight days. Originally the operation was used for temporary relief, but the lid remained in good position even after removal of the suture.   George Brown.

Schindler, Rudolf. **Treatment of essential blepharospasm.** Klin. Monatsbl. f. Augenh. 110:380-383, May-June, 1944.

The patients are asked to close their eyes as tightly as possible while looking down. After 2 to 2½ minutes the muscle is exhausted and the patients readily open their eyes and keep them open for some time. Such exercises are applicable only in cases of psychoneurotic blepharospasm.   George Brown.

Sená, J., and Cerboni, F. **Hereditary and familial xanthomatosis.** Arch. de oft. de Buenos Aires 23:79-89, June, 1948.

There are various forms of xanthalasma: simple, as of the lids, multiple or eruptive tuberous, congenital or tumor-forming, and secondary. The first of these is the best known and occurs bilaterally, chiefly in women. This paper is concerned with the second, tuberous, form. Yellowish masses of varying size occur on the lids and in other parts of the body as well, and the disease is not limited to any age or sex. The authors analyse the hypercholesterinemia, which they consider the fundamental pathologic process of this disease, and describe its fate in the body. A detailed case report with photographs of the gross and microscopic lesions is given.   A. G. Wilde.

Spaeth, E. B., and Cappriotti, O. A. **Heteroplastic and isoplastic skin grafts.** Plast. and Reconstruct. Surg. 3:707-712, Nov., 1948.

Comments are made on heteroplastic and isoplastic grafts, and brief summaries are given of the few articles published on ectropion and its repair in ichthyosis congenita. In a fifteen-year-old boy with ichthyosis congenita ectropion began to develop at the age of eight. The condition has gradually become more severe and recently a corneal ulcer developed. Intermarginal lid adhesions were made, the lid defects prepared, and thromboplastic shellac was applied to the raw surfaces. Very thin free skin grafts from the thigh of a donor whose blood matched the patient's as to type, Rh, M and N factors were fitted into the defect. After a year the author reports successful takes. (4 figures.)   Alston Callahan.

Theodore, F. H. **"Silent" dacryocystitis.** Arch. Ophth. 40:157-162, Aug., 1948.

A mild type of dacryocystitis, usually mucoid, is often the cause of persistent conjunctivitis or tearing. This "silent" type of dacryocystitis is overlooked if investigation of the tear passages is limited only to a determination of patency. If the lacrimal washings are collected, the finding of mucus or frank pus containing pathogenic organisms will indicate the presence of "silent" dacryocystitis. Treatment, consisting largely of irrigations, results in cure of the dacryocystitis and conjunctivitis. This low grade mucous dacryocystitis may eventually lead to more obvious inflammatory changes in the lacrical passages.   John C. Long.

Toselli, C. **Elongation of the lacrimal canaliculi.** Rassegna ital. d'ottal. 17:334-341, Sept.-Oct, 1948.

Toselli reviews the literature and describes two cases of elongation of the inferior lacrimal canaliculi. In one the lids seemed stuck together at the inner angle so that they were reduced in length and height. Ptosis resulted. The border of the upper lid was normal, the lower showed a bowing, the cilia were normal and the lower canaliculus was definitely elongated. The second patient suffered from epiphora, had bilateral ptosis, epicanthus, paresis of the superior rectus of the left eye and a rudimentary caruncle. The lower canaliculus was twice the length of the upper. Eugene M. Blake.

16

TUMORS

Bettman, J. W. **Treatment of malignant tumors of the retina.** Stanford Med. Bull. 6:437-443, Nov., 1948.

In about one of three cases of malignant tumor of the retina the lesion was unilateral. The average age of patients in this series in whom unilateral tumor was discovered was 3½ years, of those with bilateral lesion it was 1½ years and the prognosis is better in the former. Thorough ophthalmoscopic examination, with

a dilated pupil and under general anaesthesia, is most important in the first examination and in the monthly examinations of the sound eye.

When the lesion is unilateral immediate enucleation is definitely indicated and as large a piece of the optic nerve as is possible should be removed. The tumor is usually in an advanced stage. If a frozen section reveals neoplasm in the nerve, a radium implant is inserted but if the tumor has spread more than a few millimeters radiation is of doubtful value. If there is tumor in both eyes but only one quadrant or less and not the choroid is affected, in one eye, this eye is irradiated and the other eye is enucleated. If more is involved both bulbs are enucleated.

F. M. Crage.

Carpentdale, M. T. F. **Lymphosarcoma presenting as edema of the eyelids.** Lancet 1:305-306, Feb. 19, 1949.

Primary lymphosarcoma of the skin is very rare, although secondary lesions are not uncommon. A married woman, aged 61 years, was admitted to the hospital with a swelling about the left eye which was first noticed two weeks before and was slowly enlarging. Necropsy after ten weeks showed hemorrhage from ulcerated secondary growth in the stomach, and generalized lymphosarcoma. At first this patient was thought to have a recurrent facial cellulitis or periorbital cellulitis secondary to ethmoiditis. Other possible diagnoses were erysipelatoid and angioneurotic edema. A study of a biopsy specimen taken from indurated skin on the lateral margin of the left orbit suggested lymphosarcoma.

Theodore M. Shapira.

Dunnington, J. H. **Granular cell myoblastoma of the orbit.** Arch. Ophth. 40:14-22, July, 1948.

The histogenesis of myoblastoma, a type of tumor variously designated as myoblastic myoma, myoblastoma, rhabdomyoma and granular cell myoblastoma, is much discussed in the literature. It is believed by some to be a true neoplasm of immature, proliferating skeletal muscle cells (myoblasts) and by others to be a degenerative lesion. The author concludes that granular cell myoblastoma is a relatively common tumor and widely distributed throughout the body. Its occurrence in the orbit is rare and two cases are reported. The tumors presented no characteristic clinical picture, and the differential diagnosis was purely histologic. One was malignant although the tumor is more commonly benign.

Ralph W. Danielson.

Grom, E. **Modified epithelioma of the lacrimal gland.** Arch. d'opht. 8:593-610, 1948.

Grom reports four cases of epithelioma of the lacrimal gland, three in men of 21, 29, and 32 years, and one in a woman of 32 years. He reviews the subject of lacrimal gland tumors, with particular reference to the so-called mixed tumor, and points out that histologically the gland is similar to the salivary glands and may be simultaneously involved. Clinically these tumors are of varying malignancy; some evolve slowly over many years while others are rapidly invasive and penetrate the nasal sinuses and the brain. Metastases are rare. In all cases the epithelium is the principal tissue involved. It is disposed in canalicular-acinous, acino-canalicular, or atypical formation. Parenchymatous changes are generally fibrous but myxomatous plaques are common. The author suggests that the name "épithélioma remanié," or "modified epithelioma," is to be preferred for this type of tumor.   P. Thygeson.

Jorio, S. **Congenital epibulbar tumors.** Rassegna ital. d'ottal. 17:289-303, Sept.-Oct., 1948.

Two cases of bilateral dermoids are reported: In the first case the father of the patient, a five-year-old boy, had congenital ptosis of the right upper lid and a mass on the temporal side of each globe which resembled a dermoid. The dermoids on the boy's eyes were very extensive and were removed surgically. The other patient, a 19-year-old boy had bilateral dermoids, pre-auricular malformations, irregular dentition, facial asymmetry, underdevelopment of the mandible, deafness, mental retardation and a coloboma of the upper lip. The pathology of dermoids is discussed. (8 figures.)

Eugene M. Blake.

Posner, M., and Horrax, G. **Tumors of the optic nerve.** Arch. Ophth. 40:56-76, July, 1948.

Failure of vision in one eye combined with some degree of exophthalmos, together with a normal visual field and visual acuity in the other eye in a patient with no other evidence of an intracranial lesion, strongly suggests the diagnosis of a tumor of the optic nerve within the skull. Three cases of intracranial tumor of the optic nerve with survival from four and one-half to twelve years are reported. The prognosis is not as consistently poor as is generally believed.

Ralph W. Danielson.

Stansbury, F. C. **Lymphosarcoma of the eyelid.** Arch. Ophth. 40:518-530, Nov., 1948.

The literature is reviewed, lymphosarcoma is discussed, and a case is reported, not because it represents a rare tumor, but for its unusual features. The lesion was considered an atypical, low grade inflammatory process by all who examined the patient, and the disease progressed rapidly to a fatal termination in forty days. The neoplasm in this case is unique because of the meager amount of involvement of the lymph nodes and the rapid,

destructive spread to all the viscera and other tissues of the body. Less than one percent of all lymphosarcomas originate in the region of the eye.

Ralph W. Danielson.

17
INJURIES

Burch, E. P. **Treatment of common eye injuries.** Northwest Med. 48:104-107, Feb., 1949.

A careful history is essential for diagnostic, therapeutic, and medicolegal considerations. Examination of the deeper structures is important irrespective of how trivial an eye injury may appear externally. Local anesthesia is important in obtaining coöperation during the examination but cocaine is avoided. Tetanus antitoxin should be used cautiously. For deep wounds of the eye the author advises penicillin (300,000 units) immediately, and the next day a typhoid-paratyphoid vaccine (15 to 25 million) intravenously. The penicillin and typhoid are given alternately at least three to five times and sulfonamides are often given concurrently. Removal of all hopelessly blind, damaged eyes is suggested because of the danger of sympathetic disease. Wounds of the sclera and cornea and methods for their repair are reviewed. The complicating cataract, glaucoma and iritis and their therapy are discussed. Irrigation with a solution of 10-percent neutral ammonium tartrate is suggested for lime burns after all lime particles have been removed with an applicator impregnated with vaseline.

H. C. Weinberg.

Boshoff, P. H., and Jokl, E. **Boxing injuries of the eyes.** Arch. Ophth. 39:643-644, May, 1948.

Ten cases of ocular injury due to blows incurred in boxing are recorded. There were hemorrhages, cyclodialysis, retinal tears, retinal detachment and kerato-

conus. Boxers deliberately try to produce head injuries.   Ralph W. Danielson.

Clothier, W. L. **Treatment of extra-ocular foreign bodies.** Northwest Med. 48: 107-109, Feb., 1949.

Foreign bodies under the upper lid produce more pain than do the uncomplicated foreign bodies of the cornea. Severe corneal damage may occur when an untrained person attempts to remove what is really a pigmented mole of the iris. It is important to examine the puncta, lid margins, superior retrotarsal fold and upper and lower lids as well as the cornea in looking for foreign bodies. Adequate anaesthesia should be used. The use of a sharply pointed instrument is preferred to the spud and burr. In the removal of iron rust particles it is noteworthy that overzealous removal of stained tissue in the central corneal area often reduces vision more than if a small stained area had been left alone. It is important that vision be recorded before treatment is begun and when the patient is discharged. (1 table.)
H. C. Weinberg.

Stuart, Jean. **Clostridium welchii infection of the eye.** Brit. M. J. p. 272, Feb. 12, 1949.

Although the patient received 300,000 units of penicillin every three hours after an unsuccessful attempt to remove a piece of intraocular steel, the eye became septic and proptosed and had to be enucleated. During the operation gas and blood-stained pus escaped freely. From the pus a pure growth of Clostridium welchii was obtained. Penicillin fails to diffuse into the vitreous in appreciable quantity.
F. Grunfeld.

18
SYSTEMIC DISEASE AND PARASITES

Appelmans, M., and van Vooren, H. **The eye manifestations of myasthenia gravis.** Ophthalmologica 117:8-18, Jan., 1949.

In a girl, 8 years of age, with myasthenia gravis the mimic musculature of the face and the extraocular muscles were predominantly involved.
Peter C. Kronfeld.

Bruce, G. M. **Changes in the ocular fundus associated with pheochromocytoma of the adrenal gland.** Arch. Ophth. 39:707-730, June, 1948.

Pheochromocytomas are tumors growing from cells of the so-called chromaffin system. The dominant finding in cases of this tumor is vascular hypertension, in the course of which pathologic changes may be found in the retina or in its blood vessels or both. The findings cannot be differentiated ophthalmoscopically from those encountered in hypertensive vascular disease. Treatment consists of the surgical removal of the tumor. Three cases in children, all with pathologic changes in the retina, are reported.
John C. Long.

Cross, A. G. **Ocular disturbances associated with malnutrition.** Tr. Ophth. Soc. U. Kingdom 66:102-104, 1946.

No gross impairment of night vision was demonstrable with a Livingston rotating hexagon in 119 prisoners liberated from camps in Siam of whom 17 had nutritional amblyopia. They were always hungry and most of them had had malaria, dysentery, pellagra and beriberi. Burning of the feet often preceded the blurred vision which could be relieved by nicotinic acid, but the diet evidently contained sufficient vitamin A to maintain normal night vision.
Beulah Cushman.

Esente, I. **Further ophthalmologic observations upon tuberculous meningitis treated by the Cocchi method.** Rassegna ital. d'ottal. 17:318-333, Sept.-Oct., 1948.

Cocchi's treatment of miliary tuberculosis and tuberculous meningitis consists of the use of streptomycin, sulfone and vitamins A and D2. Esente reports upon the lesions and treatment in 150 cases and reports 85 percent greatly improved. He discusses the ocular involvement under five headings: 1. symptoms of ordinary functional disturbances, such as photophobia, ocular hyperesthesia and amaurosis; 2. symptoms of the extrinsic ocular muscles, paralysis, contracture, and nystagmus; 3. the intrinsic muscles and pupillary changes; 4. orbital affections and exophthalmos; and 5. ophthalmoscopic changes. Miliary tuberculosis of the choroid, disturbances of intrinsic and extrinsic muscles and early stages of tuberculous meningitis are benefited by streptomycin therapy.

Eugene M. Blake.

Fraser, J. D. **Ocular disturbances associated with malnutrition.** Tr. Ophth. Soc. U. Kingdom 66:96-98, 1946.

The author, a prisoner in the internment camp of Hong Kong, states that the diet was rich in carbohydrates and deficient in fats, proteins, salts and vitamins. It was associated with a syndrome characterized by edema, neuritic symptoms, a syndrome of subacute combined degeneration of the cord, mental disturbances, skin lesions, variations in blood pressure, prolonged diarrhea, dysentery, chronic malaria and diphtheria. Of 246 patients with visual complaints the cornea was involved in 119, corneal dystrophy was present in 64, retrobulbar neuritis in 43, retinitis in 2, and a central retinochoroiditis in 4. Chronic retrobulbar neuritis with partial optic nerve atrophy was noted in 174 patients. Beulah Cushman.

Grammatico, A. D. **Pneumothorax and intraocular tension.** Arch. de oft. de Buenos Aires 23:90-91, April-June, 1948.

Pneumothorax can bring about hypertrophy of the right ventricle. No coincident change in ocular tension immediately after the introduction of the air, or several hours later, could be demonstrated. A. G. Wilde.

Haynes, H. A., Jr., and Parry, T. L. **Alopecia areata associated with refractive errors.** Arch. Dermat. and Syph. 59:340-342, March, 1949.

In 61 patients with alopecia areata there was a rapid regrowth of hair in three months after the continuous wearing of glasses and no recurrence as long as the error was adequately corrected. The predominant error was a small astigmatism at an oblique axis. F. H. Haessler.

Hobbs, H. E. **Ocular disturbances associated with malnutrition.** Tr. Ophth. Soc. U. Kingdom 66:116-122, 1946.

The author discusses the data on 200 men with reduced visual acuity associated with central scotoma. Temporal pallor was common; a few patients had general pallor of the disc and attenuated blood vessels, a few had some pigmentary disturbance between the fovea and the optic disc and in eight there was macular damage. Visual fields were constricted in only those most severely affected. All were debilitated and many had suffered from several of the diseases endemic in prison camps, malaria, beriberi, famine edema, pellegra, and dysentery, and 37 had lesions of the nervous system. No clear relationship to a single disease was apparent but marked improvement occurred when animal protein was added to the diet. Beulah Cushman.

Livingston, P. C. **Ocular disturbances associated with malnutrition.** Tr. Ophth. Soc. U. Kingdom 66:19-44, 1946.

The author reviews the effect of starvation on the eyes of 3,000 Royal Air Force personnel repatriated from Japanese

prison camps after 2½ years. Defects of central vision with scotoma were found in 200. Peripheral contractions were recorded and a loss of perception established at rod level. In some patients the corneoscleral border zone was invaded by vascular loops. Grave corneal lesions were not found and the vitreous appeared normal. Degenerative changes of the retina could be seen in the macula. There were fine discrete white spots and pigmentary disturbances and the most common finding was the loss of the foveal reflex. It was often impossible to find the macula and between the macula and disc a glistening silver-gray sheet could be seen. Temporal pallor of the disc was very common and in some there was complete atrophy. There was often a wide discrepancy between the visual acuity and the appearance of the disc and the macula. Results of treatment were often better than expected.   Beulah Cushman.

Lockwood, J. H. Reiter's disease, Behcet's syndrome and Stevens-Johnson disease; a study and comparison. U. S. Nav. M. Bull. 49:41-49, Jan., 1949.

The author completely reviews the literature and the manifestations of each of these conditions of obscure etiology in turn and compares their symptoms.
                                Orwyn H. Ellis.

Lyle, T. K. Malnutritional amblyopia. Post Grad. M. J. 24:649-655, Dec., 1948.

Malnutritional amblyopia which occurred in prisoners of war in the far east is a different entity than retrobulbar neuritis. Predisposing factors are excessive manual labor and intercurrent disease. The lesion is probably a disease of the macular capillaries, bilateral, and of gradual onset. The 5° to 10° central scotoma is not dense and has sloping edges and may disappear with early treatment. The fundus may be normal, in the early stages, or have dilated veins and some

edema. In later stages, the disc may be normal or slightly pale.
                                Irwin E. Gaynon.

Philps, A. S. Ocular disturbances associated with malnutrition. Tr. Ophth. Soc. U. Kingdom 66:99-102, 1946.

The author reports on three patients with atrophy of the optic nerve after returning from the internement camps. All had beriberi, malaria, or dysentery. The smoking of the crude strong local tobacco was thought to have some influence, as the amblyopia was indistinguishable from that due to tobacco.
                                Beulah Cushman.

Ridley, Harold. Ocular disturbances associated with malnutrition. Tr. Ophth. Soc. U. Kingdom. 46:45-70, 1946.

The author reports on the eye findings of several hundred persons in Rangoon and Singapore who had been imprisoned by the Japanese in Siam, Malaya and N.E.I. and who had suffered varying degrees of starvation for three and a half years. Most men lost much weight, and some reached an extreme degree of emaciation. Nutritional diseases due to deficiency of vitamin B were common. There was less evidence of lack of vitamins A, C, and D. There were many manifestations of dry and wet beriberi. One percent of the men had impairment of vision of two to three years duration. None complained of hemeralopia. About one half of those with amblyopia had beriberi. The visual failure was accompanied by nerve deafness in many cases and in some by ataxia. No amblyopia was found among the relatively few women that were seen though their food had been little better than that of the men. Deficiency of accommodation was almost universal among released prisoners.
                                Beulah Cushman.

Shapland, C. D. Ocular disturbances as-

sociated with malnutrition. Tr. Ophth. Soc. U. Kingdom 66:77-95, 1946.

The author describes the ocular manifestations found among the prisoners of war in Singapore from 1942 to 1945. Among 975 patients 777 had refractive errors and no organic disease, 104 had had retrobulbar neuritis, 45 had a history of visual disturbances during captivity and now had temporal pallor of the discs, normal vision and no scotoma, and 49 had other ophthalmic diseases.

Beulah Cushman.

Smith, D. A. **Ocular disturbances associated with malnutrition.** Tr. Ophth. Soc. U. Kingdom 66:111-116, 1946.

The author discusses amblyopia in the inmates of a civilian camp in Hong Kong from 1942 to 1945 in relation to intake of the main nutrients, to incidence of other nutritional diseases, and to certain other extrinsic factors. There were 1,300 men, 900 women and 300 children under 16 years of age. Loss of body weight was about 26 percent. No extrinsic toxic or infective factor was found common to all, except nutritional deficiency. Thirty patients developed amblyopia who were at the time under treatment with daily injections of synthetic vitamin B, for beriberi. The provision of foods rich in B complex, soya beans, rice polishings and camp brewed yeast prevented progressive deterioration. An amino-acid may have been the missing factor.

Beulah Cushman.

Stannuss, Hugh S. **Ocular disturbances associated with malnutrition.** Tr. Ophth. Soc. U. Kingdom 66:123-126, 1946.

Many years ago the author correlated the ophthalmologic syndrome that is part of beriberi and pellagra and recent studies have made no change. It is an optic neuropathy which belongs to the group of deficiency syndromes and it may be due to

dysfunction of the capillaries supplying the neurophyl of the lateral geniculate body.

Beulah Cushman.

Streiff, E. B. **The ocular symptomatology of the posterior cervical syndrome.** Ophthalmologica 116:292-297, Oct.-Nov., 1948.

The syndrome of Barré-Baertschli comprises a number of ill-defined forms of ocular discomfort and asthenopia caused by a chronic arthritis in the region of the third to fifth cervical vertebra.

Peter C. Kronfeld.

19
CONGENITAL DEFORMITIES, HEREDITY

Dekking, H. M. **Toxoplasmosis as a cause of congenital defects.** Ophthalmologica 117:1-7, Jan., 1949.

The clinical and histologic eye findings in an infant with toxoplasmosis are reported in detail. One eye had a pseudocoloboma of the macula, the other a lesion like the congenital falciform detachment of the retina. The clinical diagnosis of toxoplasmosis was based on a positive neutralization test of the infant's blood and on the presence of multiple typical foci of calcification in the brain. Histologic examination of the brain revealed typical foci of toxoplasmosis containing the parasite. Toxoplasmosis may also cause microphthalmos, congenital cataract, and congenital total retinal detachment.

Peter C. Kronfeld.

Lloyd, R. I. **Clinical course of ocular complications of arachnodactyly.** Arch. Ophth. 40:558-569, Nov., 1948.

Observations on 21 patients over periods of 5 to 14 years and on 25 others for shorter periods have convinced the author that arachnodactyly is not always a nonprogressive, congenital defect but often a true abiotrophy. The disease is inherited as a dominant in many families and as a

recessive in others. A parent with normal eyes and some of the skeletal defects may transmit the disease in complete form. In eyes with good vision the course is uneventful and not progressive but the prognosis is poor when vision is not good because of associated progressive changes in the uvea and the tendency to complete dislocation of the lens and retinal detachment. Six case reports are given.

Ralph W. Danielson.

Rehsteiner, K. Another Swiss family with hereditary retinitis pigmentosa. Ophthalmologica 117:51-59, Jan., 1949.

Rehsteiner reports the pedigree of 70 members in four generations of a Swiss family of whom 16 had retinitis pigmentosa, 33 had normal eyes and 21 could not be examined. The transmission definitely followed the dominant mode. Visible fundus changes were present before any loss of function could be demonstrated.

Peter C. Kronfeld.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Aragañaraz, Raúl. Impressions on an educational voyage through the United States, Canada and England. Arch. de oft. de Buenos Aires 23:71-78, April-June, 1948.

The author observed the ophthalmologic facilities of the United States, Canada and Great Britain for four months. He contrasts the combined theoretical and clinical teaching in the United States, where student enrollment is limited to the available facilities, with conditions in Argentine where instruction is theoretic, the number of students unlimited and one professor may be required to teach five hundred simultaneously. The great cost of American medical education is surprising. In London the work of Dallos interested him especially. He is

perfecting a contact lens which is used without fluid. Small openings in the glass allow the intervening space to become filled with tears.

A. G. Wilde.

Ballantyne, A. J. Johannes Evangelista Purkinje. Tr. Ophth. Soc. U. Kingdom 66:503-543, 1946.

Only one or two copies of the collected works of Purkinje, which embody his contributions to clinical ophthalmology, are available. There is a photostatic copy in the Surgeon General's Library in Washington. Purkinje, born in Bohemia in 1787, is a physiologist of the senses who stands at the turning point between Goethe's age of poetry and the Platonic contemplation of nature, and the purely scientific Aristotelian era of Johannes Müller. He was professor of physiology in Breslau but it was in his own house under most unfavorable circumstances that Purkinje laid the foundation of modern physiology. He became the principal of the first physiological laboratory in 1839, and, oddly, after this time he published no discovery of first rate importance.

He was a pioneer in the description of most of the subjective visual figures, notably those obtained by galvanic stimulation, recurrent images, entoptic appearances from the shadows of retinal vessel, the dependence of brightness of color upon intensity of light, the choroidal figure, the rosettes of light produced by use of digitalis, and the peculiar radiation following the instillation of belladonna. In clinical medicine, Purkinje was the first to study the vertigo and rolling of the eyes produced by rotating the erect body in the vertical axis. He described an optometer, explained the diffraction of light from a bright object, described the manner in which the field of vision may be measured, used the blind spot to determine the place of entrance of the optic nerve, and explained how the radius of

curvature of the cornea and sclera and the prominence of the eyeballs may be measured. He described the Purkinje's images formed by the anterior and posterior surface of the cornea and the anterior and posterior surfaces of the lens. He described the transparency of the cornea and drew attention to the arcus senilis. He noted the blueness of the sclera in infants, and pointed out that change in the transparency of the aqueous or vitreous could be determined by oblique illumination. He described in detail the iris, the reactions of the pupil, and the response of the latter to belladonna and hyoscyamus.

Beulah Cushman.

Burian, H. M. **The history of the Dartmouth Eye Institute.** Arch. Ophth. 40: 163-175, Aug., 1948.

The origin of what in 1937 became the Dartmouth Eye Institute dates back to 1919, when Ames and Proctor began their research on the optical properties of the eye. The author describes the various policies and factors that ultimately resulted in the closing of the Institute. In the short span of its existence, the Dartmouth Eye Institute has made lasting contributions to the study of visual physiology. A complete bibliography of the papers published by the members of the Institute is appended.   John C. Long.

Fralick, F. B. **Emergency eye care in general practice.** J. Michigan St. M. Soc. 47:1365-1369, Dec., 1948.

The author describes the best treatment for some of the most common ocular emergencies. Removal of a foreign body from the cornea is recommended and describes in detail. Contusions with subluxation of the lens or hemorrhage are discussed and the possibility of glaucoma and corneal staining causing a loss of vision are emphasized. In the treatment

of lacerations of the lids the importance of obtaining smooth union of the lid border is emphasized. Lacerations of the lateral or medial canthi should be sutured with heavy chromic catgut (4-0) in order to prevent epiphora and to avoid additional plastic surgery. Chemical burns of the eye should be copiously irrigated with water whether due to alkali or acid. (2 figures.)

Herman C. Weinberg.

Imus, H. A. **Testing vision in industry.** Tr. Am. Acad. Ophth. pp. 261-273, Jan.-Feb., 1949.

The relative merits of the ortho-rater, sight-screener, telebinocular and clinical tests are compared in a series of industrial patients. In most of the tests, the ortho-rater was somewhat superior.

Chas. A. Bahn.

Kuhn, H. S. **An eye physician reports on the Ninth International Congress of Industrial Medicine, London, England, September 13-17, 1948.** Indust. Med. 18: 33-36, Jan., 1949.

In the "National Health Service" the ophthalmologist gets $800 a year for 46 weekly three-hour sessions at a hospital clinic. The maximum allowance is eight sessions a week if he can get them, the average is two. For 60 refractions a week he gets 100 pounds, is allowed to work 46 weeks a year and can earn $18,400 very easily.

This unusually lucrative position has been brought about mainly by the opticians who fought hard to refuse to concede important parts of the program desired by the government.

Surgical fees were not investigated. Hospitals shortages are very great, there is a backlog of six to seven month's surgery, those who can afford to, push themselves ahead and this results in delayed service for the poor.

The author has unlimited praise for

English cordiality, and she experienced no antagonism to Americans.

F. M. Crage.

Matthews, J. L. **Use of absorptive lenses: facts for the profession.** Tr. Am. Acad. Ophth. pp. 274-277, Jan.-Feb., 1949.

The retina is protected from abiotic radiation in the normal eye. Ordinarily, individuals exposed to sunlight in sports require no ultra-violet filter glasses. In industry, specific filters are recommended by the Government. Except by prolonged contact as in glass blowers the moist surface of the cornea reasonably protects the eye from infrared radiation. The normal eye under ordinary conditions has no need for mildly tinted lenses. Tinted glasses worn habitually lessen the wearer's tolerance to glare. Green glasses aggravate the defects of protanomalous persons. In industry lay safety men should be carefully instructed in the fundamentals of light filtering lenses. Chas. A. Bahn.

Verhoeff, F. H. **American ophthalmology during the past century.** Arch. Ophth. 39:451-464, April, 1948.

This historical article deals with the development of the specialty in the United States. Not one ophthalmological contribution of major importance has originated in the United States but American ophthalmologists have made many contributions of minor importance and a few of considerable importance.

John C. Long.

Vila Ortiz, J. M., and Granados, E. **Legal aspects of obstructions of the central retinal artery.** Arch. de oft. de Buenos Aires 23:94-100, April-July, 1948.

A study of the relation between degrees of exertion and general arterial tension, pressure in the central artery of the retina, and ocular tension can give results of practical value. An obstruction in any vessel may have been brought on by exertion which caused occlusion of the disturbed circulation by an unknown mechanism. A. G. Wilde.

Zobel, W. A. **Initial results of eye testing program.** Tr. Am. Acad. Ophth. pp. 277-279, Jan.-Feb., 1949.

In a visual and safety study involving 14 ordnance plant group jobs, the percentage of injury is compared in workmen with adequate and inadequate vision. A difference of 20 percent was found.

Chas. A. Bahn.

PAN-AMERICAN NOTES

ARGENTINA

THE IV ARGENTINIAN CONGRESS OF OPHTHAL-MOLOGY

This meeting, held in Mar del Plata, December 13 to 18, 1948, was a great success and was attended by ophthalmologists from all parts of the Western Hemisphere. The official subjects were "Ocular blastomas" and "The surgical treatment of strabismus." The former subject was divided into 14 parts and Dr. Algernon Reese of New York was invited to give the section on "Treatment of bilateral blastomas with X rays." Dr. Jorge Malbran presented the second official subject. Dr. Magin A. Diaz and Dr. Joaquin A. Caretti read a paper on "The prevention of blindness in the quinquenal plan of the secretariat of public health."

Courses were given during the meeting by the following ophthalmologists: Dr. Moacyr E. Alvaro, Dr. Raul Argañaraz, Dr. Archimedes Busacca, Dr. Ramón Castroviejo, Dr. Federico C. Cerboni, Dr. Baudilio Courtis, Dr. Carlos Garbino, Dr. Alfredo D. Grammático, Dr. Gunther von Grolman, Dr. Waldemar Niemeyer, Dr. Justo Lijó Pavia, Dr. Robert Pereira, Dr. Paulina Satanowsky de Neumann, and Dr. José A. Sená.

SOCIEDAD DE OFTALMOLOGIA DE CORDOBA

Newly elected officers of this society elected to serve during 1949 are: President, Dr. Roberto Obregón Oliva; secretary, Dr. Alberto Urrets Zavalia (hijo); treasurer; Dr. Roque A. Maffrand; 1st elder, Dr. Rodolof Laje Weskamp; 2nd elder, Dr. Marcos H. de Anquín.

BRAZIL

SÃO PAULO SOCIETY

The prize of the Sociedade de Oftalmologia de São Paulo for 1948 was awarded to Dr. Drino Coelho who read a paper on "Glaucomatous Syndromes."

At the joint meeting of this society with the Centro de Estudos de Óftalmologia in July, 1948, Prof. Julio Szymansky read a paper on "Keratoplasty and the demi-Elliot operation method" (demonstration on patient) and Dr. A. Busacca read one on "Clinical and anatomical observations on perivasculitis of the nodular type seen in cases of chorioretinitis." At the August, 1948, meeting Prof. Ernst Simonsen spoke on "Effects of the degree of illumination and of color upon fatigue."

CELEBRATES ANNIVERSARY

The Ophthalmologic Clinic of the Escola Paulista de Medicina celebrated its 12th anniversary in March, 1949. The occasion was marked by several special scientific meetings.

ORTHOPTIC COURSE

The second course in orthoptic training opening in May, 1949, and given by the assistants of the ophthalmologic clinic of the Escola Paulista de Medicina, could be attended by graduates in medicine, trained nurses, and social workers.

PAN-AMERICAN ASSOCIATION OF OPHTHALMOLOGY

Resolutions adopted by the Committee on Inter-American Medical Relationships in Havana, January, 1948, were:

1. For the most widespread understanding of the scientific papers presented, it is recommended that:

a. An abstract of a paper to be presented must be transmitted to the proper authorities at least six months in advance of a congress so that lantern slides of a translation may be made and shown simultaneously with the presentation of the paper. In order to provide funds for this purpose it is recommended that the fee for the IV Congress be increased to $25.00.

b. The use of recorded discs for the immediate translations or discussions to be tried.

c. All members of the Pan-American Association of Ophthalmology be urged to become bilingual for Spanish and English or Portuguese and English.

2. In the interest of closer relationships between the ophthalmologists of the Western Hemisphere, the facilities of the Pan-American Association of Ophthalmology should be utilized for the introduction of accredited members when traveling. Be it understood that any member will be welcome as a visitor to the hospitals and scientific meetings of the members resident in the city visited. Be it understood also that the resident member should not be responsible for the social entertainment of any such visiting members. It is suggested that visiting members (a) be furnished with a distinctive badge with name and address and (b) be furnished with an interpreter if necessary.

3. It is recommended that during the first three days of the Pan-American Congress, social luncheons be arranged to bring together resident members and members from the different countries.

4. It is recommended that, since the center of medical education and research has passed from Europe to the Western Hemisphere, the Pan-American Association of Ophthalmology use its full facilities for rapid interchange of information of interest to its members.

5. It is recommended that a fund be established to be known as the Pan-American Fund, which

will grant fellowships for traveling in different countries.

PERSONALS

Dr. Federico K. Cramer of Buenos Aires visited São Paulo, Brazil, from March 12 to 18, 1948. Dr. Cramer read a paper at the Sociedade de Ophthalmologia de São Paulo entitled "Technical difficulties and complications of dacryocystorhinostomy by the external method." On March 15 he gave the inaugural lesson for the 1949 class in ophthal-mology of the Escola Paulista de Medicina. His subject on that occasion was "Physiopathology of the corneal tissue."

Dr. Juan Vicente Echague, Montevideo, Uruguay, and Miss Maria Ribeiro and Dr. Paunessa, Buenos Aires, have been taking orthoptic training under the direction of Miss Lygia Alves Lima, orthoptic technician of the Centro de Estudos de Oftalmologia in São Paulo. Dr. Echague hopes to organize an orthoptic training center in Montevideo.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month

DEATHS

Dr. Wayne Bernard Granger, Emporia, Kansas, died December 26, 1948, aged 56 years.

Dr. William F. Hardy, St. Louis, Missouri, died May 4, 1949.

ANNOUNCEMENTS

PRERESIDENT TRAINING COURSE

The faculty of the College of Physicians and Surgeons of Columbia University have approved plans to enlarge the preresident training course (formerly given as basic science for the residents of the Institute of Ophthalmology and allied hospitals) so that up to 15 applicants who have received or have been promised appointments in institutions approved by Columbia University will be accepted for four months' full-time training at the Institute of Ophthalmology.

Anatomy, embryology, pathology, physiologic optics, bacteriology, pharmacology, physiology, biochemistry, and refraction will constitute the basic studies upon which further studies preparing the matriculants for training in ophthalomolgy will be founded. The course will start January 2, 1950. Applications must be submitted before November 1st to the office of the assistant dean in charge of Graduate Medical Education, 630 West 168th Street, New York 32, New York.

ORTHOPTIC TECHNICIANS EXAMINATION

All applications for the annual examination of orthoptic technicians to be conducted by the American Orthoptic Council must be received by the office of the secretary, Dr. Frank D. Costenbader, 1605 22nd Street, N.W., Washington 8, D.C., by July 1st, and must be accompanied by the examination fee of $25.

BOOKS AND PERIODICALS NEEDED

The National Committee for Chile is now receiving gifts for the library of the Medical School of the University of Chile at its new collection center, Room 318, in the Library of Congress, Washington, D.C. Periodicals, books, and reference materials of the Medical School were totally destroyed in the recent fire. Urgently needed are medical periodicals of the last 10 years and recent medical books.

DE SCHWEINITZ LECTURE

The 12th annual de Schweinitz lecture, sponsored by the Section on Ophthalmology, College of Physicians of Philadelphia, will be given on Thursday, November 17, 1949, by Dr. Arthur J. Bedell of Albany, New York. The subject of Dr. Bedell's address will be "The macula in the aged."

MISCELLANEOUS

GILL GRADUATE COURSE

The Gill Memorial Eye, Ear, and Throat Hospital has just finished its 22nd annual spring graduate course. There was a registration of 250 doctors from all parts of the United States and Canada. On the faculty were: Dr. Banks Anderson, Dr. H. W. Brown, Dr. W. B. Clark, Dr. W. P. Dearing, Dr. W. W. Eagle, Dr. Harold Falls, Dr. E. P. Fowler, Jr., Dr. N. B. Herman, Dr. L. P. Garrod, Dr. Glen G. Gibson, Dr. C. L. Jackson, Dr. Carl C. Johnson, Dr. A. C. Jones, Dr. Harold H. Joy, Dr. Louis Paufique, Dr. Peter N. Pastore, Dr. Bernard Samuels, Dr. E. W. Scheldrup, Dr. Albert E. Sloane, Dr. Claire L. Straith, Dr. A. Earl Walker, Dr. Henry Williams, Mr. L. A. Watson, and Dr. John S. Lundy.

The next course will be given beginning April 3, 1950.

GLASGOW GRADUATE LECTURES

During May, a series of lectures were held in the Department of Ophthalmology, University of Glasgow. On May 4th, Prof. W. J. B. Riddell spoke on "European vacation." Dr. Fergus Campbell discussed "Pupillary movements," on May 11th; Dr. Antionette Pirie read a paper on "The structure of the vitreous humor," on May 18th; and, on May 25th, Dr. W. O. G. Taylor spoke on "Bleeding and clotting within the eye."

Societies

A.O.S. Meeting

Papers presented at the 85th annual meeting of the American Ophthalmological Society, held at The Homestead, Hot Springs, Virginia, June 2nd, 3rd, and 4th were:

"Late fistulazation of operative wounds: Diagnosis and treatment," Dr. John H. Dunnington, New York, and Dr. Ellen F. Regan (by invitation); "Simultaneous bilateral malignant ocular melanoma," Dr. Frederick C. Cordes, San Francisco, and Dr. Robert Cook (by invitation); "Nevus flammeus associated with glaucoma," Dr. Harold H. Joy, Syracuse, New York.

"Goniotomy and the treatment of congenital glaucoma," Dr. Harold G. Scheie, Philadelphia; "Spontaneous cysts of the ciliary body simulating neoplasms," Dr. Algernon B. Reese, New York; "Clinical and experimental investigations on para-amino-salicyclic acid (PAS) and streptomycin in ocular tuberculosis," Dr. Trygve Gundersen, Boston, and Prof. G. B. Bietti (by invitation).

"Sarcoid involving the orbit," Dr. F. N. Knapp, Duluth, Minnesota; "The psychology of the poor reader," Dr. William H. Crisp, Denver; "Iris pigment flakes on the posterior surface of the cornea following cataract extraction," Dr. Walter S. Atkinson, Watertown, New York; "Lamellar keratoplasty: Technique and results. Comparative study with penetrating keratoplasties and keratectomies," Dr. Ramon Castroviejo, New York.

"Ocular conditions associated with idiopathic hyperlipemia," Dr. Edwin B. Dunphy, Boston; "Oblique muscle surgery from the anatomical," Dr. Walter H. Fink, Minneapolis; "Fat embolism of the retina: A clinical and pathologic report," Dr. Arthur G. DeVoe, New York; "Retinitis punctata albescens," Dr. Arthur J. Bedell, Albany, New York.

"Cataract surgery routine in India," Dr. Raynold N. Berke, Hackensack, New Jersey; "Temporal arteritis (The Horton-Magath-Brown syndrome) as a cause of blindness: Review of the literature and report of a typical case," Dr. Gordon M. Bruce, New York; "Intraocular diktyoma and glioneuroma," Dr. F. Bruce Fralick, Ann Arbor, Michigan, and Helenor Campbell Wilder (by invitation).

"How we can best study primary glaucoma?" Dr. Eugene M. Blake, New Haven, Connecticut; "Experimental and clinical use of aureomycin in herpes simplex," Dr. Alson E. Braley, New York; "Tonometry: The variation of ocular rigidity in chronic glaucoma and an adaptation of the Souter tonometer," Dr. Searle B. Marlow, Syracuse, New York; "Clycloelectrolysis for galucoma," Dr. Conrad Berens, New York, and Dr. Benjamin L. Sheppard and Dr. Arthur B. Duel, Jr., (by invitation).

Midwestern Research Meeting

The midwestern section of the Association for Research in Ophthalmology held its organizational meeting in the Elliott Auditorium, Oscar Johnson Institute, St. Louis, Missouri, on Saturday, March 26th. Dr. William F. Hughes, Jr., was elected chairman; Dr. William Howard Morrison, vice-chairman; and Dr. T. E. Sanders, secretary and treasurer.

The following scientific program was enjoyed by 65 ophthalmologists from Ohio, Indiana, Illinois, Wisconsin, Minnesota, Iowa, Nebraska, Kansas, and Missouri.

"Some possible applications of 'spreading factor' in ophthalmology," Dr. Philip Shahan, and W. A. Moor, A.B., Washington University; "A family of idiopathic flat detachment of the macula: Question congenital," Dr. Harold F. Falls, University of Michigan; "Motor imbalances and the fusional processes: A preliminary report," Dr. Kenneth N. Ogle, Mayo Clinic; "Cortical potential changes in amblyopia ex anopsia," Dr. Edward Bierman and Dr. Dallas Dyer, St. Louis University; "The effect of the pupil on flicker fusion fields: Preliminary report," Dr. Paul Miles, Washington University; "Antistine: A study of its toxicity on topical applications to the eye," Dr. T. F. Schlaegel, Jr., Indiana University; "Some ocular effects of sympatholytic compounds," Dr. Frank W. Newell, Dr. William L. Ridgeway, and Dr. Robert W. Zeller, Northwestern University; "Beta irradiation: An evaluation of a radium-D applicator for ophthalmic use: Preliminary report," Dr. Fred M. Wilson, University of Illinois.

Second Western Research Meeting

The second annual meeting of the Western Section of the Association for Research in Ophthalmology was held on March 25th at the University of California Medical School, San Francisco. On the program were the following papers.

"The correlation of clinical and histopathologic findings in vernal conjunctivitis," Dr. N. M. Biegelman, University of Southern California; "Tonus of the extraocular muscles: An electromygraphic study," Dr. R. M. Flanagan, Dr. B. Kvernland, and Dr. R. V. Hill, University of Oregon; "Some experimental studies on corneal transplants," Dr. A. E. Maumenee, Stanford University; "Dynamic muscle balance: Part I. Theory and technique; Part II. Some applications and results," Dr. L. Bond and Dr. Kenneth C. Swan, University of Oregon; and "Clinical experiences with vitreous replacement," Dr. G. P. Landegger, University of Southern California.

At the dinner meeting, John B. deC. M. Saunders, F.R.C.S., librarian of the Medical School Library, professor of anatomy and lecturer in medical history and bibliography of the University of California Medical School, gave the address of the evening. His subject was "Some aspects of the activities of the central nervous system."

Alabama Academy Organized

At the Jefferson Davis Hotel in Montgomery, Alabama, on April 20th, the Alabama Academy of

Ophthalmology and Otolaryngology was organized. The meeting was called by Dr. Harvey Searcy of Tuscaloosa, and Dr. Bruce Holding of Montgomery was appointed temporary chairman. Fifty-two men from all over the state were in attendance.

Officers were elected as follows: Dr. Frank Clements, Birmingham, chairman; Dr. Phil P. Gilchrist, Mobile, chairman elect; and Dr. Karl B. Benkwith, Montgomery, secretary and treasurer.

During the scientific session, Dr. John Lingo, Mobile, read a paper on "Allergy in otolaryngology," and Dr. John Keyton, Dothan, spoke on "Hormone therapy in cataracts."

BROOKLYN PROGRAM

At the 108th regular meeting of the Brooklyn Ophthalmological Society, the following brief case reports were presented: "Retinitis pigmentosa with drusen on the optic nerve," Dr. Regina V. Gilroy; "Sarcoidosis with corneal involvement," Dr. Mary G. Bruno; "Angioid streaks," Dr. A. Benedict Rizzuti; "Severe erythema multiforme bullosum with ocular complications: Treated with aureomycin," Dr. Leo Esbin; "Optic neuritis as a complication of chicken pox," Dr. Mortimer Cholst; "Sympathetic ophthalmitis," Dr. Joseph Mandelbaum; "Epithelial invasion of the anterior chamber," Dr. Morris H. Pincus; "Oxycephaly," Dr. Martin Bodian.

MILWAUKEE GUEST SPEAKER

Dr. Otis S. Lee, Department of Ophthalmology, University Hospitals, Iowa City, Iowa, spoke at the April 26th meeting of the Milwaukee Oto-Ophthalmic Society. The subject of his lecture was "Cyclodialysis."

PENNSYLVANIA ACADEMY MEETING

Dr. George M. Coates, Philadelphia, was guest of honor at the annual meeting of the Pennsylvania Academy of Ophthalmology and Otolaryngology held at Harrisburg, April 22nd to 24th. Dr. Coates spoke on "Reminiscences in otorhinology."

Other speakers were: Dr. John R. Lindsay, Chicago, "Vertigo: Differential diagnosis and treatment," and "Eustachian tube obstruction: early diagnosis and treatment"; Dr. Ralph O. Rychener, Memphis, "External diseases of the eye: Treatment and diagnosis"; Dr. C. Stewart Nash, Rochester, New York, "Functional diseases of the nose," and "The otolaryngologic consultant in compensation and liability actions"; Dr. Albert D. Ruedemann, Detroit, "Beta ray uses in ophthalmology," and

"Medical treatment of early cataract"; Dr. Ralph R. Pino, Detroit, "Economics of ophthalmology"; Dr. Arno E. Town, Philadelphia, "Fibrin closure of surgical wounds"; Dr. Harrison F. Flippin, Philadelphia, "Recent advances in chemotherapeutics."

In addition to these papers a round-table discussion on "Headache" was held, and Dr. Ruedemann and Dr. Town conducted a study club on cataract problems.

Specialists from all parts of Pennsylvania, as well as from surrounding states, attended the meeting. Officers elected for the following year were: President, Dr. Daniel S. DeStio, Pittsburgh; president elect, Dr. Jay G. Linn, Pittsburgh; secretary, Dr. B. F. Souders, Reading; treasurer, Dr. Bruce A. Grove, York.

GUEST LECTURERS AT WEST VIRGINIA

Guest lecturers at the meeting of the West Virginia Academy of Ophthalmology and Otolarygology held at Martinsburg on May 13th and 14th were: Dr. Glen G. Gibson, Temple University, Philadelphia; Dr. Walter Klingman, University of Virginia, Charlottesville; Dr. G. Slaughter Fitz-Hugh, University of Virginia, Charlottesville.

Among the papers presented were: Dr. William Stone, Jr., "The Stone-Jardon implant"; Dr. Glen Gibson, "Medical and neurologic ophthalmology"; Dr. Walter Klingman, "Pain mechanisms associated with headache"; Dr. James K. Stewart, Wheeling, "Penicillin in acute otitis media"; Dr. G. S. Fitz-Hugh, "Treatment of facio-maxillary fractures"; Dr. Charles T. St. Clair, Bluefield, and Dr. Ben W. Bird, Princeton, "Allergic manifestations of the eye."

PAN-AMERICAN-N.S.P.B. MEETING

At a recent meeting of the officers of the Pan-American Association of Ophthalmology and of the National Society for the Prevention of Blindness, it was decided to have a joint meeting of the two organizations in Miami Beach, Florida, March 26 to 30, 1950.

For the National Society for the Prevention of Blindness, this would be their annual meeting; for the Pan-American Association of Ophthalmology, this would be an interim meeting, inasmuch as the next Congress of the Pan-American Association of Ophthalmology will be held in Mexico City early in 1952.

The headquarters of this joint meeting will be at the Floridian Hotel, Miami Beach, Florida. Summer rates will prevail.

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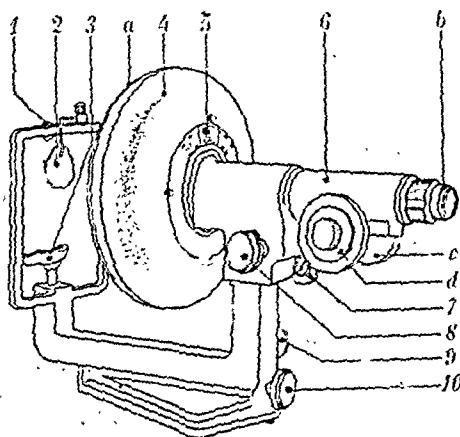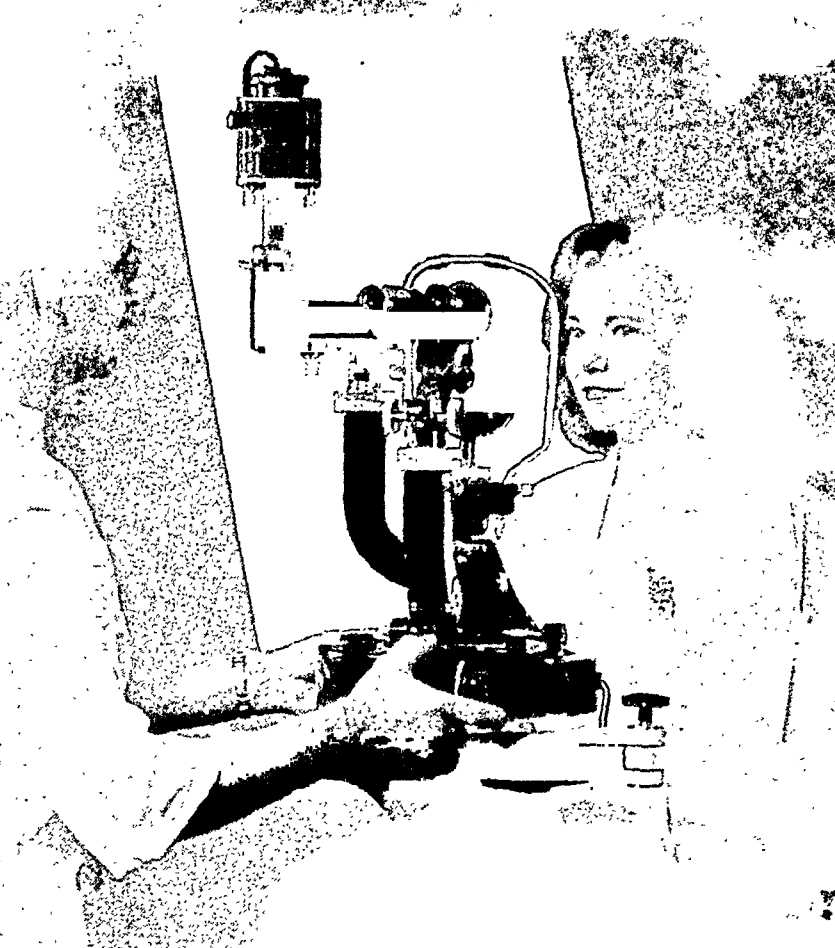
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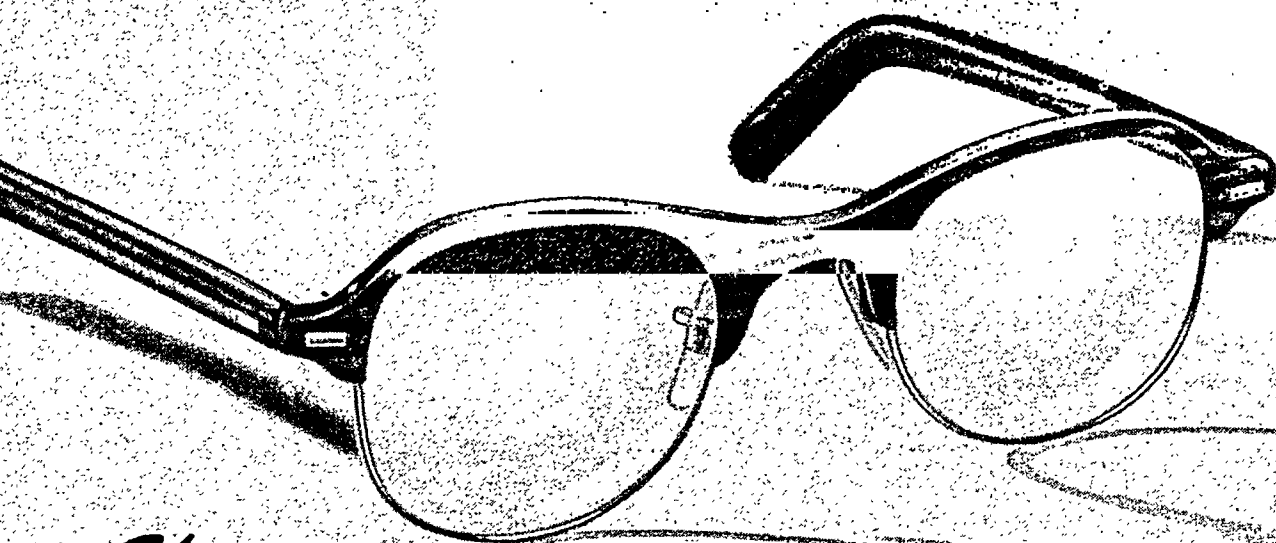
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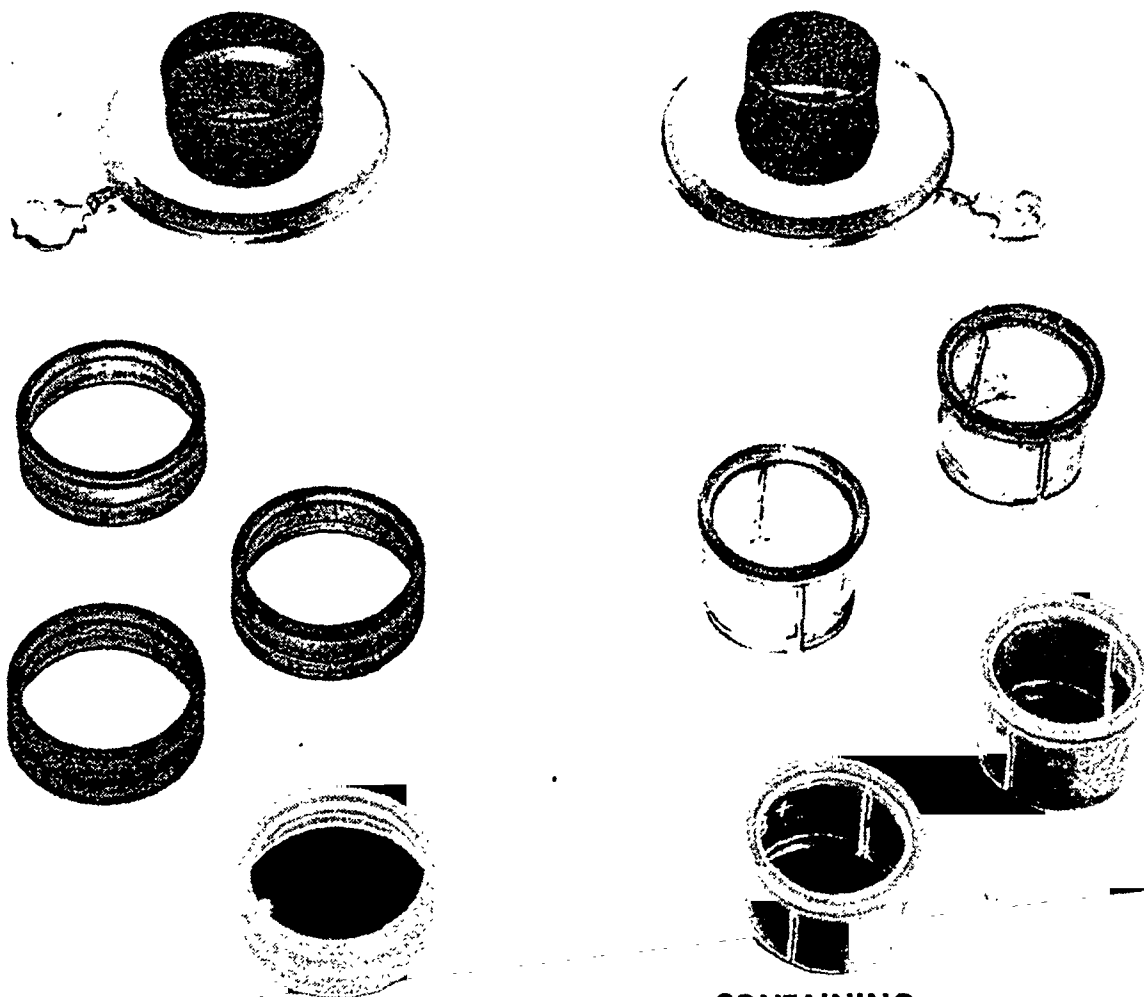
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1. Friedlaender, A. S., and Friedlaender, S.: Annals of Allergy, 6: 23-29, Jan.-Feb., 1948.

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A way around the difficulty was found to be the use of two different sized lenses. On one side we used a lens 38 mm wide and 44 mm long and on the other side with the low eyebrow, the lens used was 34 mm wide and 44 mm long.

Some care was used in figuring where to put the optical centers. The 38 mm wide lens was ordered with the optical center in the geometric center of the lens and the 34 mm wide lens was ordered with the optical center 2 mm above the geometric center.

In this case, the use of dissimilar sized lenses resulted not only in correctly centered and positioned lenses but also in a pair of glasses that are cosmetically satisfactory to the patient.

CONTENTS

STUDIES ON THE CLINICAL PHYSIOLOGY OF THE CORNEA*

THE INTERRELATIONSHIP OF CORNEAL TURGESCENCE, EPITHELIAL EDEMA, BULLOUS
KERATOPATHY, AND INTERSTITIAL VASCULARIZATION

THE THIRD FRANCIS I. PROCTOR LECTURE[†]

DAVID G. COGAN, M.D.
Boston, Massachusetts

It is the purpose of this address to present a resume of some recent experimental work on the cornea done at the Howe Laboratory and to point out the clinical significance of these primarily laboratory observations.

TURGESCENCE

Much of our original interest in corneal turgescence stemmed from the simple fact that an excised button of corneal tissue placed in almost any aqueous solution (including blood plasma or aqueous humor) had a capacity to take up water over and above its normal content far in excess of any other biologic tissue (fig. 1). It is an intriguing question to ask what are the factors preventing it from swelling in vivo and what function is served by this normal maintenance of a deturgesced state of the cornea.

To answer these questions, Dr. V. E. Kinsey and I carried out a series of studies, at first on excised corneal buttons, then on excised whole corneas, and finally on corneas in vivo, with the following results: Corneal pieces immersed in solutions whose osmotic pressure was varied over a wide range (0 to 2.0 molar) showed no inhibition of turgescence comparable to that which exists during life.[1] Likewise, corneal pieces placed in solutions of various hydrogen and hydroxyl-ion concentration similarly failed to show an in-
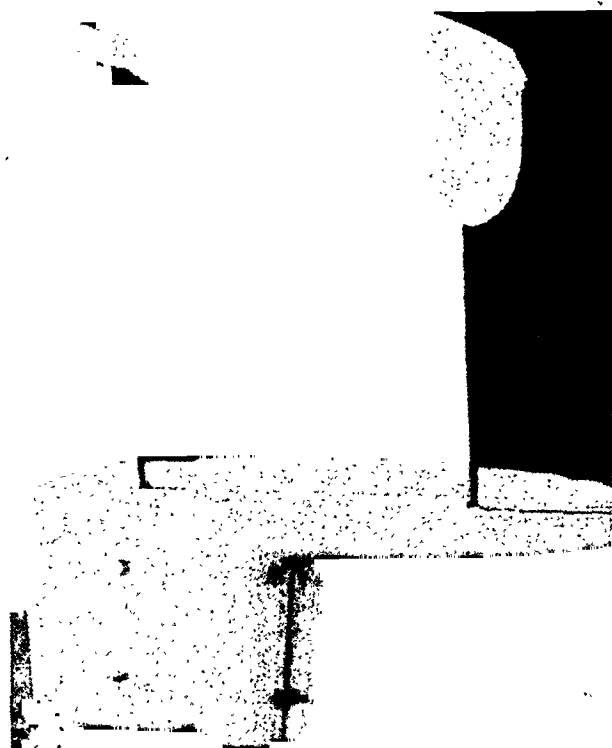

Fig. 1 (Cogan). Two buttons of cat corneas which had equal diameters when excised. The button on the left has been freshly excised; that on the right has been immersed in physiologic saline solution for several hours.
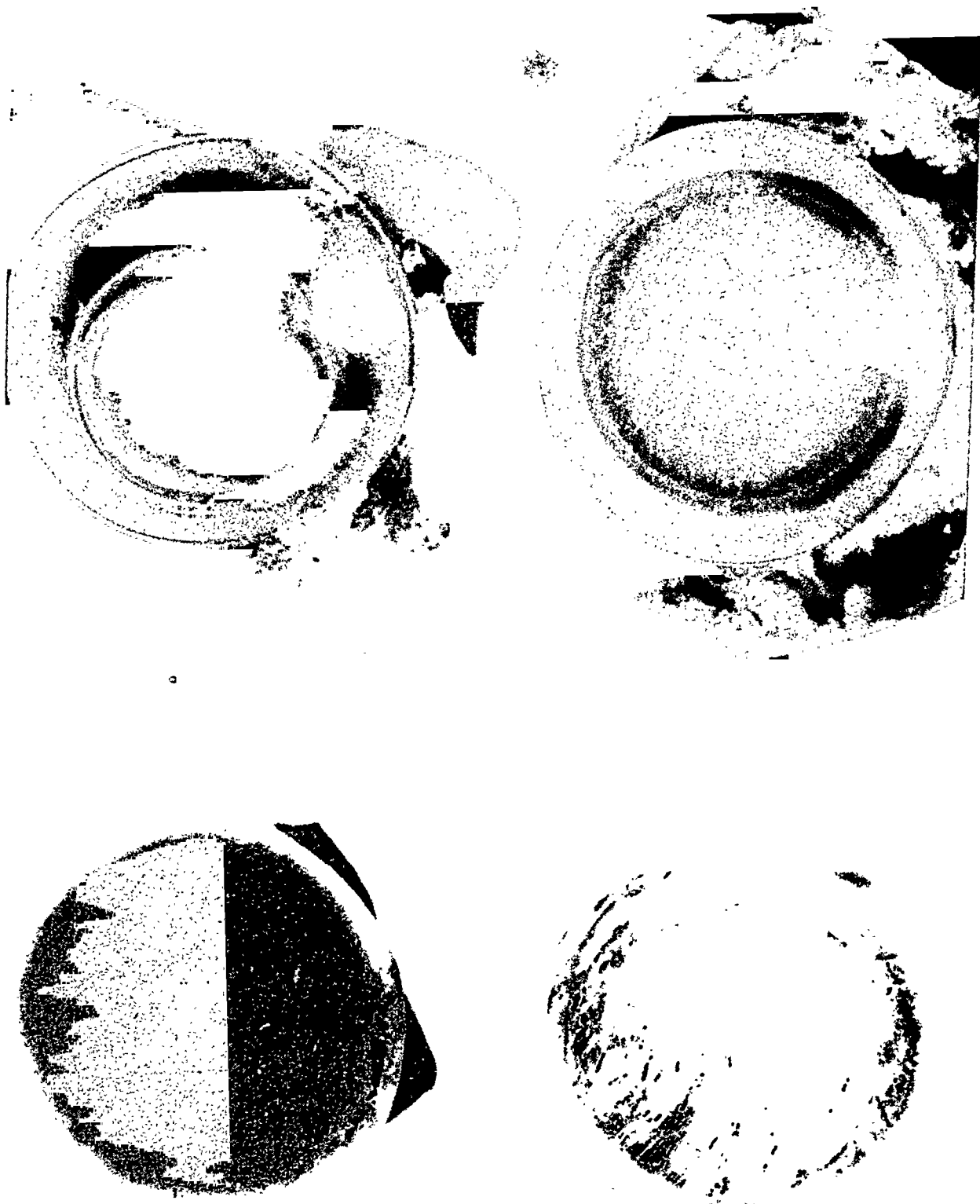
Fig. 2 (Cogan). Pictures showing relative opaqueness of cornea on hydration (above) and relative transparency of sclera on dehydration (below). The upper pictures are those of cat corneas which have been tied onto the ends of tubes (photographed end-on); the upper left has been kept relatively dehy-

hibition of turgescence over a range that might be considered to exist under physiologic conditions (pH 6 to 8).[1] Hydrostatic pressure had a definite inhibitory effect on turgescence, but the pressure necessary to maintain a state of deturgescence of the same order of magnitude as that which exists during life was much greater than could be accounted for by the normal intraocular pressure. Hence, it was concluded that the partially dehydrated state of the normal cornea was determined neither by the osmotic tension nor by the hydrogen-ion concentration of the interstitial fluid, and that the intraocular pressure was insufficient to account for more than a small part of it.

An explanation for the maintained deturgescence of the cornea was found, however, in a study of the permeability properties of the corneal epithelium and endothelium. While freely permeable to water,[2] these surface membranes were found to be extraordinarily impermeable to electrolytes[3] and to nonlipid soluble nonelectrolytes.[4] The semipermeability properties of the corneal epithelium (with respect to sodium chloride) were found to be far greater than for any other known biologic membrane and, indeed, approached those of a theoretically perfect semipermeable membrane. The corneal endothelium was less accessible for quantitative testing than was the epithelium but, in so far as it could be tested, it showed the same semipermeable properties as the epithelium.

In the presence of such effective semipermeable membranes, it is possible, therefore, to maintain a relatively deturgesced state of the cornea by having fluid on the surface of the cornea hypertonic to that within the stroma. This may readily be demonstrated for the excised cornea where the osmotic concentration of the fluid outside of the cornea can be made hypertonic at will and is presumed to apply in vivo[5] where the tear fluid on the anterior surface of the cornea and the aqueous humor on the posterior surface are believed to be hypertonic to that of the corneal stroma. According to this concept, the fluid within the corneal stroma is derived from the limbal blood vessels, and so long as the surface membranes of the cornea are intact and the fluids on the front and back surfaces of the cornea are hypertonic to that within the stroma, there will be continuously a net loss of water out of the cornea with consequent deturgescence of the stroma.

The function served by this deturgescence is transparency. To maintain transparency it is essential to keep the cornea relatively dehydrated. Since the structural and fluid components of the cornea have different refractive indices,[6] transparency will be approached only in so far as one of these components, in this case the fluid component, is kept at a minimum. The fundamental optical difference, then, between cornea and sclera (assuming the structural and fluid components of the sclera are also anisoindicial) is due to the fact that the former has a dehydrating mechanism in its semipermeable membranes not present in the latter. In consequence, the sclera is normally hydrated to its maximum under physiologic conditions and therefore opaque, while the cornea is kept relatively dehydrated and transparent. But if the cornea is allowed to imbibe water fully, as is the case with the normal sclera, it becomes opaque; and conversely, if the sclera is artificially dehydrated so that, like the normal cornea, it contains only a fraction of the water capable of being imbibed, it also becomes transparent (fig. 2).[7]

drated by having epithelium intact and the fluid in contact with the epithelial side hypertonic to that on the stromal side; the upper right had the epithelium removed and is in consequence swollen. The lower pictures are those of albino rabbit scleras similarly tied onto the ends of tubes (photographed end-on); the lower left is the freshly excised sclera; the lower right has been allowed to dry in the air and is in consequence dehydrated and transparent.

EPITHELIAL EDEMA AND BULLOUS KERATOPATHY

Whereas maintenance of the normally deturgesced state of the cornea requires an osmotic gradient such that the fluid on the anterior (and posterior) surface of the cornea is hypertonic to that within the stroma, epithelial edema and bullous keratopathy result when the osmotic gradient is reversed, that is, when the osmotic tension of the tear film becomes equal to, or less than, that within the stroma. This may be brought about ex-

formly edematous and loose. Gross bullae develop, at first singly but, becoming confluent, raise up the whole epithelium in one large bulla that ultimately bursts.[1]

The determining factor in epithelial edema and bullous keratopathy of human beings is probably not a primary hypotonicity of the tears but rather an increase in the tonicity of the stromal fluid. This is brought about through endothelial damage with consequent percolation of hypertonic aqueous humor into the stroma. The development of the epi-
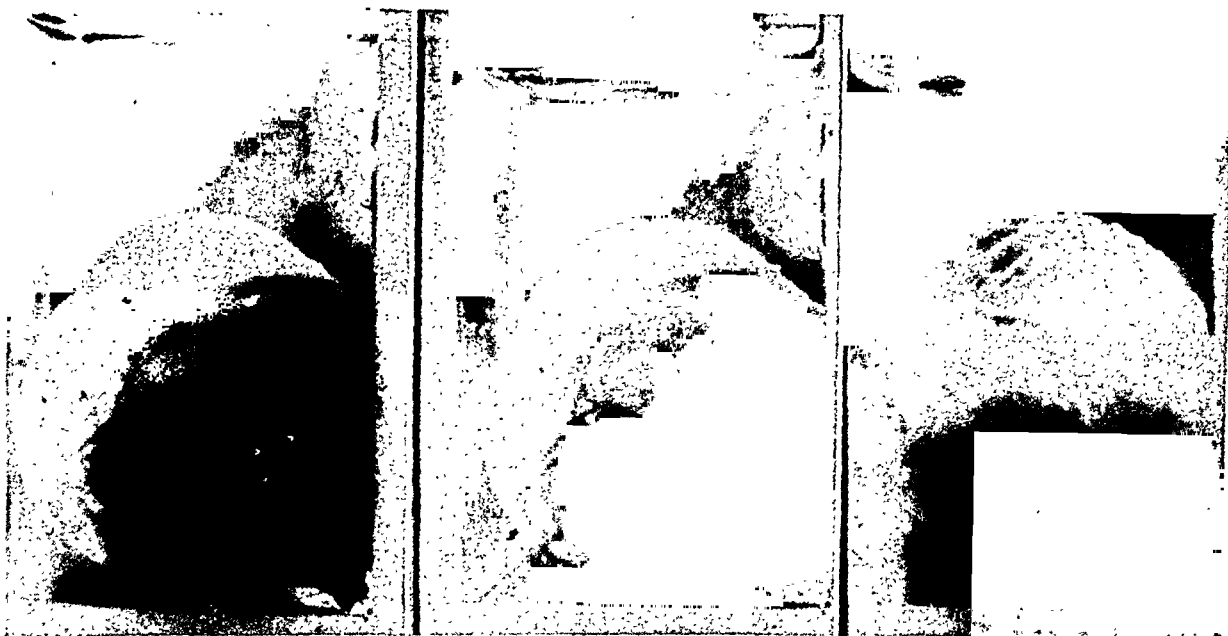

Fig. 3 (Cogan). Development of "bullae" in the enucleated cat eye by injection of three-percent sodium chloride solution into the anterior chamber and immersion of the whole eye into a flask of water. The pictures were taken at 5, 15, and 60 minutes after the injection.

perimentally by making the tear fluid hypotonic (placing water bath on eye) or by making the stromal fluid hypertonic (injecting 3-percent sodium chloride into the cornea or into the anterior chamber). The development of the bullae can perhaps be most strikingly induced by injecting hypertonic solutions into the anterior chamber of the enucleated eye and immersing the eye in a flask of water (fig. 3) or, alternatively, by tying the endothelial-less cornea on the end of a tube and making the fluid on the anterior or epithelial side hypotonic to that on the posterior side. The epithelium becomes uni-

thelial changes will be influenced by a variety of factors. Noteworthy is the exaggeration of the edema by prolonged closure of the eyes (for example, after sleep) where the effect of evaporation in concentrating the precorneal tear film is reduced to a minimum. Moreover bullous keratopathy is infrequent where there is an open blood-aqueous barrier; it is found predominantly in conditions where the aqueous is believed to have an osmotic tonicity equal to or greater than that of the blood, as in primary keratopathies or with glaucoma. In other words, epithelial edema and bullous keratopathy are found

most marked where the osmotic tension of the tear fluid is less and where that of the aqueous humor or, more properly, that of the corneal stroma is greater than that of the blood.

It is possible to have swelling of the cor-

the endothelium. In all these conditions the osmotic tension of the aqueous humor is presumably lower than normal since it approaches that of the blood. Conversely epithelial edema and bullous keratopathy might be expected to occur without swelling of the

Fig. 4 (Cogan). (A) Bullous keratopathy in a human eye three weeks after a perforating injury. The picture illustrates the looseness of the epithelium and the presence of subepithelial debris. (Low-power magnification.) (B). Same in high-power magnification. The subepithelial debris appears to be cytoplasm of the disrupted basal epithelial cells and contains free floating nuclei which are interpreted as being derived from the burst basal cells.
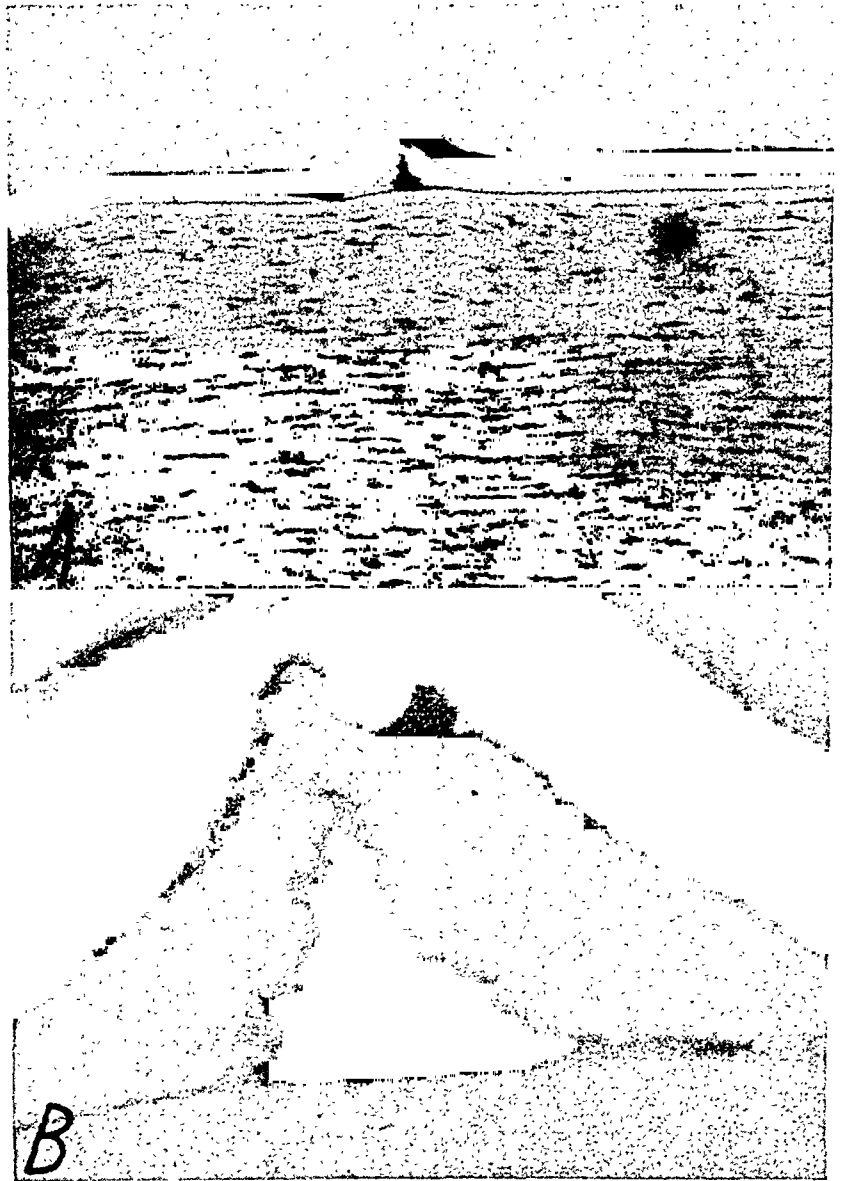
nea without epithelial edema or bullous keratopathy. Such might be expected to occur when, in the presence of endothelial damage, the blood-aqueous barrier no longer maintains the hypertonic state of the aqueous humor. Such swelling of the cornea without bullous keratopathy is indeed found to be the case with hypotony in instances of phthisis bulbi, chronic uveitis, and following a paracentesis when there has been an abrasion of

cornea in conditions wherein the stromal fluid became hypertonic through excessive movement of its water into the aqueous humor. Such may be the explanation for the epithelial edema in some cases of glaucoma. In other cases of glaucoma, however, the endothelium appears to have been damaged by the intraocular pressure, and the cornea becomes swollen as well as having edema of its endothelium.
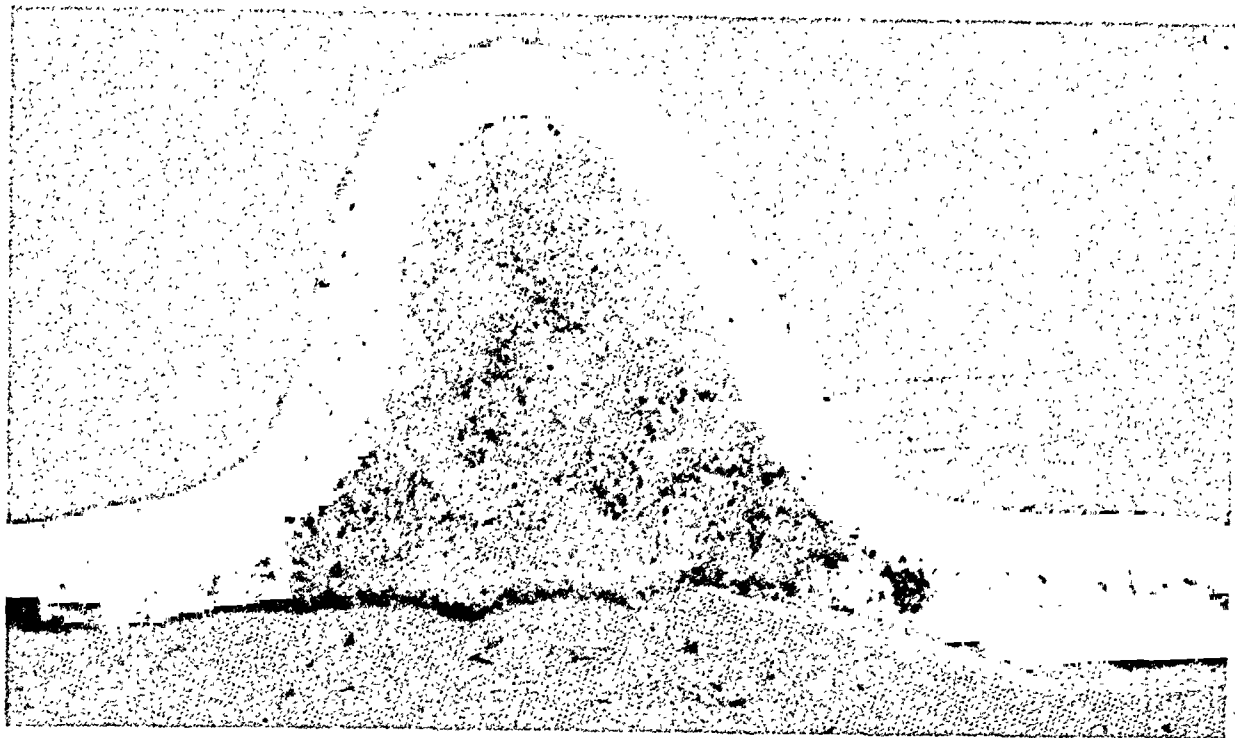
Fig. 5 (Cogan). "Bullous keratopathy" in the enucleated cat eye induced by injection of three-percent sodium chloride into the anterior chamber and immersion of the eye in a flask of water for one hour. The subepithelial debris appears to consist of ruptured epithelial cells and free floating nuclei.

By piecing together the observations in acute experimental bullous keratopathy and those in the subacute and chronic clinical variety, it is possible to reconstruct the chain of events which lead to the characteristic histologic picture of epithelial edema and bullous keratopathy.[8]

The initial changes in bullous keratopathy are the swelling of the basal epithelial cells (edema) and the accumulation of fluid between the epithelium and Bowman's membrane. The basal cells swell to the point of bursting and disgorge their cytoplasmic and nuclear contents beneath the epithelium forming, with the subepithelial fluid, a bulla (figs. 4 and 5). This amorphous debris in the bulla becomes invaded by cells which, although appearing to come from the epithelium, assume spindle-shaped processes and come to be laid down anterior to Bowman's membrane in a manner indistinguishable from connective-tissue cells (fig. 6). In the course of time these cells develop laminas of collagen not unlike that of true corneal tissue (fig. 7).

In interpreting the sections of any one case of bullous keratopathy, it is important to remember that this disease is characterized by cycles of activity. The aforementioned early changes consisting of epithelial edema and bursting of the basal cells with the production of subepithelial cytoplasmic debris and free floating nuclei are to be found only when the histologic sections are made through an area which was actively developing a bulla at the time of enucleation. During a quiescent interval the epithelium appears relatively normal, the outstanding abnormality being laminas of flattened cells and (depending on the duration) a varying amount of collagen separating the epithelium from Bowman's membrane or from the superficial stroma.

VASCULARIZATION

There appears to be a significant relationship between swelling of the cornea and new blood-vessel formation in the stroma of the cornea.[9] Neovasculogenesis occurs only when the corneal stroma adjacent to the

preëxisting vessels swells. Moreover, the morphologic changes in these vessels suggest that the initial events are induced by a reduction in the tissue compactness of the cornea. There is first a dilatation of the vessels, chiefly of the veins and capillaries, with saccular outpouchings of the vessel walls. Such dilatation must be brought about either by increase in the intravascular pressure or decrease in the extravascular pressure. There is no evidence to support the former, but the facts, that the dilatation occurs only as the area of swelling extends to the vessels and that the saccular outpouchings are to be found on the sides of the vessels toward the greatest swelling, support the assumption that the early morphologic changes are due to decrease in extravascular pressure.

It is to be remembered that the normal cornea is maintained in a state of compact-ness by the unique deturgescing forces which operate on its surfaces. Swelling of the stroma appears to result in a reduction of this compactness and the evidence suggests this softening of the stroma is the factor precipitating the dilatation of the vessels. As the swelling of the cornea increases, the dilatation of the vessels increases until ultimately each of the saccular aneurysms bursts and numerous tiny hemorrhages can be seen extending into the adjacent stroma. The further sequence of events consists of a riddling of the hemorrhagic zone with new capillaries. Forming at first a profligate network, these ultimately become resolved into one or more loops with regression of the rest of the capillaries.

Obscure as are the factors responsible for the later stages, the early events of interstitial vascularization in the cornea appear to
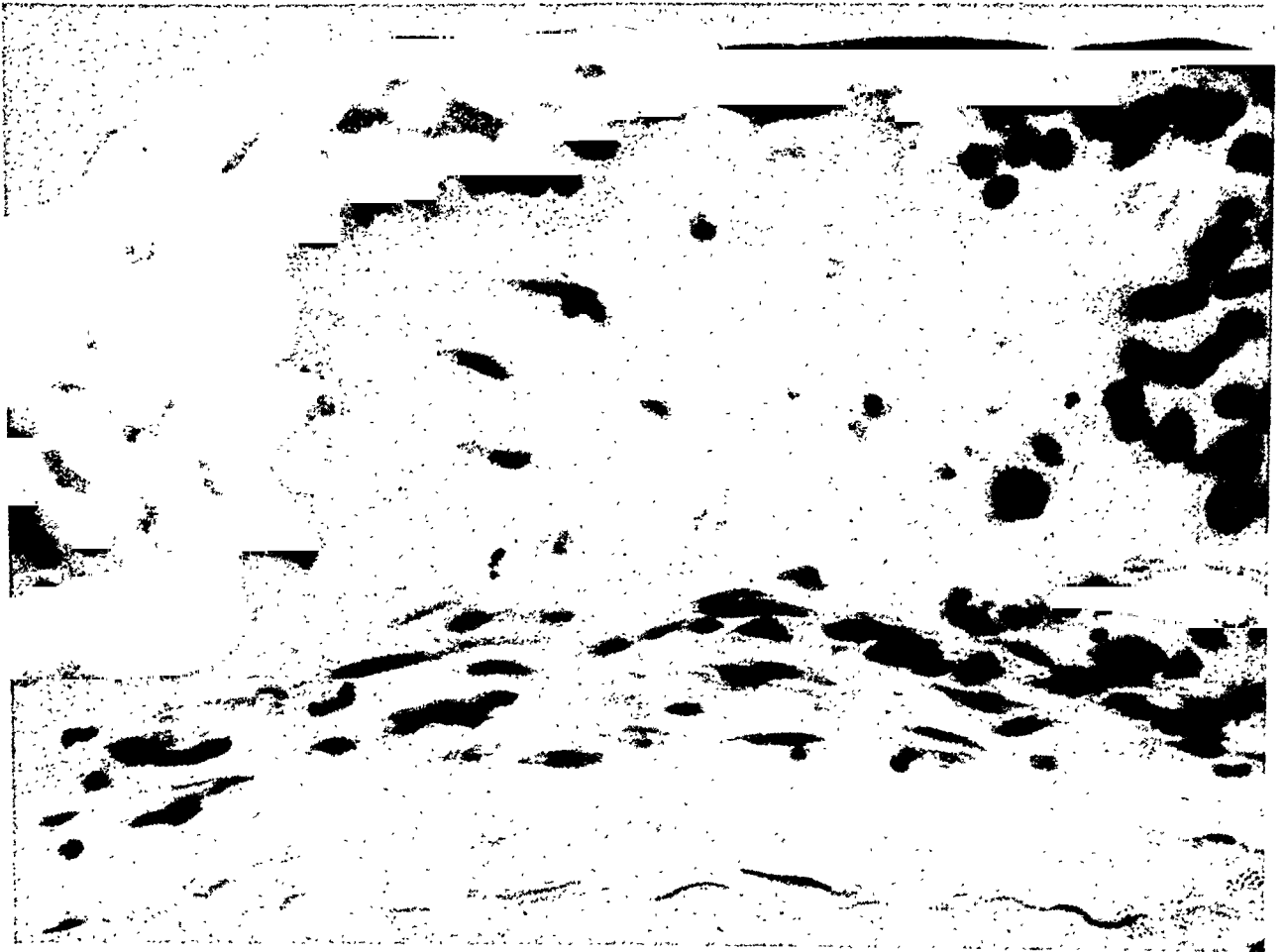

Fig. 6 (Cogan). An "active" bulla in a human eye. The cells within the bulla appear to develop spindle-shaped processes and come to be laid down in a stratified manner anterior to Bowman's membrane.

be initiated by the simple mechanical factor of softening of the adjacent stroma. It should be emphasized that it is the adjacent stroma which is important. Swelling of the axial portions of the stroma not extending to the limbus does not become vascularized. Thus swelling of the cornea in guttate dystrophy, long-standing glaucoma, and other
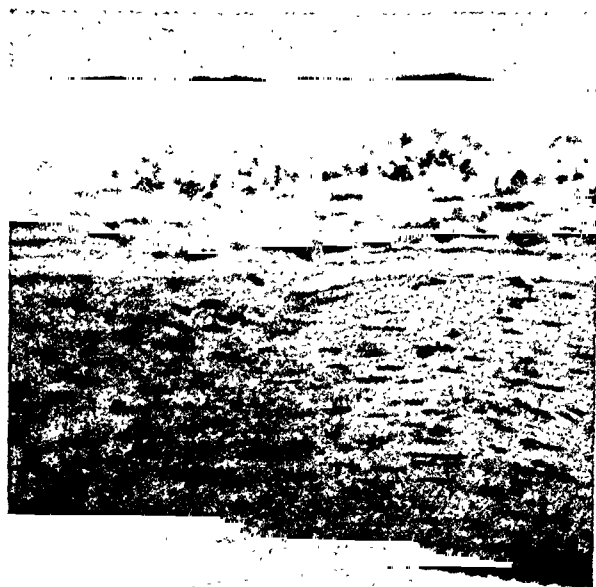

Fig. 7 (Cogan). An "inactive" stage of bullous keratopathy in a human eye showing stratification of collagen-rich tissue anterior to Bowman's membrane.

conditions having a nonswollen peripheral ring of cornea remain unvascularized indefinitely; whereas, comparable swellings extending to the limbus become promptly invaded by blood vessels.

TURGESCENCE, BULLOUS KERATOPATHY, AND VASCULARIZATION OF THE CORNEA

The observations thus far enumerated have been published elsewhere together with detailed protocols. The thesis which I should now like to develop and which, to the best of my knowledge, is new is that swelling of the peripheral cornea sets up, through neovasculogenesis, a cycle that is self-corrective. It is proposed not only that the swelling of

the cornea initiates the neovasculogenesis but that the neovasculogenesis in turn corrects the swelling and the accompanying bullous keratopathy.

The evidence for this is simply that corneas which are swollen and have bullous keratopathy become deturgesced as blood vessels grow into the stroma, while those corneas which do not develop interstitial vascularization are apt to remain swollen and bullous. Several examples of this may be cited.

Luetic interstitial vascularization shows a uniformly swollen cornea which becomes deturgesced as the new blood vessels grow in. The same phenomenon is strikingly seen in vascularization of the rabbit cornea. On the other hand, swelling of the cornea and bullous keratopathy are apt to be permanent when they accompany long-standing glaucoma, guttate dystrophy of the posterior corneal surface, or occurring idiopathically, and in these types it is noteworthy that no neovasculogenesis occurs since there is a peripheral zone of nonturgid cornea across which the vessels do not pass.

On the other hand, swelling and bullous keratopathy of the *peripheral* cornea do become vascularized and, as the new vessels grow in, the swelling decreases, and the bullous keratopathy disappears. This is seen often in sclerokeratitis or in a variety of conditions where, through inflammatory deposits or other foreign material, the posterior surface of the peripheral cornea is eroded.

The probable theoretical basis for this beneficial effect of neovascularization on bullous keratopathy and swelling of the cornea is as follows. The cornea becomes swollen as a result of the impaired endothelial function with consequent percolation of hypertonic aqueous into the stroma. Bullous keratopathy results when the normal osmotic gradient between tear fluid and stromal fluid is reversed. As new blood vessels grow into the cornea, the stroma becomes more nearly isosmotic with the blood and therefore hypo-

tonic to the precorneal tear film. Then, in spite of persistent damage to the posterior corneal surface, water will be abstracted through the anterior surface with consequent cure of the bullous keratopathy and (so long as the water abstracted from the anterior surface of the cornea exceeds the net amount entering from the blood vessels and the posterior surface) deturgescence of the cornea.

It is, moreover, not impossible that the deturgescence in itself may be responsible for the subsequent collapse and partial obliteration of the blood vessels, through restoration of the normal compactness of the cornea, thereby completing the cycle of turgescence, vascularization, deturgescence, and devascularization. But it should be emphasized that this applies to interstitial vascularization only. There is no theoretical nor practical evidence to suggest that superficial vessels, such as occur in pannus, have any such deturgescing effect.

An analogy may be drawn between the dynamics of a vascularized cornea and that which normally obtains at the limbus. In both cases the stroma is in relatively intimate equilibrium with the blood and is relatively refractory to the development of corneal swelling and bullous keratopathy. Thus,

when the posterior surface of the cornea is abraded with a "magnetic flea," it is predominantly the central portions of the cornea which become swollen and opaque.[10] This is true even when the abrasions are made most markedly at the periphery. Similarly, experimental bullous keratopathy, induced by the injection of hypertonic salt solution into the anterior chamber, is much more marked in the normal cornea than in the vascularized cornea. In both instances it is presumably the equilibrium with the blood which maintains the relative hypotonicity of the stromal fluid and consequent deturgescence of the cornea.

From a practical point of view the obvious corollary of all this is that persistent swelling of the cornea and bullous keratopathy should be curable by inducing interstitial vascularization of the cornea. Such treatment will in itself induce some opacification of the media and whether or not it is indicated will depend on a number of factors such as persistence of the process, degree of discomfort, and visual acuity. To date I have employed it as a form of treatment in only a few cases and with equivocal results. I shall have to await further trial before drawing any practical conclusions.

243 Charles Street (14).

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AN OPERATION FOR CHRONIC PRIMARY GLAUCOMA*

GONIODIALYSIS COMBINED WITH SCLERECTOMY AND IRIS INCLUSION

JOSEPH LAVAL, M.D.
New York

I am sure most eye surgeons have done this operation in part many times. The sclerectomy, the iris inclusion, the goniodialysis—all these have been done by many surgeons. I am suggesting only that all of these be done at one time and also that the incision be made by the ab externo route as originally advocated by Ernst Fuchs.

The operation is indicated for cases of chronic primary glaucoma either with or without acute exacerbations. It can also be used for the intractable borderline case of secondary glaucoma; that is, the case which is difficult to classify as true primary glaucoma and in which often more than one operation has been done with no permanent control of tension.

This operation has been done at Mt. Sinai Hospital and at the Manhattan Eye, Ear, and Throat Hospital on a total of 50 eyes of 43 patients, 20 of whom were men and 23, women. The ages ranged from 43 to 79 years. The duration of the glaucoma varied from 1 year to at least 8 years before operation. The tension before operation with miotics varied from 30 mm. Hg to 80 mm. Hg (Schiøtz).

The visual fields varied from almost normal to telescopic, with various sizes of paracentral scotomas and enlarged blindspots extending almost to fixation. In no case was the field made worse or the visual acuity impaired by the operation. No patients developed lenticular opacities as a result of the operation. Visual acuity before operation ranged from 5/400 to 20/20.

Some cases have been followed for three years, and some for only one month. Three patients had had prior operations for relief of tension in eyes operated on by the method described in this paper. Of these three cases, one was a failure after 8 months with this operation. Any case which needed miotics after the operation more than 3 times a day to keep the tension normal was considered a failure. The one failure was in a Negro who had syphilis and whose right eye was lost following several unsuccessful operations to control the tension, including cyclodiathermy. The left eye had one operation for glaucoma with no reduction in tension, following which the operation I shall describe was performed by the surgeon in charge of the case. The tension was controlled for 8 months but then rose again and could not be controlled with miotics.

OPERATIVE PROCEDURE

The operative procedure is simple and requires no great amount of surgical skill. It can be done under intravenous or local anesthesia. On the day of the operation, I use no miotics, in this way making it easier to withdraw the iris from the wound.

In the cases done under local anesthesia, I use a lid block according to Van Lint's technique, two sutures through the upper lid, and one through the superior rectus. No suture is needed for the lower lid. Two cc. of 2-percent novocain with adrenalin are injected retrobulbarly above and also some subconjunctivally above, ballooning up the conjunctiva between the limbus and the upper fornix.

The incision is made one centimeter above the limbus and rather wide, as one does for a trephination. Tenon's capsule is also opened rather wide. As one approaches to within 5 mm. of the limbus the incision goes through all the layers down to sclera. This

incision must also be made wide to avoid a small filtration area which would stand out like a knuckle.

The dissection is carried down to the corneoscleral margin and here a partial splitting of the cornea, as for a trephination, may be performed, only it does not have to be carried into corneal tissue for any considerable distance.

With a keratome or a knife, a 5-mm. incision is made through sclera, 2 mm. above the corneoscleral margin. This line is scratched deeper and deeper until the uveal tissue is reached. If scleral bleeding is annoying, it is easily controlled by applying thrombin topical on an applicator.

Then an iris repositor is inserted through the wound, hugging the under surface of the sclera. If the repositor does not enter easily, the incision with the keratome is repeated, going a bit deeper this time. The repositor is tried again and, as it enters, it is placed gently into the anterior chamber, entering through the iris angle. The repositor is swung gently from side to side opening the angle over as great an area as possible.

With a Stevens scissors, two incisions are made 3 mm. apart at right angles to the original scleral incision going down to the corneoscleral margin. This piece of sclera is then picked up in toothed forceps and excised.

The iris is then gently grasped with iris forceps near the pupillary margin and, with a gentle side to side swaying motion it is carefully, gently, and very slowly withdrawn through the scleral wound until the black pupillary portion is visible. One incision is made through half of the withdrawn iris to the pupil and this pillar allowed to recede. The other portion of the iris, which is still in the iris forceps, is allowed to lie on the sclera just as it falls. No attempt is made to straighten the iris or to place the pigmented layer of the iris against the sclera.

The conjunctiva is now closed with a

Fig. 1 (Laval). The ab externo scleral incision is made 5 mm. long with the point of a keratome 2 mm. above the corneoscleral margin until the uveal tissue is reached.
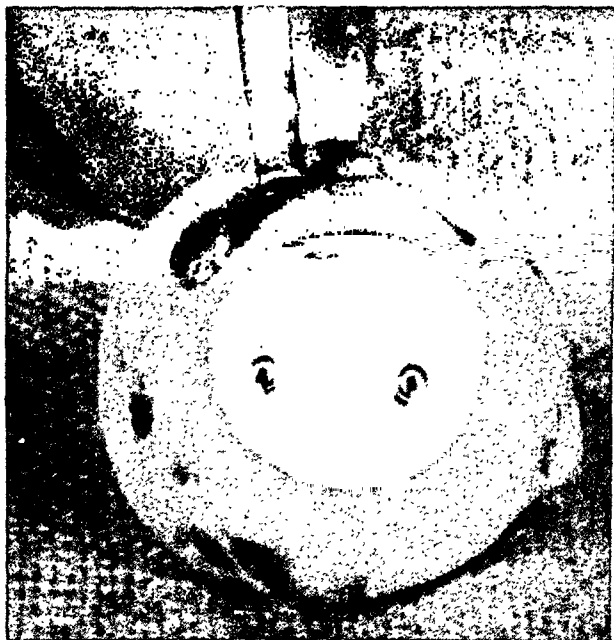

Fig. 2 (Laval). An iris repositor is then placed in the wound, hugging the inner scleral surface, and gently continued forward until the repositor enters the anterior chamber. The repositor is then moved from side to side freeing the angle (gonio-dialysis).
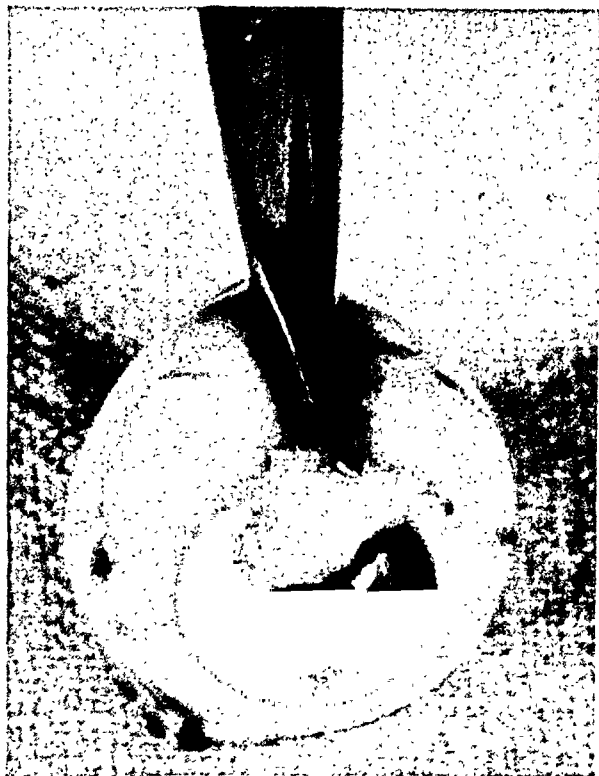
Fig. 3 (Laval). Two incisions, 3 mm. apart, are then made in the sclera toward the corneo-scleral margin for a distance of 1 mm.

running silk suture; a knot is tied at both ends and the bites are taken rather closely together. In this way a tight closure is obtained and the ends of the suture can be
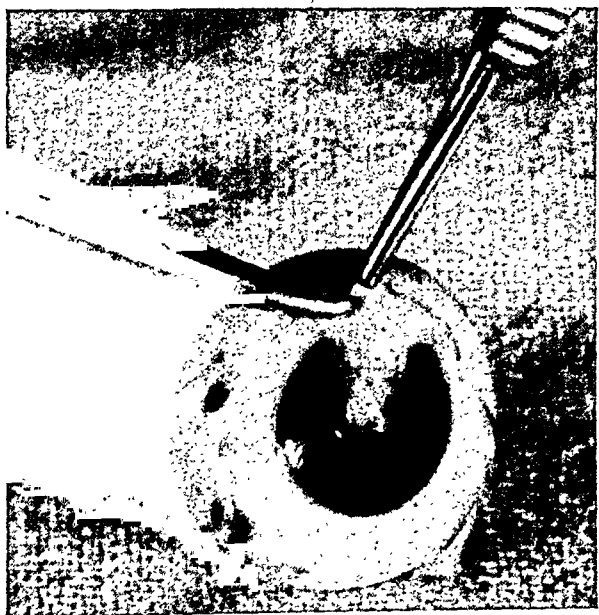

Fig. 4 (Laval). This piece of sclera is cut off with scissors giving a scleral opening measuring 3 by 1 mm.

Fig. 5 (Laval). A scleral tongue 2 by 5 mm. has been excised. This has been made extra large for purposes of demonstration but in actual practice does not exceed 1 by 3 mm.

cut quite short. One drop of 1-percent atropine is instilled and the eye bandaged.

EXPERIMENTAL OBSERVATIONS

I was curious to know what structures my iris repositor traversed as it passed from the scleral incision, 2-mm. above the corneo-scleral margin into the anterior chamber. Accordingly, I obtained a normal globe from the Eye-Bank, made the scleral incision, and
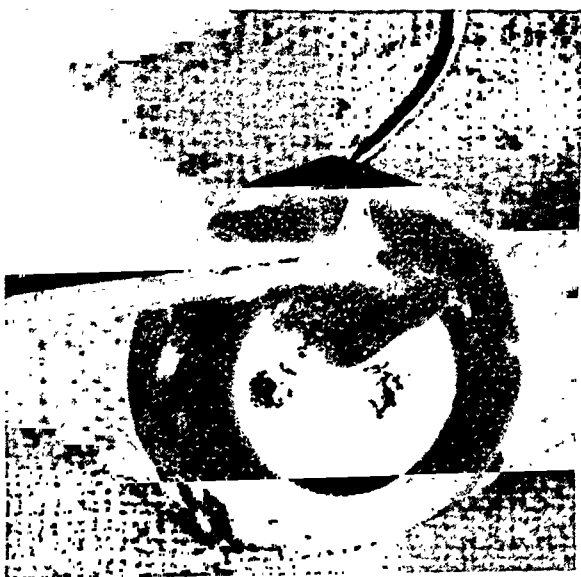

Fig. 6 (Laval). The iris is withdrawn until the black pupillary seam is seen; then it is cut half-way across.

inserted along the path of the repositor a piece of black silk suture material. The eye was fixed in Bouin's solution, sectioned, and stained with hematoxylin-eosin. Figure 9 shows the site of the scleral ab externo incision, (S) the suture material entering the sclera and passing through the ligamentum pectinatum (L).

In other words, the goniodialysis succeeds in cutting the trabeculas and freeing any anterior peripheral synechias, if present. A filtration tract is thereby formed connecting the anterior chamber through the angle with the outer surface of the globe. This tract is kept patent by the inclusion of iris tissue in the entire length of the channel. The length of the tract is cut in half by removing a 1-mm. piece of sclera, thus bringing the opening in the sclera near the filtration angle. Furthermore, by withdrawing and cutting the iris after the sclerectomy, the iris is cut directly at its root.
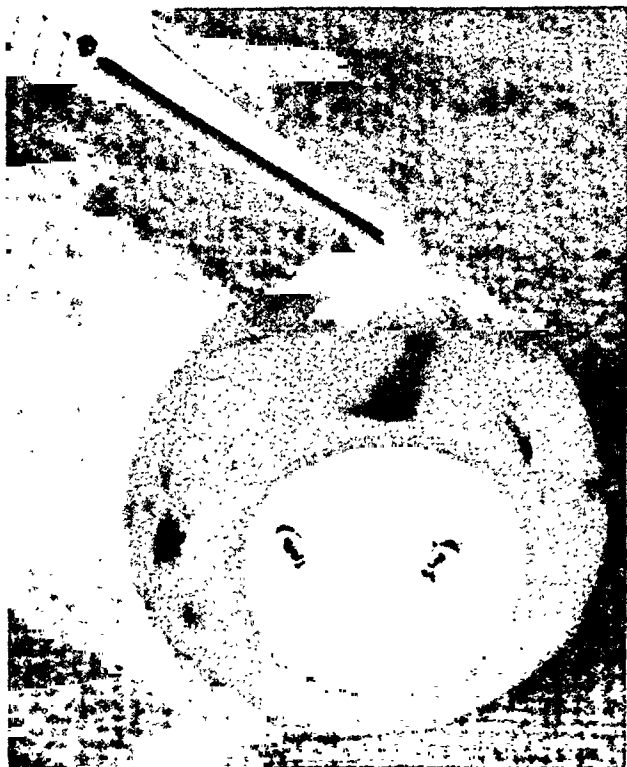

Fig. 8 (Laval). The conjunctival flap covers the iris.

Fig. 7 (Laval). The iris which is in the forceps is allowed to lie on the sclera as it falls; no attempt is made to turn the pigment surface face up or down.

Summary

The operation is advocated because: (1) It is simple and requires no great amount of surgical skill; (2) a thick covering of the filtration area is obtained instead of a very thin covering as in a trephination; (3)

regardless of the use of gonioscopy before the operation this procedure can still be carried out because the goniodialysis cuts through the filtration angle and any adhesions, if present; (4) by using the ab externo route for the scleral incision with the

Fig. 9 (Laval). Section of eye fixed in Bouin's solution and stained with hematoxylin-eosin. (S) Site of incision. (L) Ligamentum pectinatum. (M) Scleral meshwork. (Sc) Schlemm's canal.

keratome, the danger of injury to the lens is removed and one is also assured of making an unbeveled incision directly over the filtration angle; (5) the size of the scleral excision, which can be varied to suit the individual case, will be determined by the amount of tension with and without drops.

Addendum

It is of interest to note here that an article recently appearing in the Brazilian ophthalmic literature reports an operation of simple goniodialysis executed in a manner somewhat similar to the one I have described, but without sclerectomy and without iris inclusion. The author, R. Granville,[2] performed the goniodialysis on 4 patients in 2 of whom the tension was satisfactorily controlled.

To accept the concept that a goniodialysis alone will reduce intraocular pressure one would have to suppose that enough of the aqueous in the anterior chamber cannot get into Schlemm's canal because the fibrillas of the meshwork of the filtration angle are so thickened and closely woven to each other as to block the aqueous at (L) in Figure 9. The remainder of the fibrillas of the meshwork (the scleral meshwork—M) would have to be normal in thickness to permit the aqueous to reach Schlemm's canal (Sc), which must also be considered patent and functioning. The goniodialysis makes an opening in the thickened arc of fibers at (L) and permits the aqueous to get to (M) where the spaces in the meshwork are sufficient in number and size for the aqueous to get into Schlemm's canal (Sc).

According to Barkan,[1] his technique of goniotomy for congenital glaucoma "makes the incision only in the meshwork of the filtration angle" and goes through the same thickened arc of fibers at (L) in Figure 9. The direction of the incision in Barkan's goniotomy is from the anterior chamber outward through the thickened area into the supposedly normal fibers of the scleral meshwork. Schlemm's canal is not incised and, again, one must suppose that Schlemm's canal is normal and that the aqueous has been kept from Schlemm's canal only by the thickened area of fibers of the meshwork at the filtration angle.

Accordingly Barkan, in his goniotomy with the aid of a surgical contact glass, is accomplishing the same thing that I accomplish with the goniodialysis by the ab externo route (trabeculotomy as Barkan suggested). Believing this to be true, I have performed a goniodialysis over one third of the area of the filtration angle in a case of congenital glaucoma in which an earlier iris-inclusion operation had failed to control the tension.

The incision in the sclera extended over one third of the circumference of the globe, 2 mm. behind the corneoscleral incision. The iris repositor was inserted and the iris angle freed over this entire area. The conjunctiva was sutured with a continuous plain catgut suture with a knot at each end to insure tight closure. There was no reaction and the tension fell from 40 mm. Hg (Schiøtz), before operation, to 20 mm. Hg (Schiøtz), after the operation. It has remained at 15 mm. Hg (Schiøtz) for the past three months. Of course, this is an absurdly short observation period but time and more cases will give the verdict.

Granville, the Brazilian ophthalmologist, was able to separate a large area of the angle through a 4-mm. scleral incision, but I found it difficult to manage and also quite indefinite of execution. My next case will have a series of three 5-mm. incisions about 5 mm. apart and, through these, the areas of goniodialysis can all be connected quite simply.

136 East 64th Street (21).

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2. Granville, R.: Goniodialise. Revista Brasileira de oftal., 5: No. 4 (June) 1947.

SUTURES USED IN CATARACT SURGERY: A REVIEW*

Dudley P. Bell,† M.D.

Piedmont, California

There has been a great deal written concerning the value of sutures as used in cataract surgery, and there will be a great deal more written regarding the relative merits of various sutures used in cataract surgery. The purpose of this paper is to present a review of the subject to date, with comparisons, rather than to introduce any new methods of technique.

Historically, according to Brown,[1] some form of surgical treatment for cataract dates back 2,000 years or more. This early form of treatment was crude in relation to present surgery, with couching and reclination being the methods of choice. Charles de St. Yves[2], 1707, was probably the first to remove a lens through a corneal incision; however, this was on a lens previously dislocated into the anterior chamber following an accident.

It is generally felt that the honor and the credit should go to Jean Jacques Daviel,[3] 1745, as being the first to perform the modern cataract extraction. His method, as originally described, has not been changed to any great degree up to the present time.

The first to use a suture in the closure of a cataract incision was Henry W. Williams,[4] 1867, of Boston. Dr. Williams was the president of the American Ophthalmological Society and ophthalmic surgeon to the City Hospital of Boston. The first suture he described was corneoscleral in type, later to be modified by himself as a scleroconjunctival suture. It seems timely to present the following from the original article by Dr. Williams:

"The advantage of the corneal flap extraction may be much enhanced, and its dangers materially lessened, in my judgment, by the use of a suture to retain in apposition the edges of the wound. Securing a more immediate union, we not only avoid ulceration of the border of the flap and prolapsus iridis with its attendant evils, but obtain the more prompt restoration of the fullness of the globe, and of the normal relations of its several parts, lessen the chances of irritation from pressure of any cortical fragments or remnants of capsule upon the delicate contiguous structures, and the occurrence of iridocyclitis. This suture, a single strand only of the finest glover's silk, passed through the edges of the wound by means of a very minute, short needle, held by forceps, can be tolerated, without detriment, even in the cornea; but at present I am disposed to extend the corneal flap at its apex a little way into the conjunctiva, so as to allow of the placing of the suture in this membrane, where it is more easily inserted than through the tougher corneal tissue."

Williams used the corneoscleral suture in 48 cases which he reported. In the same year probably the second surgeon to use the corneoscleral suture was R. Chisholm.[5] He reports its use in one case and should be given due credit for being an early advocate of suture in cataract surgery, although his name has long been forgotten in this connection.

Sutures of this type or of any type were not used to any extent until revived by Kalt,[6] in 1894. Even then the majority of ophthalmic surgeons were not in favor of using sutures and this feeling is not entirely dispelled today. Many arguments were raised against the use of sutures some of which were: the procedure was too time consuming, it might endanger the eye due to inflammation, the sutures were too apt to be cut during section, the procedure was too complicated. Some authors went so far as to say

that the worry regarding sutures spoiled the thrill of a perfectly executed section. Gradually sutures became more accepted, and the discussion in the literature shifted from whether or not to use sutures to an attitude of what is the best type of suture to use. Actually there can only be a few basic types of procedures; but the modifications are legion.

The advent of adequate anesthesia in ophthalmic surgery has done much to advance the use of sutures; since, in the past, the element of time would not permit its use. As late as 1917, McCorry and Shanker,[7] writing in defense of the conjunctival flap (without sutures), felt that this added procedure did not take too long. Their time was from 1 to 3 minutes from start to finish (not counting dressing) for a cataract operation. E. E. Maddox,[8] feeling that adequate closure was necessary, advocated using, and did use for a while, newly melted wax, but the results not being uniform he gave this up for sutures, in 1911.

TYPES OF SUTURES

Ellett,[9] in 1921, felt there were only two main types of sutures to be classified; one in the ocular coats and a second as a conjunctival flap or bridge. This is inclusive but does not break the various types down to their actual finer points. The following five principal processes and their advocates, as presented by Bonfioli,[10] seem to cover suture types adequately:

I. Conjunctival—Conjunctival

A. Classic conjunctival flap—Arruga, Elschnig, Sinclair, and Tersion.

B. Conjunctival recovering—Faure, Van Lint, Federici, Birch-Hirschfeld, Clark, Villard, Bartels, Gifford, Olah and Wood.

C. Conjunctival bridge—Chuckie, Wenzel, Desmarres, Hazner, Lamb, Pavia, Dusseldorp, Patton, Eber, Pochissoff, Salaviev, and Slocum.

II. Cornea—Conjunctival

Frisch, Verhoeff, and Scandbygaard.

III. Sclera—Conjunctival

Derby, Walker, VanPoole, Horwath, Verhoeff, and DeVaul.

IV. Corneoscleral

Suarez de Mendoza, Kalt, Liegard, Piccaluga, Baldino, Saint-Martin, Stallard, Olmos, and Corboy.

V. Corneoscleral—Conjunctival

Frisch, Gomez, Marquez, Wolfe, McLeod, Rabinowisch, Stallard, Leech, Sugar, Lindner, McLean, Verhoeff, and Castroviejo.

The Van Lint[11] flap differs from the Kuhnt[12] flap in its manner of preparation rather than in its function, as both are functionally of the recovering type.

A Van Lint flap is made by a limbal incision, the conjunctiva is dissected back freely so it will slide over the incision and about one third of the cornea, being then sutured in its new position at the 3- and the 9-o'clock positions.

In forming a Kuhnt flap, the limbal incision is made similar to the Van Lint, and then a secondary incision is made in the conjunctiva a few millimeters above the limbus. The undermining is not carried out to the extent necessary for the Van Lint flap, as the secondary incision allows the free movement of the newly formed flap in its covering of the incision and of the cornea. The sutures are placed as in the Van Lint flap but not so far down, with the resultant flap covering a smaller area of cornea.

Figure 1 is self-explanatory for most of the conjunctival sutures; however, it is of interest to note that Van Poole[13] used preplaced sutures of human hair stretched across the cornea. Using this material he had no cases of corneal ulceration or inflammation, and he routinely removed the sutures on the 4th postoperatvie day.

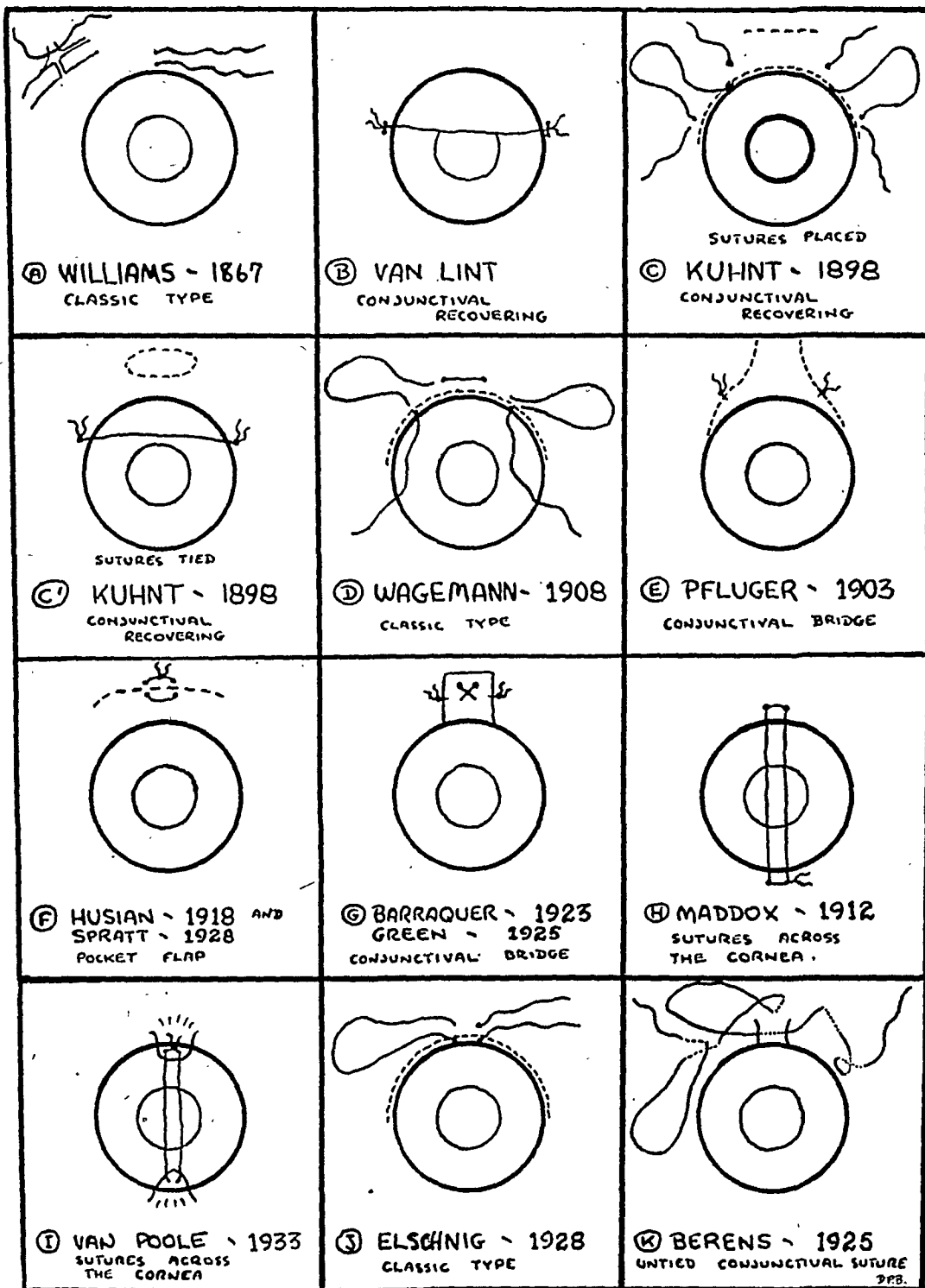Also of note is the untied conjunctival su-

Fig. 1 (Bell). Examples of conjunctival-conjunctival sutures.

ture of Berens[14] which is placed after the section and conjunctival bridge have been completed. The suture is 45 cm. long and made of No. 3 twisted black silk impregnated with paraffin. It is introduced by means of a small curved cutting needle. Berens felt that the only contraindication to the use of this type of suture would be extreme atrophy of the conjunctiva.

The scleral sutures as seen in Figure 3 may be divided into two types; those which are sclera-conjunctival as described by Verhoeff, Derby, and Horwath, and those which are sclera-sclera as to apposition of tissue,
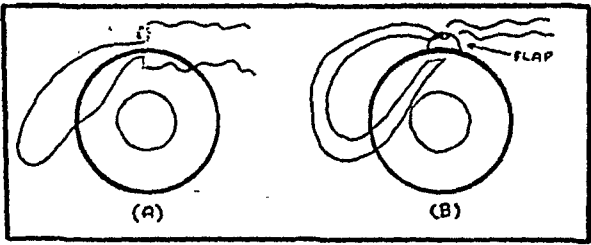
Fig. 2 (Bell). Scandbygaard's two variations
of cornea-conjunctival sutures.

with a secondary closure of conjunctiva. Examples of the latter type were described by Walker, DeVaul, and Hymes. All three of the sclera-conjunctival types have a small flap of conjunctiva turned down, and the suture is placed through sclera and conjunctival flap for closure.

In the sclera-sclera type with secondary covering by conjunctiva, the suture is preplaced, both bites in scleral tissue. The manner of scleral preparation is different with each advocate of this type. Walker[15] attained an exact appositional suture by first making a scleral groove with a guarded cataract knife parallel to the limbus and 2 to 3 mm. back in scleral tissue. This groove went to about one third of the scleral depth and then a tongue of sclera was split out by means of a keratome incision in the lip nearest to the limbus.

DeVaul[16] makes a scleral tunnel with a cataract knife parallel to the limbus. The tunnel is divided in its long axis and then
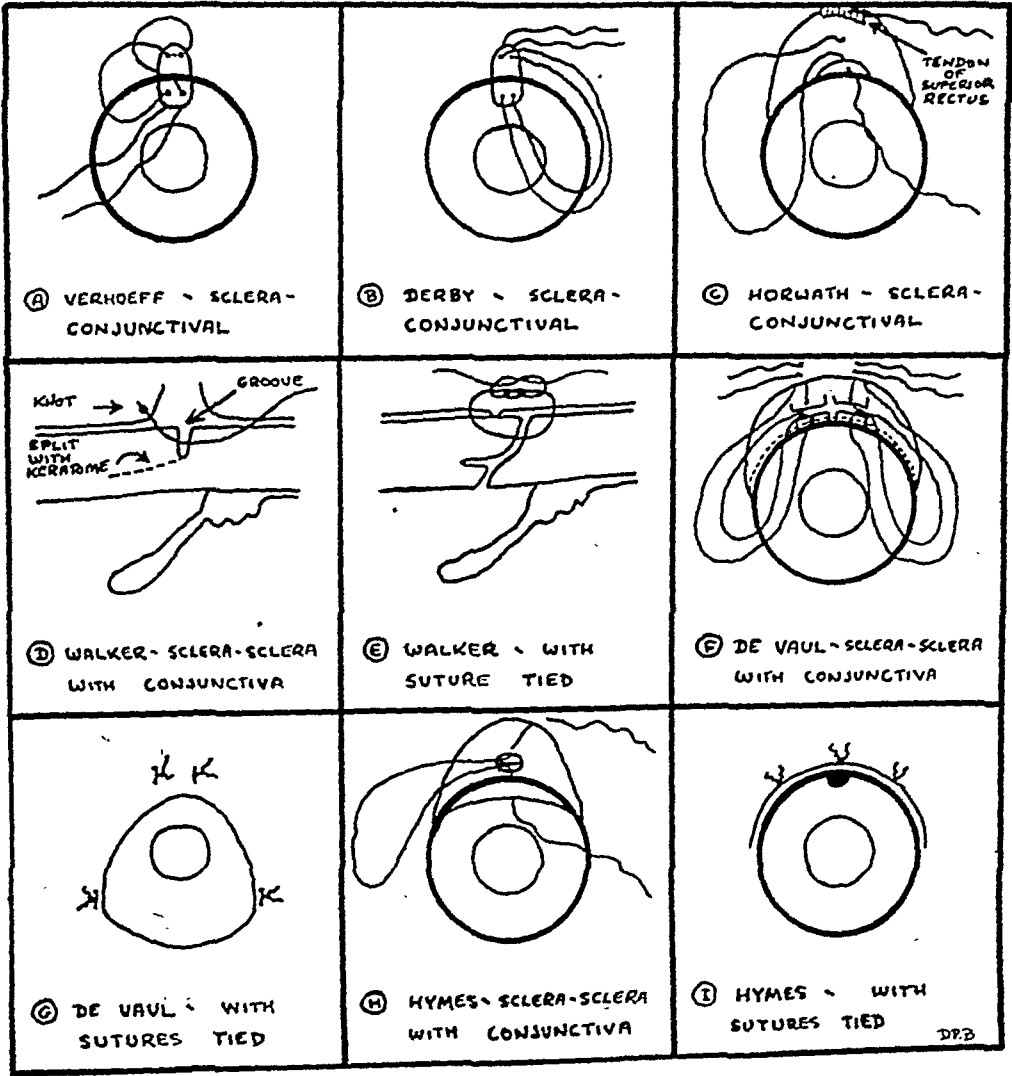

Fig. 3 (Bell). Sclera-conjunctival sutures and sclera-sclera sutures with conjunctiva incorporated.
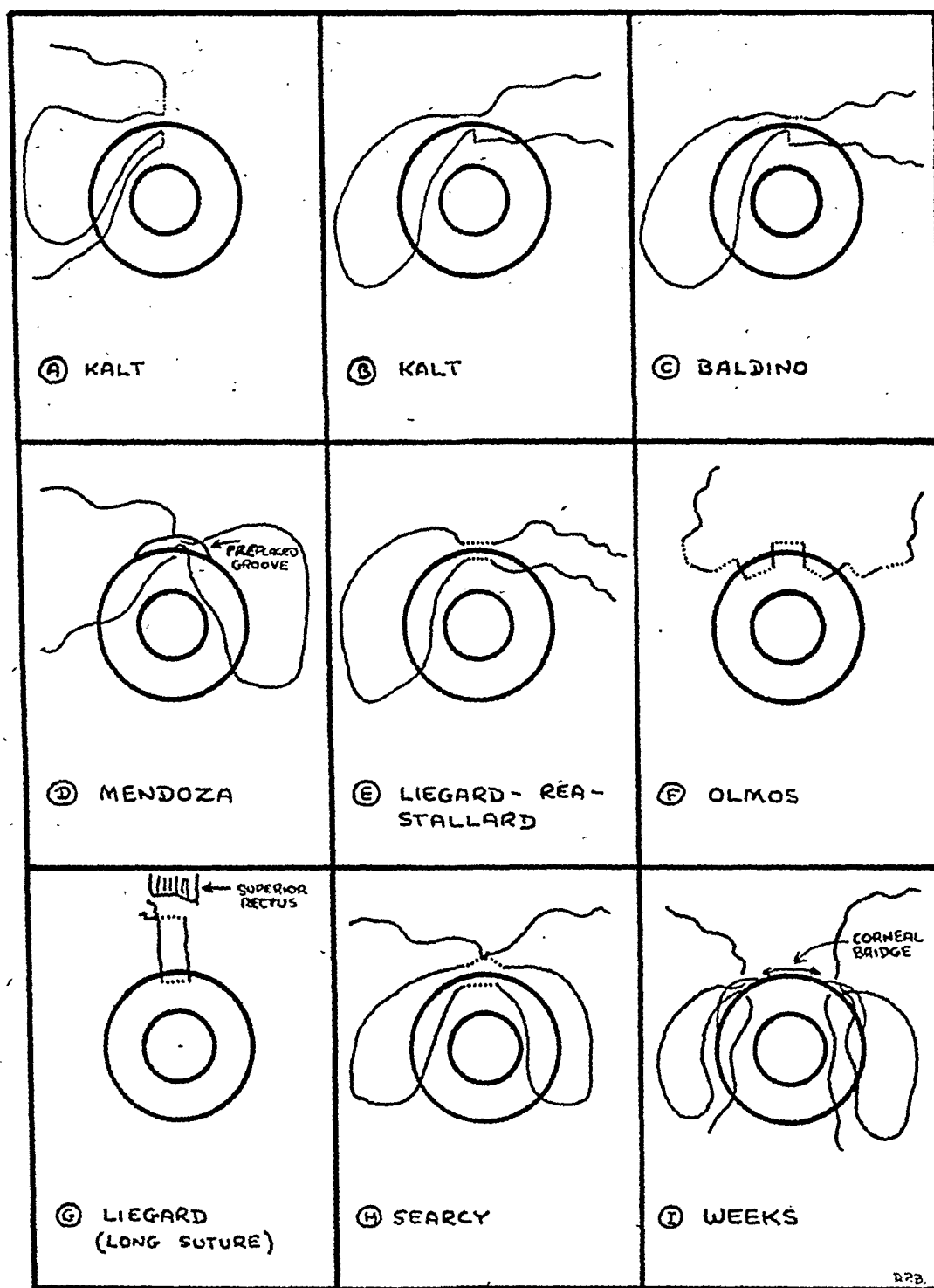
Fig. 4 (Bell). Corneoscleral sutures.

bisected to form four small flaps in which the sutures are placed. Hymes[17] makes a concentric wedge-shaped scleral flap at the 12-o'clock position by means of a concave scleral knife. This incision is closed with a single scleral-scleral suture and two conjunctival sutures.

Closure with scleral-scleral apposition is more firm than with scleral-conjunctival. It is, however, somewhat more difficult to place the purely scleral type of suture according to DeVaul.

The corneoscleral suture as used today was very probably described first by Kalt[18] in 1894. The following is taken from his paper on the subject: "The suture consists
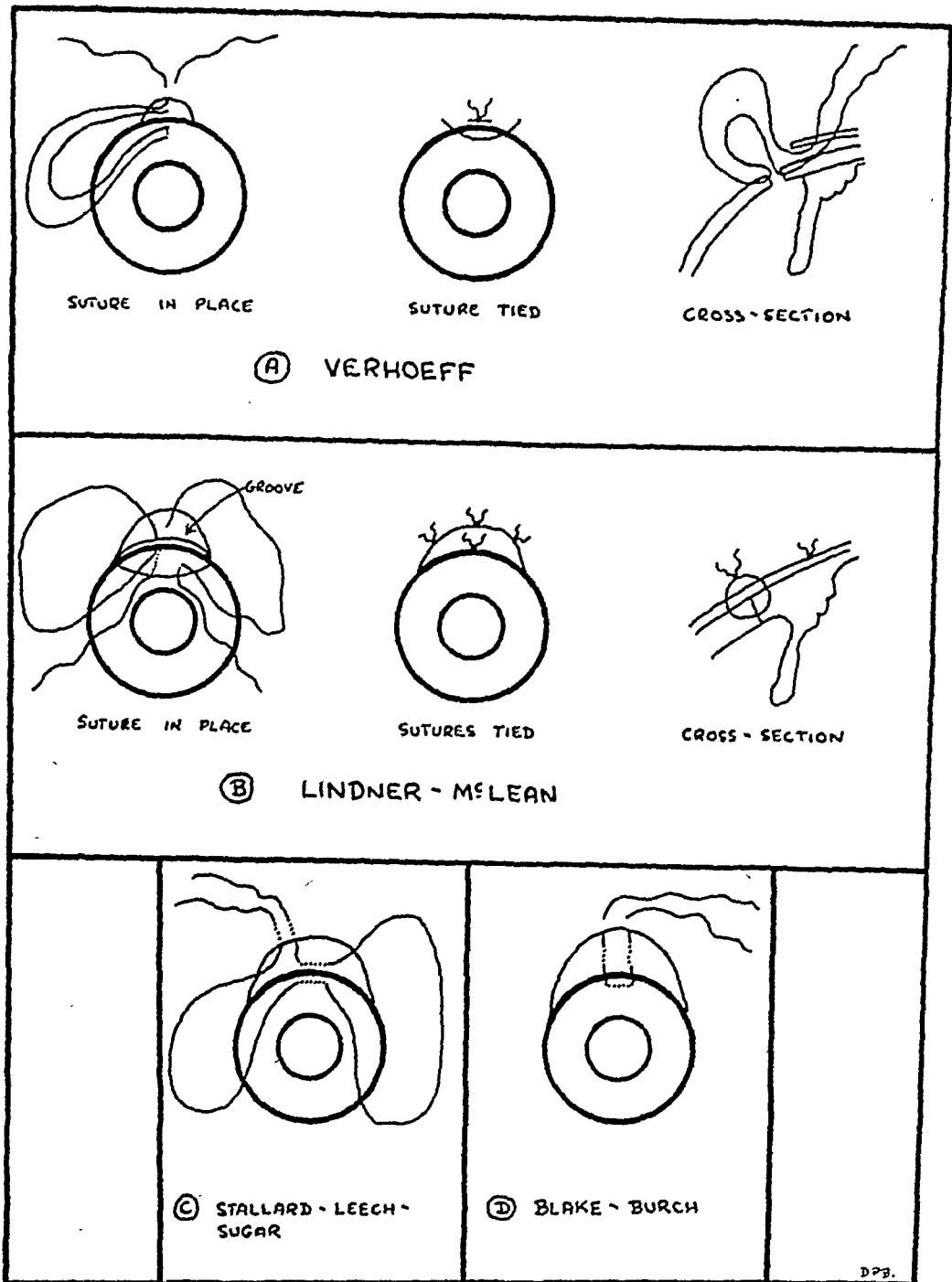
Fig. 5 (Bell). Corneoscleral-conjunctival sutures.

of a vertical corneal portion and a transverse episcleral portion. The whole forms a T with a gap between the junction of the horizontal with the vertical portion. The length of each of the portions does not exceed 1 mm. The vertical intracorneal branch follows the vertical corneal meridian and stops exactly at the junction of the transparent portion with the sclera. The horizontal portion traverses

the opaque part of the limbus as near the cornea as possible. An interval of 0.5 mm. corresponding to the limbus is ample to permit the passage of the knife."

From Figure 4 it is clear that the sutures of Kalt, Baldino, Liegard, Rea, and Stallard are all quite similar. Mendoza's differed from the previously mentioned sutures in that he used a preplaced groove. Olmos used

a complicated running type of suture with five scleral bites and two corneal bites while Searcy[19] used a single corneal bit with two scleral bites with the tie at the apex of the two scleral bites.

All of the above corneoscleral sutures are preplaced, while that of Weeks[20] differs in this respect. He makes the section, all except a corneal bridge at the 12-o'clock position, of about 2.4 mm. A small iris hook is then slid under the bridge and a corneoscleral suture is placed on either side of the bridge. The sutures are held out of the way and the section is completed by cutting the bridge with scissors.

In Figure 5 the first corneoscleral-conjunctival suture is one described by Verhoeff,[21] in 1927, and is a preplaced corneoscleral suture with a limbal flap allowed to retract away from the limbus. The suture may be inserted in more than one way according to the author. The third suture (C in Figure 5) is similar to the regular Stallard-type suture with the exception of the limbal conjunctival flap.

The suture termed the Lindner-McLean, which was described by McLean[22] in 1940, has a turn down flap 1 to 2 mm. from the limbus and extends from the 3- to the 9-o'clock positions. A small slot is made at the base of the flap with a Lundsgaard or other type of knife and extends about halfway through to the anterior chamber. The suture of fine black silk is run through the flap, reversed, and run back through sclera and cornea, coming across the preplaced groove or slot. This gives exact apposition of tissue (corneoscleral). More than one suture of this type may be preplaced as desired. The conjunctiva likewise may then be closed by additional sutures as desired. Figure 5-D is a transverse corneal bite with two vertical scleral bites augmented by a flap of conjunctiva incorporated into the closure.

Types of suture material

Davis,[23] in a preliminary report (1944), mentions his use of 5-0 plain catgut after the section. A double knot cut short was used and showed very little reaction except for some slight conjunctival edema in a few cases. Absorption was complete in 7 days and showed about the same amount of reaction as seen in other suture material. The author and his associates used plain catgut with good results in 70 cataract operations.

Hughes, Guy, and Romaine,[24] in 1944, made comparative studies using nylon, twisted and braided; plastic material, single strand and braided; 3-0 surgical gut, plain and chromic; and 5-0 surgical gut, plain and mildly chromicized. These materials were compared to 8-0 black surgical silk in the closure of cataract incisions, with the following conclusions:

1. Absorbable material probably more desirable and eliminated complications at time of removal.

2. The best size was 5-0, fine caliber, surgical gut.

3. Mildly chromicized gut held edges 14 days but caused objectionable reaction in tissues.

4. Plain surgical gut (5-0) held 5 days with only a slightly greater reaction than silk.

5. The knot is too bulky to be tied over corneal tissue.

6. Plain surgical gut (5-0) is not so flexible as silk but nearly approaches it. It is an advance but doesn't meet all requirements of the ideal suture.

Experimental work

In 1939, Hilding[25] felt that the handling of limbic incisions in cataract surgery had never been entirely satisfactory from the standpoint of preventing postoperative wound gaping and prolapse of the iris. He experimented with ox eyes, making various incisions and closures comparable to those used in cataract surgery. A manometer was used, making the measurements in millimeters of mercury, to determine at what pressure the iris would prolapse.

When a simple linear incision was used, the iris prolapsed at 30 mm. Hg pressure. With the incision covered by a conjunctival

flap, the iris prolapsed with 40 mm. Hg pressure and, when the lips of the wound were closed with one sclerocorneal suture, it took 240 mm. Hg pressure to prolapse the iris. Combining one sclerocorneal suture with an iridotomy, the iris could not be made to prolapse at the greatest pressure recorded on the type of manometer the author used. Hilding concluded that sutures placed directly in the lips of the incision, plus an opening in the iris, were effective in holding the wound closed and in preventing herniation of the iris.

Continuing his studies on the mechanics of iris prolapse and safety factors in cataract

corneoscleral sutures and 3 peripheral iridectomies) showed only half the amount of very tiny iris prolapses as did operation No. 2 (4 corneoscleral sutures and no iridectomies).

STATISTICAL STUDIES

Prior to the use of the suture which bears his name Stallard[27] had postoperative hyphemia in 30 to 35 percent of his cataract patients. In using this suture in 107 consecutive operations (79 extracapsular and 28 intracapsular cataract extractions) no hyphemia was seen in the postoperative period.

Visual acuity is one of the most important end results of cataract surgery. Klein,[28] in

TABLE 1

COMPARISON OF COMPLICATIONS USING THREE TYPES OF WOUND CLOSURE*

Type of Closure	Prolapse of Iris and Vitreous; Incarceration of Iris	Hyphemia	Anterior Chambers Not Reformed
Conjunctival flap without sutures	12 cases (8.0%)	9 cases (6.0%)	11 cases (7.3%)
Conjunctival flap with sutures	10 cases (6.6%)	17 cases (11.3%)	9 cases (6.0%)
Corneoscleral suture (Stallard type)	6 cases (4.0%)	7 cases (4.6%)	4 cases (2.6%)

* Survey by Leech and Sugar.

closure, Hilding,[26] in 1945, reported on 187 cataract operations. He felt that the mechanics of iris prolapse were an intact iris over a sudden defect in the outer coat plus the pressure from the posterior aqueous, which then pushed the iris through the opening or incision. He is of the opinion that one corneoscleral suture will prevent gaping in roughly 25 to 35 degrees of arc of the incision. An iridectomy or iridotomy guards 5 to 10 degrees of the arc on either side from iris prolapse. Roughly, this would mean that, in the average incision of 140 degrees, one would use for protection at least 4 corneoscleral sutures or 6 to 8 iridotomies. However, in using combined protection at 5 points, 3 sutures and 2 iridotomies would provide adequate protection.

An interesting point of comparison was shown by Hilding in the two types of operations used in this series. Operation No. 1 (2

1939, reported that visual acuity was better with the Liegard suture or the flap section than with a Kuhndt apron-type of closure. In 1942, Klein[29] felt, in reviewing cases, that there was a greater incidence of hyphemia seen where sutures were used. However, since most hemorrhages occur on the 5th to 6th day and he removed the sutures on the 5th or 6th day, he felt there might be a correlation in these incidences. He felt that Stallard's suggestion of not removing sutures until the 14th day might prevent many cases of hyphemia.

An impartial survey of the records at the Illinois Eye and Ear Infirmary, by Leech and Sugar,[30] in 1939, disclosed some interesting facts. They wanted to see whether the suturing of cataract wounds was of value or not in preventing postoperative complications. In the study three types of cases were reviewed:

1. Those in which conjunctival flaps were used without sutures.

2. Conjunctival flaps with sutures.

3. Corneoscleral sutures (Stallard type).

One hundred and fifty histories for each of the above groups were tabulated with the following postoperative conditions being considered:

1. Prolapse of iris or vitreous or both.

2. Hyphemia.

3. Delayed closure of the anterior chamber.

Table 1 shows the complications they found with the various types of wound closures.

When the corneoscleral suture was used, Hilding[31] found the postoperative astigmatism in 62 percent of his cases to be 1.5D. or less. When patients with other preëxisting pathologic changes were eliminated, 90 percent had normal or near normal vision.

CRITERIA FOR THE CLOSURE OF CATARACT WOUNDS

In a survey of the literature, the criteria for the closure of cataract wounds by McLean[32] seem to be inclusive and are herein reproduced:

A. The suture should be inserted in solid corneal and scleral tissue and not in loose yielding conjunctiva.

B. The suture should be placed before the section is made and should not require extensive manipulation after the eye is opened.

C. It should go through, not over, the lips of the wound so as to give firm closure and exact preoperative apposition.

D. The entire wound should be covered by conjunctiva as an added protection and better surgical closure.

E. The method should not be too complicated for the average surgeon.

INSTRUMENTS AND SUTURES

The essentials for a proper wound closure in cataract operations are:

1. Adequate fixation with scleral forceps, scleral pick, hook, or special instruments.

2. Sharp atraumatic needle and fine black-silk suture.

3. Needle holder of excellent design which will prevent turning of needle.

Ellett[33] stressed the fact of always using the best type of needle and suture; the needle to be curved and round rather than to have a cutting edge. To be firm, the bite of the needle should not be at the wound edge, but far enough back. His choice of needles was the semicircular, curved type of Kalt, Chevallereau, and Toulant, the length being from 18 to 12 mm.

To prevent slipping of the needle, Higgens[34] devised a modification of the Kalt needle holder. The tip is made with a convex upper jaw and a concave lower jaw which fits the curve of the needle.

It is generally agreed that the time to remove sutures is from 7 to 14 days postoperatively. A good and safe method for the removal of sutures is the one advised by Hilding.[35]

With good illumination and adequate anesthesia, they are removed in 7 days. The lid retractor is held in the left hand, and the scissors in the right hand are pointed upward and away from the cornea. Cut the sutures, lay down the scissors, and remove sutures with forceps, grasping each suture above the cornea and pulling toward the center of the cornea.

SUMMARY

There are dozens of sutures mentioned in the literature for the closure of cataract wounds. There are, however, only five main classifications based on types of insertion:

1. The conjunctival-conjunctival.

2. The cornea-conjunctival.

3. The sclera-conjunctival.

4. The corneoscleral.

5. The corneoscleral-conjunctival.

It is evident that many of the types described in the literature are actually minor modifications of types already in use. Since all of the sutures in use are designated by a

different surname, it makes for great confusion. To clarify some of the resulting confusion, it would seem advantageous to think in terms of tissue involved rather than in men's names. An anatomic nomenclature would make for greater simplicity and clarity.

The advantages of sutures over conjunctival bridges is best summed up by Elschnig:[36]

1. All work in the anterior chamber is made easier with sutures because of the improved exposure.

2. Wound closure with suture is much more secure both primarily and in the healing period.

3. Vitreous prolapse is often prevented.

4. There is less chance of infection.

5. With peripheral iridotomy and sutures, there is rarely an iris prolapse.

To the above list might be added:

1. There is less postoperative hyphemia when sutures are used.

2. There is less postoperative astigmatism.

3. There is a greater mobility for elderly patients and less danger for those unable to coöperate.

CONCLUSIONS

1. Some form of suture should be used in the closure of all cataract wounds. The principle of suturing wounds should be followed as dogmatically in ophthalmic surgery as it is in all other branches of surgery.

2. The corneoscleral (preplaced in groove) truly appositional type of suture seems to afford the most perfect closure.

3. Most of the comparison of types of sutures as reported in the literature is based upon clinical evidence rather than upon experimental evidence. At the present time, there is need for more experimental study, regarding sutures in cataract surgery.

4. At present, silk is the best form of suture material for use in the closure of cataract wounds.

5. Until overwhelming experimental and statistical evidence piles up in favor of the one-perfect type, many types of wound closures will continue to be used.

141 Caperton Avenue (11).

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AMOUNT OF EYE MOVEMENT OBJECTIVELY PERCEPTIBLE TO THE UNAIDED EYE*

ELEK LUDVIGH, PH.D.

Boston, Massachusetts

Several ophthalmic tests involve the examiner watching the patient's eye to determine whether the eye has moved, as in loss of fixation during campimetric or perimetric examination or during the determination of the angle kappa. Other tests, such as the cover test for squint and the transfer cover test for phoria, require the examiner not only to detect a movement of the patient's eye but also to determine the direction of the movement whether up or down, right or left.

When the examiner, as is ordinarily the case, is using his unaided eye, what accuracy can be expected of such tests? In order to throw some light on these and similar problems, a simple investigation was performed to determine the amount of eye movement objectively perceptible to the unaided eye.

Eye movements of various magnitudes were produced as follows. The examinee was seated facing a wall, 3.5 m. distant, on which was fastened a white sheet of paper at eye level. On the paper, in ink, were printed five dots in a horizontal row. The dots subtended 3 minutes of arc at the examinee's eye and the distance between the centers of two adjacent dots subtended 14 minutes of arc. The examinee fixated the center dot and on signal from the examiner, transferred fixation from the center dot to one of the other four dots. Thus, excursions of the examinee's eyes of 14 or 28 minutes of arc to left or right were obtained.[†]

[†] Excursions of as little as 10′ or as much as 57′ were occasionally produced for particularly good or poor examiners.

The examinee determined the direction and magnitude of each excursion by reading it off the top card of a pack which was shuffled before each series of observations. The examiner, seated facing the examinee, stated after each excursion in which direction the eye had moved. If in doubt, the examiner was forced to guess. An analogous procedure was carried out with the dots in a vertical row.

Each examiner selected what he considered to be ideal conditions for the observation. The room could be partially darkened, movement in the background or periphery was eliminated, some examiners

judgments was computed. The results are presented in Table 1.

Results vary from day to day and from examiner to examiner. In this investigation the same examinee was used for all examiners. It seems likely that the eye movements of some individuals are more readily perceived than are those of others.

It may be seen from the figures given in the table that vertical movements appear to be more difficult to discern than horizontal movements but this may well be attributable to chance since application of the t-test[2] shows that $P > 0.2$.

The results show, in general, that, even

<div style="text-align:center">TABLE 1</div>

RESULTS IN TESTS OF EYE MOVEMENT PERCEPTIBLE TO THE UNAIDED EYE

Examiner	Horizontal Movement in Δ Necessary for		Vertical Movement in Δ Necessary for	
	95% Correct	99% Correct	95% Correct	99% Correct
A	1.9	2.5	1.3	1.7
B	.6	.8	1.0	1.3
C	.9	1.1	2.0	2.6
D	1.2	1.6	.6	.8.
E	.6	.8	.8	1.1
F	2.0	2.6	1.0	1.3
G	.9	1.2	.8	1.0
H	.6	.8	1.1	1.4.
I	.8	1.1	2.3	3.0
J	.6	.8	3.2	4.2
K	.6	.8	1.0	1.3
Average	1.0	1.4	1.4	1.8

used flashlights held in their hands or clamped to a stand. Some examiners gave the signal to change fixation by tapping rather than orally since they believed the jaw movement involved in saying "now" hindered observation.

The classical method of right and wrong cases[1] was employed to determine the probable errors of the data and from these the amount of eye movement necessary to produce 95-percent and 99-percent correct

under ideal conditions, excursions of much less than 1^Δ to 2^Δ cannot reliably be perceived by the unaided eye. In usual clinic conditions and with much less coöperation from the examinee, it seems advisable to adopt at least the upper limit of 2^Δ. This means that if it is desired to detect eye movements of $1°$ or less, either a subjective test should be employed or the examiner should use magnification.

243 Charles Street (14).

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REGENERATION OF NERVES IN EXPERIMENTAL CORNEAL GRAFTS IN RABBITS*

CLINICAL AND HISTOLOGIC STUDY

WALTER KORNBLUETH,† M.D., AND A. EDWARD MAUMENEE, M.D.
San Francisco, California
AND
JANE E. CROWELL
Baltimore, Maryland

The various factors which influence the final clarity of a corneal graft cannot be properly evaluated until it has been determined whether the elements of the donor cornea are replaced or survive. In a previous study,[1] histologic examinations of clear corneal grafts, stained with hematoxylin and eosin, revealed that the donor's corneal lamellae and Descemet's membrane were not replaced.

There was no destruction or replacement of a large number of stromal cells at any one time, but it could not be determined whether there was a gradual replacement of these cells or not. Endothelial cells were always found on the grafts 4 to 5 days after operation, but it was impossible to determine in all cases whether these cells had migrated from the recipient cornea· or belonged to the donor cornea.

The epithelium of the graft always sloughed and was replaced in 4 to 5 days by cells from the recipient epithelium. The fate of the corneal nerves was not discussed in the previous report because these structures were not visible in routine histologic preparations. The following report is based on a study of the clinical sensitivity of grafts to touch and histologic examinations of silver-impregnated frozen sections of corneal grafts.

REVIEW OF LITERATURE

Clinical and histologic reports on corneal grafts both in man and experimental animals have been numerous, but regeneration of corneal nerves into the tissue has not been extensively investigated. The sensibility of corneal transplants has been studied by several investigators, but the results of these workers have differed slightly.

Ascher[2] found that sensibility returned in two clear grafts but did not return in cloudy grafts. In one patient with a staphyloma of the cornea a whole corneal transplant was done. The graft became completely opaque except for a small translucent area in the center. In this case the graft was insensitive except for the small central translucent area.

Elschnig[3] stated that complete sensibility of the implant did not develop even in the oldest cases of transparent implants, but a sensibility to heavy touch was observed. Imre[4] noted that sensibility of the graft returned 10 to 12 months after operation.

Morone[5] was able to detect the return of sensibility in both clear and cloudy grafts one year after operation. He thought the return of sensibility did not depend on the degree of clarity, course of healing, or vascularization of the graft. He also observed that the host's cornea became hyposensitive following operation. Morone stated that Magitot believed the sensibility of the graft is connected with vascularization.

Thomas[6] tested 29 experimental grafts in rabbits and found no return of sensibility in 5 grafts which remained clear, but 21 of the 24 grafts which were cloudy did regain some sensibility. Thomas concluded that the ingrowth of blood vessels was essential for the return of sensibility to the transplant.
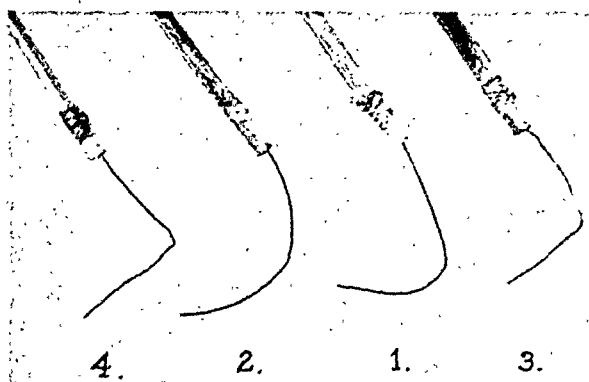
Fig. 1 (Kornblueth, Maumenee, and Crowell). Test object for determination of corneal sensitivity. (1) Equivalent to pressure of 25 mg. (2) Equivalent to pressure of 100 mg. (3) Equivalent to pressure of 300 mg. (4) Equivalent to pressure of 1,000 mg.

Galante[7] observed 8 translucent to opaque heterografts in dogs and rabbits and found that the transplants became sensitive at the periphery 10 days after operation. At the end of one month the sensibility of the grafts was equal to that of the recipient corneas.

Histologic studies for nerves in corneal grafts have been made less frequently than clinical observations on the return of corneal sensibility.‡

Babel and Campos[8] and Franceschetti and Babel[9] have reported histologic studies of nerves in grafts. In their first publication they examined four opaque human transplants which were removed in order to insert second grafts. In one of these grafts, removed 36 days after operation, no nerves were found. The remaining three grafts were removed from 10 months to 7 years after transplantation. In these specimens nerves were found entering the grafts adjacent to invading blood vessels deep in the stroma, but no nerves were found in the subepithelial region in any of the grafts.

In their second paper they reported a study of a clear human transplant obtained 7 years after operation. In this case they

found a well-developed subepithelial nerve plexus in the graft, but there were no nerves in the deeper structures except in one area where a few blood vessels had entered the margin of the graft. From these studies they concluded that, if a graft does not become vascularized, nerves other than those of the subepithelial plexus do not invade the tissue. They also suggested that the ingrowth of nerves into the subepithelial region of the graft might be essential for the continued clarity of a transplant.

EXPERIMENTAL OBSERVATIONS

All of the grafts used in the present investigation have been partial penetrating, full-thickness homografts in rabbits. The grafts were cut with a 4.5-mm. trephine blade attached to a dental drill. The transplants were held in place by continuous crisscross corneal sutures inserted into the recipient cornea as closely as possible to the edge of the graft. The sutures were removed on the 7th postoperative day.

a. *Clinical study*. The clinical sensibility of 12 clear and 10 cloudy grafts has been tested by touching the grafts and observing the blink reflex. The hairs near the eyes were clipped before examination to avoid a false blink reflex caused by touching these structures. The materials used for testing the corneal reflex were somewhat similar to v. Frey hairs. Pieces of sutures 2 cm. long were secured to match sticks and were bent to a right angle at 1 cm. from the tip of the suture (fig. 1). When the tip of the bent suture was pressed with maximal force onto a weighing pan of an analytical scale the first was just strong enough to lift 25 mg., the second 100 mg., the third 300 mg., and the fourth, 1 gm.

The blink reflex is admittedly not a very accurate test of corneal sensitivity in rabbits; nevertheless, it gave a general idea of the degree of sensibility of the grafts. The results obtained were about the same in the clear and cloudy grafts. The transplants were insensitive until about the 4th to 6th

‡ After this report was submitted for publication, an excellent study on degeneration and regeneration of nerves in corneal transplantation by Humberto Escapini was published in the Arch. Ophth., 39: 135, 1949.

week after operation, then they developed a slight sensibility to pressure (300-mg. test object) in the periphery of the graft. This gradually spread over the graft and by the 11th to 13th week the grafts became sensitive to lighter touch (100-mg. test object). On the whole the grafts did not regain as complete sensibility as the surrounding normal cornea.

These clinical observations on corneal transplants correspond well with the recent work of Marcus Jent.[10] In 1945 he made a careful study of the regeneration of the corneal nerves in rabbits following an incision through the cornea around the entire periphery down to Descemet's membrane. In these experiments he found that the sensibility of the cornea returned first to the cicatricial ring in about 4 weeks and then gradually progressed over the entire cornea.

b. *Histologic study.* Seventeen clear and 13 cloudy grafts removed from two days to one year after operation were examined. No appreciable difference was found in the regeneration of the nerves in the clear and cloudy grafts. There was a variation of the ingrowth of the nerves from animal to animal but on the whole the invasion of the nerves and further developments coincided within a week to two weeks in all specimens.

Perpendicular and horizontal frozen sections were made on equal halves of the grafts and surrounding corneas. The staining method used was essentially the same as Campos's modification[11] of the silver impregnation technique of Bielschowsky and Gros. The slight modification of Campos's method devised by one of us (J. E. C.) gave good and uniform staining of the corneal nerves. The details of the technique used follow.

DETAILS OF TECHNIQUE

1. Fix the whole eye for 24 hours or longer in neutral formalin, 10 percent (formalin neutralized to pH 7.4 with aqueous calcium oxide not more than 0.1 percent. Filter aqueous calcium oxide before neutralization).

2. Remove cornea from globe.

3. Wash cornea in running tap water 1 to 2 hours, then wash in distilled water. Change distilled water every half hour for 6 hours.

4. Cut frozen horizontal sections 50μ and collect in distilled water. Vertical sections should be cut 75 to 80μ.

5. Mordant overnight (about 18 hours) in solution of silver nitrate (10 to 15 percent) in the dark.

The following steps are facilitated by placing the sections in 50-cc. beakers. Add and decant the various solutions.

6. Wash in distilled water and decant as quickly as possible (15 to 30 seconds).

7. Wash in 3 changes of neutral formalin (1 percent). Add about 10 cc. of neutral formalin for each washing. Total time, 2 to 3 minutes. Formalin will become brown or turbid occasionally during washing.

8. Wash sections in silver ammonium solution and decant immediately. (This is done to remove any trace of formalin which may have remained in beaker. Formalin in the presence of silver-ammonium solution will cause sections to turn bright yellow.) Add 10 cc. of silver-ammonium solution and allow sections to soak for one hour. Decant. (The silver ammonium solution is prepared as follows: Concentrated ammonium hydroxide is added slowly to 10 to 15-percent silver nitrate until precipitate is completely dissolved. Agitate constantly while adding ammonium hydroxide. After precipitate is completely dissolved, add an excess of one drop of ammonium hydroxide per cc. of solution. Prepare fresh each day and keep in tightly stoppered dark bottle.)

9. Add 10 to 15 cc. of 0.5-percent neutral formalin to sections. Stir or shake until sections become a uniform light yellow-brown color. If color is slow in appearing (longer than one-half minute) decant and add 1-percent neutral formalin. If the proper color still does not appear, decant and add 2-percent neutral formalin. The latter step (2-percent neutral formalin) is seldom necessary. Check sections under microscope. Nerve fibers and nuclei should be dark brown, stroma colorless.

10. When sections have the desired tint, wash them in running water (drop by drop) for a half hour. Cover beaker with layer of gauze to prevent loss of sections.

11. Wash in 20 cc. distilled water for two minutes.

12. Tone with gold chloride (2 drops of a 1-percent aqueous solution of gold chloride to 5 cc. of distilled water) until brown nerve fibers and nuclei are colored dark gray to black.

13. Fix in 5-percent sodium thiosulfate for 1 to 2 minutes.

14. Wash in distilled water. Dehydrate in 80-percent, 95-percent, and two changes of absolute alcohol. Clear in thin cedarwood oil and mount in balsam.

Histologic examination of the stained

sections revealed the following general pattern of reaction of the corneal nerves after keratoplasty.

During the first 3 days after operation the nerves in both the graft and the surrounding cornea began to show signs of degeneration in the form of segmentation, lighter staining and curling of the fibrils, and finally disappearance of the nuclei of Schwann's sheath cells (fig. 2).

penetrating the scar and entering the margin of graft (figs. 4 and 4a).

During the following weeks these small fibers became more numerous and penetrated to the center of the graft. The number of fibers in single nerves increased and, about 12 weeks after operation, nerves could be found in the midstroma which contained 5 to 10 fibers (fig. 5). At about the same time, small fibrils could be seen in the
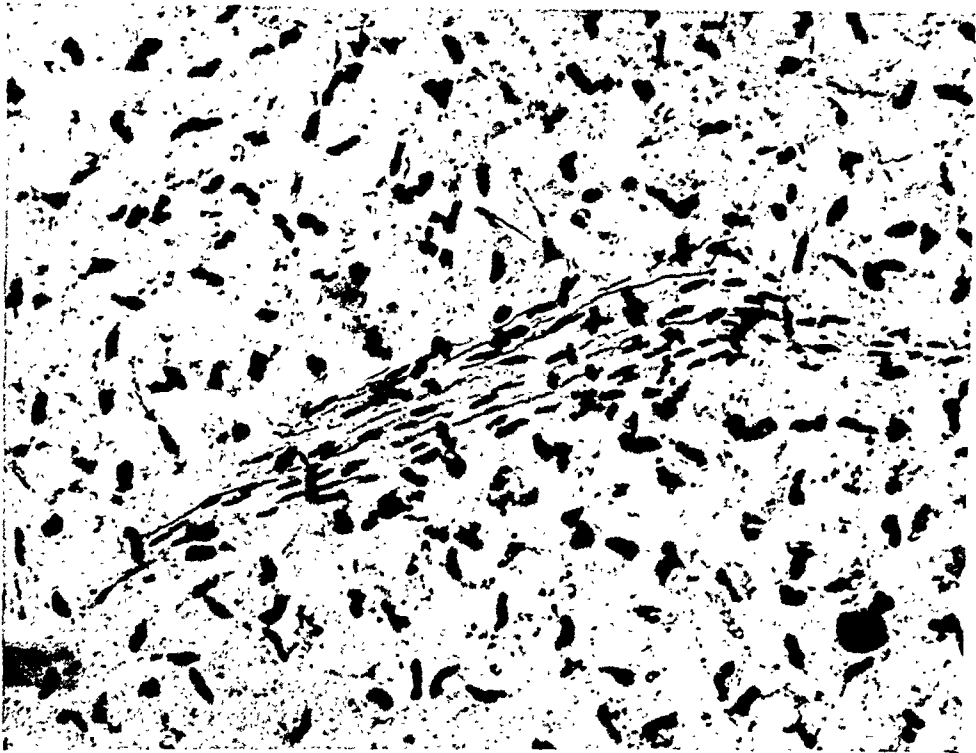

Fig. 2 (Kornblueth, Maumenee, and Crowell). Section of homogenous corneal graft (3 days after operation) showing a degenerating nerve. (Silver impregnation ×125.)

By the end of the second week practically all of the nerves had disappeared from the graft. In the recipient's cornea most of the nerve fibers for a distance of about 2 mm. from the incision disappeared and nerves in the periphery showed signs of ascending degeneration.

By 3 weeks newly formed fibers approached the scar on the edge of the graft. These frequently turned back into the recipient cornea or turned and ran parallel to the scar (fig. 3). By 4 to 6 weeks single nerve fibers could be found in the midstroma,

subepithelial and epithelial region in the grafts (figs. 6 and 6a).

During the first two months after operation the nerves in the recipient's cornea at the edge of the graft were usually composed of 1 or 2 fibers but, after 3 to 6 months, nerves containing 6 or more fibers reached the scar tissue surrounding the graft (fig. 7).

COMMENT

In this study the return of clinical sensibility coincided well with the anatomic findings. One month after operation only the
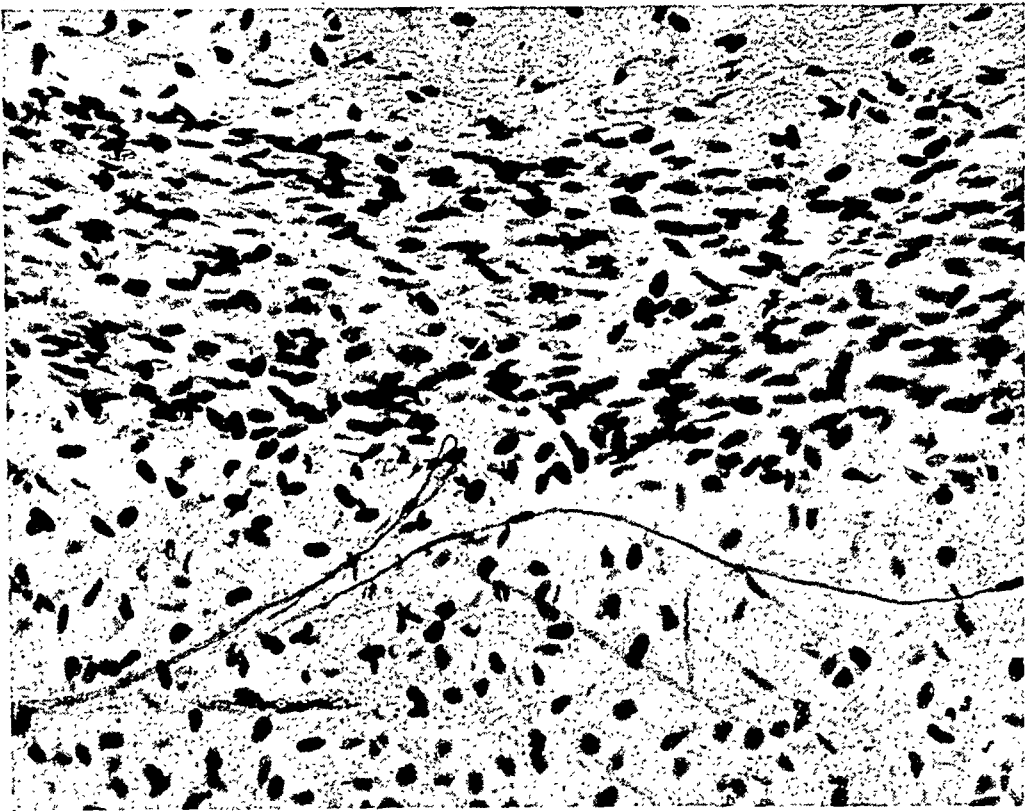
Fig. 3 (Kornblueth, Maumenee, and Crowell). Section of homogenous corneal graft (20 days after operation) showing newly formed nerve fibers in the recipient's cornea approaching the scar on the edge of the graft. (Silver impregnation ×125.)
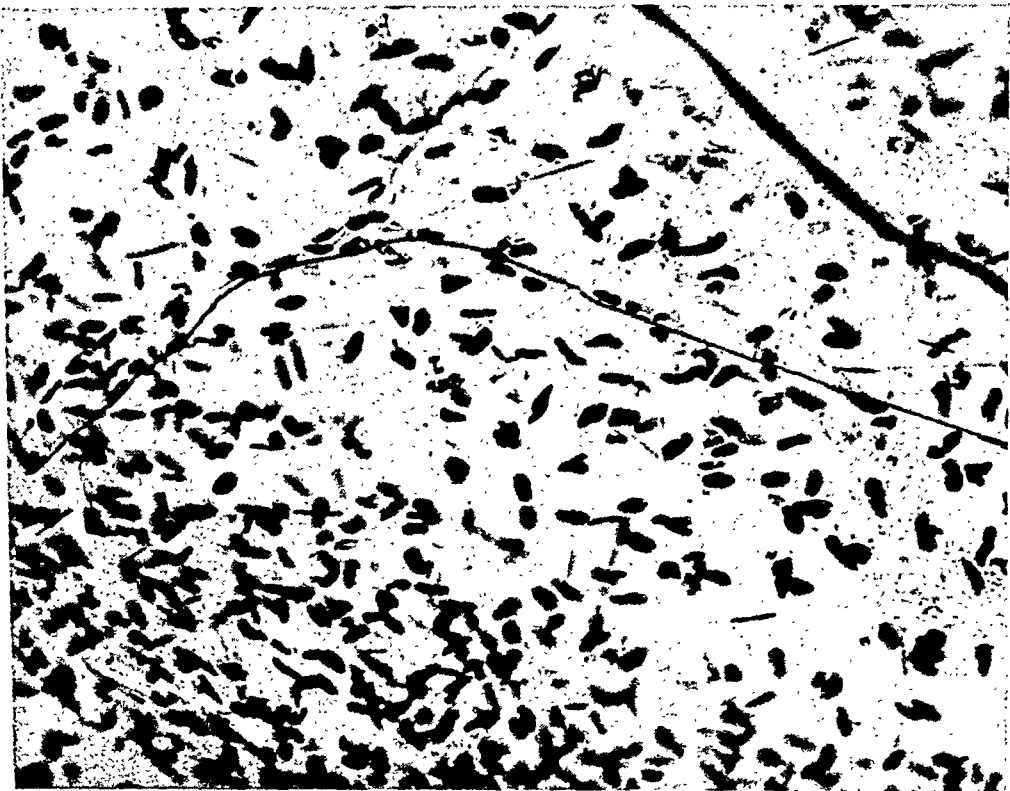

Fig. 4 (Kornblueth, Maumenee, and Crowell). Section of clear homogenous corneal graft (1 month after operation) showing a nerve fiber entering the margin of the graft. Scar at junction of graft and recipient cornea is seen at the lower left. (Silver impregnation ×125.)
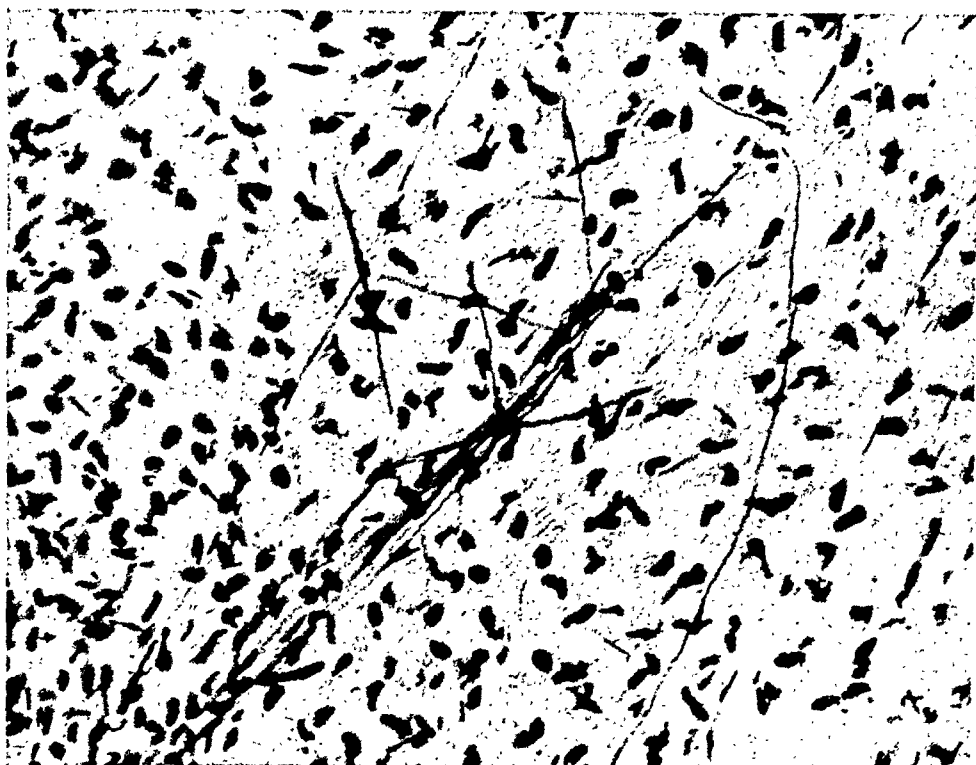
Fig. 4a (Kornblueth, Maumenee, and Crowell). Section of cloudy homogenous corneal graft (6 weeks after operation) showing nerve fibers entering the margin of the graft. Scar at junction of graft and recipient cornea is seen at the lower left. (Silver impregnation ×125.)
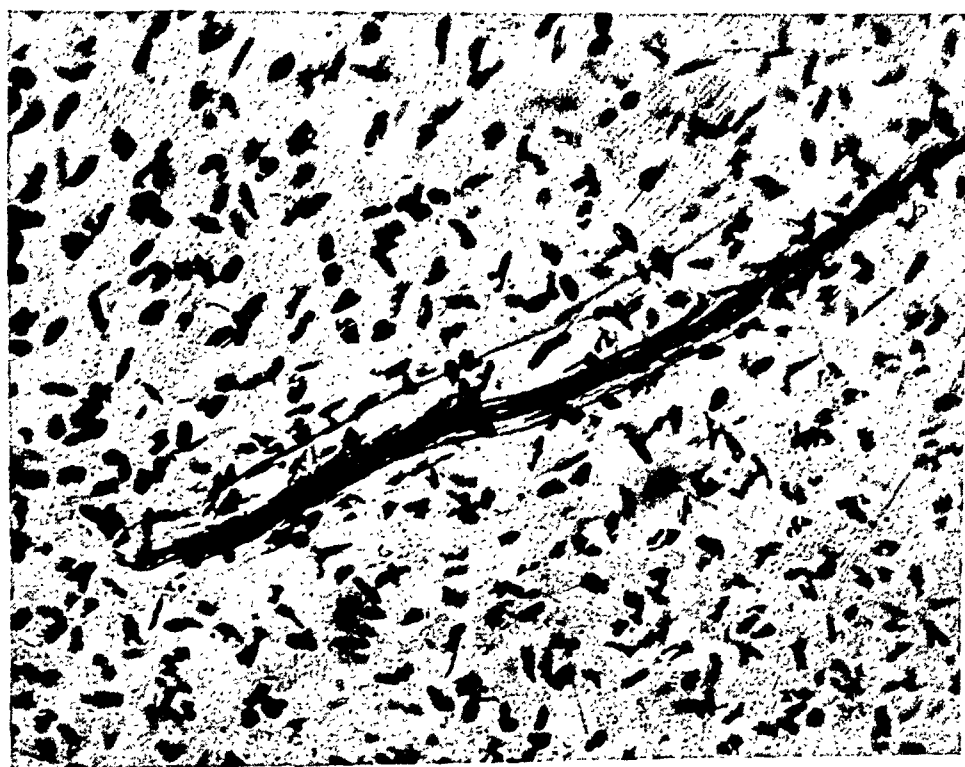

Fig. 5 (Kornblueth, Maumenee, and Crowell). Section of homogenous corneal graft (3 months after operation) showing a thick nerve in the midstroma of the graft. (Silver impregnation ×125.)
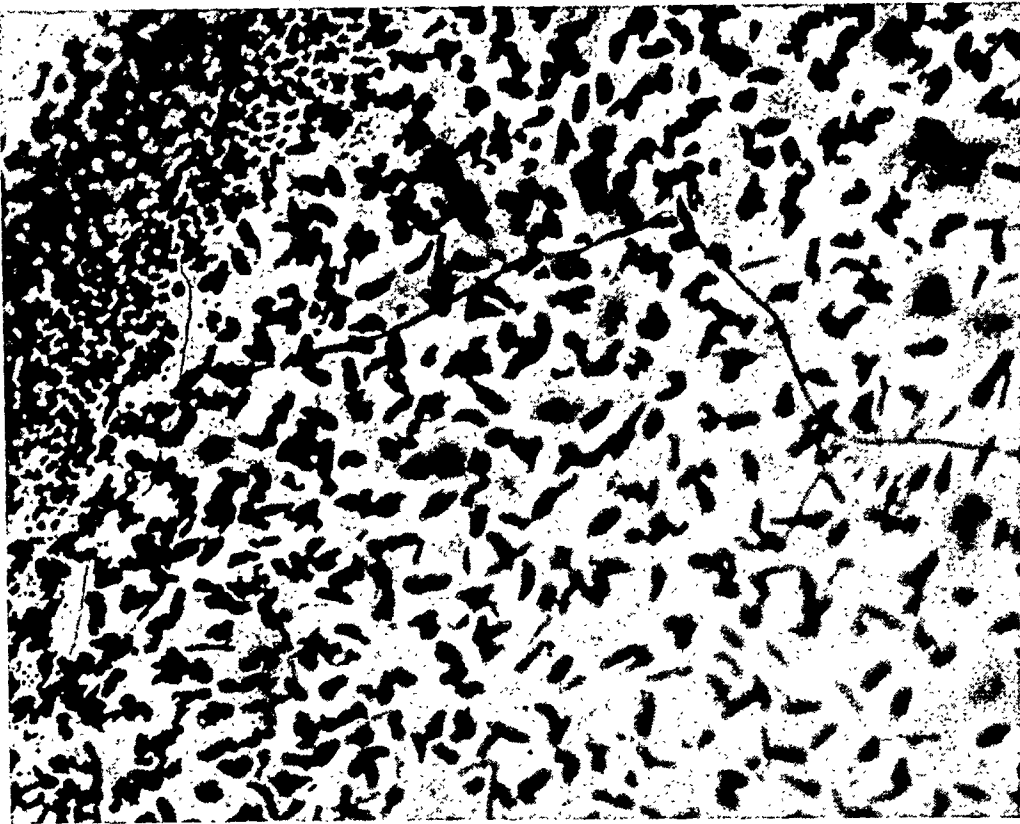
Fig. 6 (Kornblueth, Maumenee, and Crowell). Section of clear homogenous corneal graft (7 months after operation) showing a small nerve fiber entering the epithelium of the graft. Epithelium is at the upper left. (Silver impregnation ×125.)

Fig. 6a (Kornblueth, Maumenee, Crowell). Section of cloudy homogenous corneal graft (3 months after operation) showing a small nerve fiber entering the epithelium of the graft. Epithelium is at the upper left. (Silver impregnation ×400.)
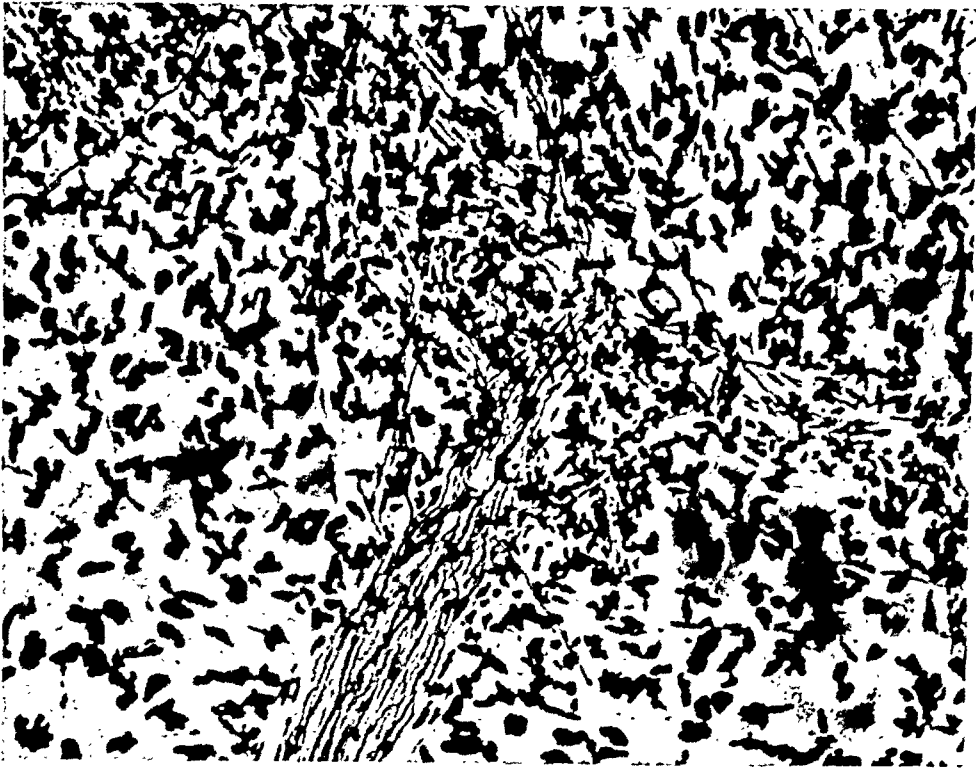
Fig. 7 (Kornblueth, Maumenee, and Crowell). Section of homogenous corneal graft (7 months after operation) showing a thick nerve in the recipient's cornea entering the scar tissue at the edge of the graft. (Silver impregnation ×125.)

margins of the grafts were sensitive to heavy touch (300-mg. test object). During the course of the next few weeks sensitivity to heavy pressure was acquired by the whole graft. This corresponded to the time when only single nerve fibers were found in the midstroma of the transplants. After 3 to 4 months, corneal sensitivity to light touch (100-mg. test object) could be perceived.

At this time, on histologic sections, numerous nerves and nerves with multiple fibers were observed in the midstroma of the graft, and small nerve fibers were found in the subepithelial and epithelial regions. The ingrowth of nerves and return of corneal sensibility was approximately the same in clear and cloudy grafts.

There was no correlation between the invasion of blood vessels and nerves into the graft as had been suggested by Thomas, Babel and Campos, and Franceschetti and Babel. Blood vessels could be found in cloudy grafts 1 to 2 weeks before the nerves entered the graft, and even then the nerves did not necessarily take the same course as the invading capillaries. On the other hand, nerves were found in entirely clear grafts which did not contain blood vessels.

We were also not able to confirm Franceschetti and Babel's suggestion that the presence of subepithelial nerves in grafts was essential for the final clarity of transplants. In our experiments both clear and cloudy grafts showed thin nerve fibers entering the subepithelial and epithelial region several months after operation (figs. 6 and 6a).

SUMMARY

The return of corneal sensitivity was tested in 12 clear and 10 cloudy transplants. The ingrowth of corneal nerves was studied histologically by the use of the silver-impregnation technique in 17 clear and 13 cloudy grafts. The return of deep sensibility in the grafts in 4 to 6 weeks corresponded to the ingrowth of nerves into the midstroma. The acquisition of light sensibility in 3 to 4 months corresponded to the

penetration of nerves into the subepithelial and epithelial regions of the grafts. No appreciable difference was found in the regeneration of nerves into clear or cloudy grafts. The ingrowth of nerve fibers was not dependent on the invasion of the grafts by blood vessels.

Stanford University Hospitals (15).
The Johns Hopkins Hospital (5).

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A CASE OF SENSITIVITY TO GOLD-BALL ORBITAL IMPLANT*

ECZEMATOUS CONTACT-TYPE DERMATITIS DUE TO 14-KARAT GOLD

H. WALTER FORSTER, JR., M.D., AND ROBERT F. DICKEY, M.D.
Philadelphia, Pennsylvania

The medical literature contains numerous references to dermatitis following parenteral administration of gold compounds in the therapy of arthritis, lupus erythematosus, vitiligo, and so forth. Ophthalmologists and dermatologists frequently see contact dermatitis due to monel metal (an alloy of copper and nickel) and "white gold" (an alloy of gold, copper, and nickel), which are used extensively in spectacle frames[1] and jewelry. The offending allergen in these cases is considered to be nickel or its salts.

The important synergistic action between pyogen and nickel allergy has been emphasized by Cormia,[2] Stokes,[3] and others. Gold chloride is said to cause dermatitis among photographers,[4] but our review of the literature failed to find any report of contact dermatitis due to gold leaf.

Gold, silver, tin, and copper in pure metallic form are not considered primary irritants or sensitizers. Most reports of sensitivity to these metals from their use in industry or in daily life emphasize the fact that usually the offending allergen is a salt of the metal concerned.

The subject of this case report showed a marked sensitivity clinically and by patch tests to a 14-karat gold ball which, 5 years previously, had been implanted into Tenon's capsule at the time of enucleation of the left eye. This sensitivity was manifested by a recurrent seropurulent orbital discharge and an eczematous contact-type dermatitis of the lids and adjacent skin.

CASE HISTORY

S. B., a 29-year-old woman, was admitted to the eye ward of the Hospital of the University of Pennsylvania on May 11, 1939. The ophthalmic history dated back to the age of six years when she started school and was found to have subnormal vision in each eye uncorrectible by glasses. She had had numerous operations on both eyes elsewhere. On admission here, the visual acuity of the right eye was hand movements; of the left eye, no light perception. The diagnosis was bilateral congenital dislocated lenses with uveitis and secondary glaucoma. The left eye was blind and painful. Enucleation was performed and a 14-karat gold ball, 14 mm. in diameter, of the standard variety used at that time, was implanted into Tenon's capsule. Recovery was uneventful. A glass prosthetic shell was procured.

She was next seen in the eye dispensary on April 23, 1942, at which time the left orbit was clean and well healed without any signs of irritation.

On September 9, 1944, 5 years after implantation of the gold ball, a purulent discharge from the left orbit developed. This failed to improve under treatment with 5-percent sodium sulfathiazole solution and the lids became excoriated. A culture made in November, 1944, showed hemolytic Staphylococcus aureus and diphtheroids. Medication was stopped because of possible sulfathiazole sensitivity, and the patient was advised to discontinue wearing her glass prosthesis. The only treatment permitted was boric-acid irrigations for removal of secretions from the socket. No improvement resulted, and a patch test on the skin for sulfathiazole sensitivity was negative.

In January, 1945, four months after the development of the orbital discharge, penicillin drops and ointment were tried with sulfadiazine systemically. The treatment, administered in the ward, rapidly cleared up the cellulitis of the lids, but the discharge from the orbit continued for another week and then stopped. The patient was again able to wear her glass prosthesis.

When the discharge recurred three weeks later, dermatologic consultation was obtained. At that time the patient presented an erythematous, oozing, vesiculopapular dermatitis of left eyelids and adjoining malar region. The diagnosis was acute recurrent infectious eczematoid dermatitis secondary to the seropurulent discharge from the left orbit. There was considered to be an associated eczematous contact-type dermatitis due to sensitivity to locally applied medicaments. The question of sensitivity to the glass prosthesis was again raised. Use of the prosthesis was discontinued, and potassium permanganate injections were tried. Four days thereafter the orbit appeared clean, but the lids were still inflamed.

In April, 1946, the patient was readmitted to the ward because of continued orbital discharge and edema of the lids. She was thoroughly studied from the standpoint of allergy and focal infection, including the lacrimal sac. The positive findings included marked skin sensitivity to a 1:100 dilution of Squibb's Staphylococcus ambotoxoid, and a culture of the orbital discharge showed hemolytic Staphylococcus aureus.

Patch tests to numerous cosmetics and locally applied medicaments showed positive reactions only to penicillin and sulfathiazole. She had previously shown no skin sensitivity to sulfathiazole. Because the lid excoriation and discharge cleared up and recurred many times in a most annoying and inexplicable manner, malingering was suspected. During this period of hospitalization the patient was closely observed for evidence of self-inflicted excoriations. This could not be proved.

A course of desensitization with Staphylococcus ambotoxoid was given from May, 1946, to February, 1947. The discharge im-

proved and relapsed frequently, and in October, 1946, tyrothricin 0.5 mg./cc. locally was started. This was followed by improvement for two weeks and then a relapse. X-ray studies of the nasolacrimal apparatus filled with Beck's paste showed no obstruction, and repeated culture of the discharge showed again hemolytic Staphylococcus aureus and diphtheroids.

Flare-ups alternated with remissions approximately every two weeks, and in February, 1947, the patient received two treat-

next remission, she was admitted to the eye ward for the fourth time.

It was determined that 14-karat gold is composed of 60-percent fine gold, 35-percent copper, 5-percent silver and tin. Standard, closed patch tests to the following metals and their salts were performed (table 1). All positive tests increased in severity for 24 to 48 hours following removal of test substance.

Skin sensitivity to the gold salt, gold leaf, and 14-karat gold ball was most marked

TABLE 1

REACTION TO PATCH TESTS OF METALS AND THEIR SALTS

Material Tested	Site of Testing	Reaction*
Copper sulphate (1% solution)	Forearm, volar aspect	1 plus
Gold sodium thiosulphate (0.5% aq. sol.)	Forearm, volar aspect	1 plus
	Upper chest	2 plus
	Upper back	2 plus
	Forehead (removed after 4 hrs.)	4 plus
Pure silver leaf	Forearm, volar aspect	0
Pure tin leaf	Forearm, volar aspect	0
Pure copper leaf	Forearm, volar aspect	0
Pure gold leaf	Forearm, volar aspect	2 plus
14-karat gold ball	Forearm, volar aspect	1 plus
	Upper arm	2 plus
	Right side of forehead (removed after 10 hrs.)	4 plus
Plastic ball	Left side of forehead	0

* Reactions were graded as follows (after Bloch):
  1 plus = erythema.
  2 plus = erythema and edema and/or beginning papulation or vesiculation.
  3 plus = fully developed vesiculation, papulation, edema, bullae.
  4 plus = strongest reaction—denudation, necrosis, and so forth.

ments with intermediate X ray after which there was again marked improvement for three weeks.

The patient had been seen repeatedly in the staff conferences of the ophthalmology and dermatology departments and finally the possibility of allergy to the gold-ball implant as an etiologic factor was considered. Such an allergy has never been reported in the literature to our knowledge. However, the situation was becoming desperate from the standpoint of the psychiatric status of the patient. Accordingly, during the

on the forehead; that is, the site nearest the patient's orbital implant. Removal of this implant was done on April 9, 1947. A plastic ball implant was substituted into Tenon's capsule. The patient had previously been patch-test negative to this plastic ball.

Five days later, there was practically no operative reaction. Because of the uniqueness of this case, and also because of the incredulity with which a gold-ball sensitivity was viewed, the patient was skin tested with the gold ball removed at the time of the operation. This gold ball was placed on the

left forearm in light contact with the skin, being held in place with a dry gauze dressing. Twelve hours later the gold ball had to be removed because of marked erythema, edema, and vesiculation at the site of the skin test; there was associated urticaria over both arms, face, neck, chest, and back.

Three days later, after this reaction subsided, the gold ball was placed on the right forearm and in 12 hours the same systemic reaction was produced, involving in addition the skin of the legs. There was a marked eczematoid reaction over a 10 by 15-cm. area at the gold-ball test site. The reaction again subsided in 3 days. This second test was performed because it seemed most unusual that the patient should manifest what was apparently an epidermal and generalized dermal sensitivity to supposedly inert 14-karat gold.

The patient was discharged to the eye clinic. All treatment was stopped and a new plastic prosthesis was obtained. One week after removal of the gold ball she was comfortable and without any abnormal secretion from the left orbit. At 2 weeks she still had no discharge. At 6 months and 8 months the orbit was completely normal, and according to the patient had given her no trouble. She was delighted with the result. At the time of this report two years have elapsed since removal of the gold ball and the patient has had no recurrence of her disfiguring orbital discharge which for 3 years prior to removal of the gold ball had made her life miserable.

COMMENT

Since contact sensitivity to metallic gold was not known to occur, and because the gold ball contained in Tenon's capsule was not in direct contact with conjunctiva or skin, the true diagnosis was not suspected until 3 years after the onset of symptoms.

It is not known why the patient did not develop generalized allergic symptoms, such as were manifested on subsequent patch testing, but instead showed sensitivity only of the conjunctiva, eyelids, and adjacent skin. The tip-off to the correct diagnosis resulted from a consideration that one or more of the metals in the 14-karat gold ball might be acting in a manner analogous to the well-known synergistic nickel-pyogen allergy.

Throughout the entire course of this patient's symptoms, repeated cultures showed pathogenic hemolytic staphylococci, coagulase positive, to which the patient was markedly sensitive by intradermal testing.

The patch-test reactions to the gold ball, 0.5-percent gold sodium thiosulphate, and gold leaf, not only showed marked erythema, edema, and vesiculation but also small pustules at the test sites. This reaction is similar to the patch-test reactions with proper strength solutions of nickel salts.

It is important to note that this patient apparently manifested not only marked local epidermal sensitivity when patch tested with the gold ball removed from her orbit, but also showed seemingly generalized dermal sensitivity in the form of pruritus and urticaria.

SUMMARY

1. A case is reported showing clinical sensitivity to a 14-karat gold orbital implant.

2. Patch tests to the 14-karat gold ball and to pure gold leaf were strongly positive; whereas, similar patch tests with other metallic components of 14-karat gold were negative.

3. Importance of synergistic metal-pyogen allergy is emphasized.

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HEPARINIZATION OF THE EYE*

Malcolm W. Bick, M.D.
Springfield, Massachusetts

This study was undertaken to investigate the use of heparin as a means of reducing postoperative scarring. Fibroblastic proliferation is a frequent cause of failure in glaucoma operations. There is good experimental and theoretical evidence to indicate that heparin might produce such a desired result by virtue of its growth-retarding characteristics, as well as its fibrin-inhibiting effect.

Goerner[1] demonstrated that heparin inhibited the growth in tissue culture of the Flexner-Jobling rat sarcoma. Fischer and Parker,[2] and later Zakrewski[3] demonstrated that proliferation of normal tissue fibroblasts in culture was depressed and differentiation enhanced by the use of heparin. Zakrewski thought that an antagonism existed between prothrombin and heparin. Prothrombin favored proliferation and growth, while heparin caused differentiation. Guy,[4] in the tissue-culture laboratory at The Johns Hopkins Hospital, observed that tissue growing in a heparinized media fails to grow in tissue sheets, that the normal bridging material between cells is not laid down, and that individual cells separate easily. Heparin is also known to inhibit the growth of yeast.[5]

Widstrom and Wilander,[6] in 1936, demonstrated that experimental pleurisy in rabbits could be modified by local heparinization, rendering exudate so incoagulable that it all was absorbed and no residual of the pleuritic process could be observed. Control animals developed dense pleural adhesions. In 1940, Lehman and Boys[7] reported on the intraperitoneal injection of heparin in rabbits and dogs to prevent the adhesions of experimental peritonitis. They were able to eliminate the reformation of adhesions in a large percentage of cases.

Laufman and Heller,[8] in 1942, tested the strength of abdominal wounds in systemically heparinized dogs. Up to the 5th day, there was delayed union, weakness of the wound, and less fibrin than in the controls. Even with poorly controlled heparinization, they were able to prevent healing until the 5th day.

CHARACTERISTICS OF HEPARIN

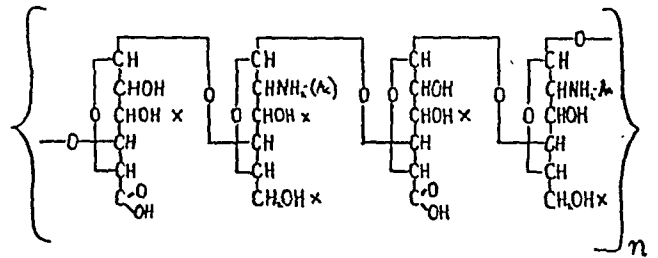Heparin is a nontoxic polysaccharide and is present in connective tissue in association

Fig. 1 (Bick). Formula for herapin as proposed by Charles and Todd.

with the metachromatic staining granules of the mast cells of Erlich. These cells give the same reaction with toluidine blue as heparin.[9] The heparin content of a tissue is proportional to the number of mast cells found therein. Commercially, heparin is obtained from ox lung, 100 gm. of which yield 1 gm. of heparin. The chemical formula suggested by Charles and Todd is given in Figure 1, which represents a carbohydrate complex having a configuration of two hexuronic molecules and two hexosamine.[10] The amino groups are acetylated, and the hydroxyl groups indicated by x are thought to be sulfated. Heparin is the strongest known organic acid found in the body. It combines with protein and especially with protamine, which inactivates the anticoagulant activity.[11]

Heparin readily forms stable salts with protein.

Heparin has a strong electronegative charge and shifts the isoelectric point of protein in neutral solution to the acid side. Precipitated protein can be peptized by adding heparin.[12] Thus, at pH 5 casein is insoluble, but heparin casein is soluble at this hydrogen-ion concentration.

Heparin is freely soluble in aqueous media. When used intravenously, it has no effect on the sugar, calcium, uric-acid, non-blood stream, the intestinal tract is the only tissue where the heparin content increases. The rapid disappearance of heparin from the blood stream is postulated to be due to an enzyme, heparinase.[13] Recent evidence indicates that a very small portion of heparin is excreted in the urine.[14]

Heparin has no effect on the capillary permeability in inflammation, the localization of leukocytes at an inflamatory site, or the phagocytosis of staphylococci by polymorphonuclear leukocytes.[15] It has no effect on

TABLE 1

THE EFFECT OF INTRAVENOUS HEPARIN ON THE COAGULATION
TIME OF THE ALBINO RABBIT

Dose*	C.T.† (Min.)	Blood Coagulation Time (B.C.T.)							
		At ½ Hr.	At 1 Hr.	At 2 Hr.	At 3 Hr.	At 4 Hr.	At 5 Hr.	At 5.5 Hr.	At 12 Hr.
		(Min.)	(Min.)	(Min.)	(Min.)	(Min.)	(Min.)	(Min.)	(Min.)
0.5	2.5	8	10	2					
1.0	3.0	10	12	2					
2.0	2.0	30	15	2					
4.0	2.5	120	—	55	5	2			
5.0	2–3	Inf.‡	—	—	—	4.5	2		
10.0	2–3	Inf.	—	—	—	4.0	2		
15.0	2–3	Inf.	—	—	—	55	3.5	2	
20.0	3.5	Inf.	—	—	—	30	3.5	—	
25.0	2–3	Inf.	—	—	—	35	12	10	2

* Dose given as milligram per kilogram.
† C.T. is clotting time.
‡ Inf. is infinity.

protein-nitrogen, phosphatase, red-cell, white-cell, and hematocrit determinations. It has no effect on the body temperature or blood pressure. Also, it is nonantigenic and can be used repeatedly.[9]

Heparin appears to be the normal anticoagulant of the blood. There is evidence to indicate that heparin acts as an antiprothrombin as well as an antithrombin. It counteracts the effect of thrombokinase which normally converts prothrombin to thrombin. When heparin is injected into the the phagocytosis of foreign particulate matter by the reticulo-endothelial system.[16]

A Howell unit is that amount of heparin which maintains 1.0 cc. of cat's blood fluid in the cold for 24 hours. A heparin unit or Toronto unit is equal in activity to 0.01 mg. of crystalline barium salt. This is approximately equal to 5 Howell units. One mg. of commercially pure heparin salt is equal to 100 Toronto or 500 Howell units.[9]

Before the local potentialities of heparin could be studied, it was necessary to deter-

mine the most efficient method of heparinizing the eye. The simplest means of following the concentration of heparin is by observations on the blood coagulation time. By knowing the effect and utilization of a given intravenous dose, one can compare its anticoagulant properties with that of a similar amount of heparin introduced into other tissues. In this manner, one can obtain indirect evidence as to the concentration of heparin in the tissues. This method proved to be of value in exploring the manner in which heparin enters and leaves the eye.

UTILIZATION OF INTRAVENOUS HEPARIN

A series of experiments were undertaken to determine what effect a given intravenous dose has on the B.C.T. (blood coagulation time) of the rabbit.

Albino rabbits were used in this and in all subsequent experiments. Nembutal anesthesia was injected into the ear vein 5 minutes prior to the injection of heparin. The dosage of anesthesia was 300 mg. per kg. of body weight which corresponds to 0.5 cc. in our preparation. The dosage of nembutal was calculated accurately because barbiturates are known to increase the effectiveness of heparin. For convenience, a commercially available sodium heparin preparation containing 10 mg. of sodium salt per cc. was employed and was injected into the ear vein.

The B.C.T. was determined one-half hour after the heparin injection and as often as necessary thereafter to obtain a curve.

The clotting time was determined by the capillary tube method[17] run in duplicate to check each determination. A new Bard-Parker blade was used to sever an ear vessel transilluminated by a small electric bulb. Freely flowing blood was permitted to run into two capillary tubes. A stop watch was started and the tubes were broken at regular intervals. The observation of a fine coagulated elastic thread stretching between the broken ends of capillary tubing was regarded as the end point. This end point was checked

by breaking the second tube. If clotting had not occurred two hours after the blood had been drawn, it was regarded as incoagulable. The results of these experiments are summarized in Table 1 and are plotted in Figure 2.
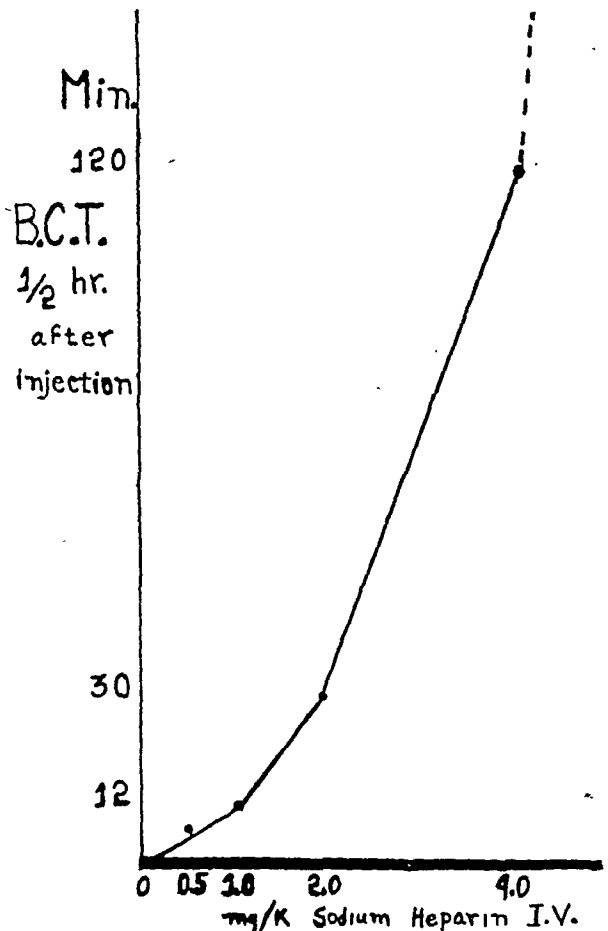
It is concluded from this data that, within

Fig. 2 (Bick). The effect on the blood coagulation time of an intravenous dose of herapin. Determinations were made one-half hour after administration.

a critical range of dosage of from 1 to 4 mg. per kg., there is a rapidly progressive increase in the effect on the clotting time. Above 4 mg. per kg. of body weight this relationship is not maintained and the blood becomes incoagulable. Above 4 mg. per kg., heparin acts like a threshold substance inasmuch as any dosage over this affects the coagulation time in the same way, and for the same length of time. In general, it may be concluded that a single intravenous dose in the rabbit producing a safe clotting time

cannot exceed 4 mg. per kg., and such an effect lasts only 3 hours. Even for dosages that render the blood incoagulable, it is impossible to produce elevated clotting time over 4 or 5 hours with a single intravenous dose.

HEPARIN CONCENTRATION AND COAGULATION TIME

The second experiment was performed to determine the relationship between the quantity of heparin present in the blood and the coagulation time such a level produces. There is no difference in the potency of

TABLE 2

RELATIONSHIP BETWEEN HEPARIN CONCENTRATION AND COAGULATION TIME OF RECALCIFIED RABBIT BLOOD

Solution Tested	B.C.T. (min.)	mg. Heparin per cc. Blood
0.1 mg. Sodium Heparin	Inf.*	0.5
0.01	30	0.05
0.001	18	0.005
0.0005	12	0.0025
0.0001	4	0.0005
0.00001	3.25	0.00005
0.000001	4.00	0.000005
Saline	3.50	0.0
Blank	4.00	0.0

* Inf. is infinity.

heparin in vivo and in vitro.[18] The concentration of blood heparin necessary to establish a given coagulation time is readily determined in vitro.

If known quantities of heparin are added to blood and the coagulation time determined, one can obtain a series of values by which the quantity of heparin present in the blood can be determined by observing the clotting time.

For convenience, blood which has been rendered incoagulable by decalcification with oxalate is employed. A known amount of heparin is added to the blood and the blood is recalcified. The recalcified clotting time is determined, and any elevation over the normal controls is attributed to the presence of heparin.

Rabbit's blood drawn from the heart of two rabbits and pooled was used for this experiment.

The determination was carried out as follows. One cc. of 1 molar sodium oxalate and 9 cc. of heart's blood from one rabbit were mixed thoroughly. This was pooled with a specimen of blood similarly prepared from a second rabbit.

One tenth cc. normal saline containing heparin was mixed with 0.2 cc. of oxalated rabbit blood on a clean watch glass. Twenty-five thousandths of a cc. of 1 molar calcium chloride was placed alongside the blood on the watch glass and mixed thoroughly with a clean glass rod for 2 seconds. A stop watch was started and the watch glass was gently rocked every 15 to 30 seconds until the blood was completely clotted. Clotting was considered complete when the watch glass was placed at a 90-degree angle to the table without fluid running off. Each specimen was run in duplicate and checked within 30 seconds of each other. The average reading for each dilution of heparin is reported in Table 2.

While decalcification and recalcification are described as increasing the speed of clotting[19] by the release of thromboplastin, no appreciable decrease in clotting time was observed in this experiment.

This study indicates that dilution of the blood by the test solution in itself has no effect on the clotting time. The clotting time of the controls was between 3.5 and 4.0 minutes. One half of a microgram of heparin per cc. of rabbit's blood had no effect on the clotting time; whereas 2.5 micrograms delayed clotting for 12 minutes. Within a range of concentration there appears to be a logarithmic relationship between clotting time and the heparin concentration (fig. 3). By knowing the clotting time of rabbit's blood in this range, one can calculate the concentration of circulating heparin. For example, if the clotting time of an animal were 30 minutes, the heparin

concentration would be approximately 50 micrograms per cc. The validity of this figure can be tested as follows.

Rabbit H-27 weighing 2.4 kilograms was given an intravenous dose of 2 mg. per kg. and the B.C.T., 15 minutes later, was found to be 30 minutes. Approximately 10 percent of the body weight is due to blood.[20] Therefore, 4.8 mg. was distributed in about 240 cc. of blood or 20 micrograms per cc. These figures of heparin concentration in vitro and
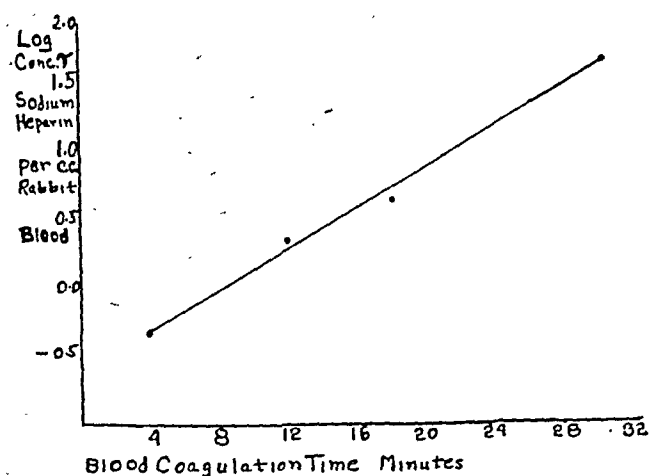

Fig. 3 (Bick). Each point plotted represents two determinations which checked within 30 seconds.

the estimated blood concentration are of the same order of magnitude.

HEPARIN AND THE AQUEOUS

The next problem was to determine if heparin enters the intraocular fluids.

The quantity of anticoagulant in a fluid can be determined by the technique described in the previous experiment; that is, known quantities of heparin were added to decalcified rabbit blood and the various unknowns were set up in the same way. On recalcification, the clotting time was determined.

Three rabbits were used receiving the dose indicated in Table 3. The intravenous dose was given under nembutal, the aqueous was removed from both eyes one-half hour after injection of heparin, and B.C.T. of the rabbit was determined simultaneously.

Within the sensitivity of this experiment,

TABLE 3

ANTICOAGULANT EFFECT OF PRIMARY AQUEOUS FOLLOWING INTRAVENOUS HEPARIN

Dose Sodium Heparin	B.C.T. (min.)	Aqueous+ Blood C.T.* (min.)	
Rabbit 0.5 mg./kg.	8	R.E.	4.0
		L.E.	4.5
Rabbit 2.0 mg./kg.	30	R.E.	4.5
		L.E.	3.5
Rabbit 3.0 mg./kg.	120	R.E.	4.0
		L.E.	4.5
Standard 0.5 Gamma		12	
0.1 Gamma		4	
Control		4	

* C.T. is clotting time.

which was 5 gamma of heparin per cc. of aqueous, no heparin was found in the primary aqueous.

It was found that the sensitivity of the method could be increased by using freshly shed human blood collected and stored in silicon-treated glassware. Silicon is a plastic material which prevents clotting for about one hour without the addition of anticoagulant. As soon as the blood comes in contact with ordinary glass, clotting begins. Human blood contains less circulating thromboplastin and does not clot as rapidly as rabbit blood. On one occasion, sensitivity to one-one hundredth of a microgram of sodium heparin was obtained.

The method using human blood was as follows. A sterile silicon-coated needle and syringe were used to draw 10 cc. of blood from the antecubital vein, and the blood was then carefully transferred to a silicon-coated test tube. The blood was pipetted into tiny test tubes used for prothrombin time determination in the proportion of 0.2 cc. of blood to 0.1 cc. of solution to be tested. The solution was placed in the tubes before the blood was added and the tubes were agitated for 2 or 3 seconds following the addition of the blood to insure thorough mixing. The stop watch was started the instant the glass

TABLE 4

ANTICOAGULANT EFFECT OF RABBIT AQUEOUS FOLLOWING INTRAVENOUS HEPARIN

Test Solution		Clotting Time (Minutes)		
Sodium Heparin 0.01 mg./cc.		Inf.*		
Sodium Heparin 0.001 mg./cc.		13		
Sodium Heparin 0.0001 mg./cc.		9		
Sodium Heparin 0.00001 mg./cc.		9		
Saline Control		9.50		
Saline Control		9.50		
Rabbit 1—mg./kg.	Primary Aqueous	(R)	8.25	(L) 9.75
	Secondary Aqueous	(R)	8.50	(L) 9.25
	Tertiary Aqueous	(R)	8.50	(L) 10.25
Rabbit 3—mg./kg.	Primary Aqueous	(R)	8.75	(L) 10.50†
	Secondary Aqueous	(R)	13.00	(L) 11.75
	Tertiary Aqueous	(R)	11.75	(L) 10.75

* Inf. is infinity.
† Bloody tap.

pipette came in contact with the blood in the silicon coated test tube. All transfers were completed within a minute after the initial contact with glass. The tubes were partially inverted every 30 seconds until clotting was completed. This was verified by complete inversion of the tube. For each determination, standards of known amounts of heparin

TABLE 5

ANTICOAGULANT EFFECT OF RABBIT AQUEOUS FOLLOWING INTRAVENOUS HEPARIN

Test Solution		Clotting Time (Minutes)
Sodium Heparin		
0.01 mg.		Inf.†
0.001 mg.		22
0.0001 mg.		13
0.00001 mg.		11.5
0.000001 mg.		8.5
Rabbit 10—mg./kg.		
Primary Aqueous	(30)*	6.5
Secondary Aqueous	(45)	14.5
Tertiary Aqueous	(55)	37.0
Rabbit 20—mg./kg.		
Primary Aqueous	(30)	5.0
Secondary Aqueous	(45)	42.0
Tertiary Aqueous	(55)	27.0
Saline Control		6.25
Saline Control		7.00

* Parenthesis figure indicates number of minutes after heparin was administered intravenously.
† Inf. is infinity.

were set up with saline controls in duplicate.

The first experiment using the siliconed human-blood technique described above was to determine the concentration of sodium heparin in the primary, secondary, and tertiary aqueous with moderately small doses of intravenous heparin. Two albino rabbits anesthetized with nembutal (300 mg. per kilogram) were given heparin in the ear vein. Aqueous was withdrawn with a hypodermic needle on a tuberculin syringe 15 minutes, 30 minutes, and 45 minutes following the injection. About 0.25 cc. of primary aqueous could be withdrawn, and 0.2 cc. of secondary and tertiary aqueous was obtained. Care was exerted not to damage the iris vessels with the point of the needle. An oblique puncture through the cornea was found to be important to prevent the escape of aqueous around the needle and the subsequent leaking of aqueous after withdrawal of the needle. The results of this experiment are summarized in Table 4.

Using higher concentrations of heparin, the experiment was repeated (Table 5). It is concluded that the primary aqueous contains no heparin. When the blood-aqueous barrier is disturbed by paracentesis, heparin enters the aqueous in concentrations proportional to the blood level.

REMOVAL OF HEPARIN FROM THE AQUEOUS

If heparin is placed in the anterior chamber by paracentesis, one inadvertently disturbs the blood-aqueous barrier, but since heparin is not present without such a disturbance, a study of its removal under such circumstances is desirable. To follow the removal indirectly by observing the clotting time of the animal, is a simple method when one knows the effects of a similar intravenous dose.
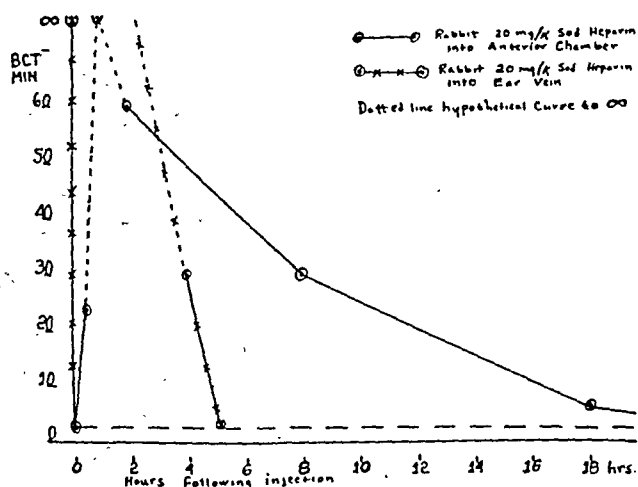

Fig. 4 (Bick). Comparison of the anticoagulant effect of heparin given intravenously with that administered by an anterior-chamber injection.

Sixty mg. of sodium heparin were taken up in 0.2 cc. of physiologic saline. The primary aqueous of an albino rabbit, weighing 2.9 kg. and anesthetized with sodium pentobarbital, was allowed to drain off through a hypodermic needle. The heparin dose was divided between the two eyes. The results of this experiment are summarized in Figure 4.

Ordinarily, in 5 hours, such a dose given intravenously would be entirely disposed of. At the end of the 18 hours following injection into the anterior chamber, there was still some elevation of the clotting time.

Intravenously, such a dose produces an immediate rise in the coagulation time to infinity. It takes approximately an hour for the blood to become incoagulable when the same quantity of heparin is put into the anterior chamber. This indicates that heparin meets some resistance to its arrival in the blood stream. This resistance accounts also for the elevation of the coagulation time for almost 24 hours. Some free heparin must, therefore, remain in the aqueous for this length of time.

CONCLUSIONS

In order to heparinize an eye effectively, one must either break down the blood aqueous barrier, or one must place the heparin directly into the eye. Even a concentration of heparin which renders the blood incoagulable will not produce heparinization of the intraocular fluids until something is done to disturb the capillary permeability. The concentration of anticoagulant in this secondary aqueous, as may be expected, is proportional to the level of heparin in the blood.

When heparin is placed inside the eye on the aqueous side of the barrier, there is a delayed anticoagulant effect on the blood as compared with a similar intravenous dose. This slowness of absorption into the blood indicates resistance to the passage of heparin out of the aqueous.

Unless a continuously high blood level of heparin is maintained, and the capillary permeability is continuously increased, heparinization of the eye by the parenteral route would be impossible. Although one might produce a continuously high blood level by divided dosage or using various heparin binders, or Pitkin's menstruum, it would be difficult to guarantee a high capillary permeability except for a short period of time.

Therefore, the most practical means of heparinizing the eye is by introducing the heparin directly.

SUMMARY

A brief review of the pertinent facts regarding heparin are given. The relationship between dosage, blood concentration, and coagulation in the rabbit was studied. The

manner in which heparin enters and leaves the intraocular fluid was investigated. It is concluded that the most practical and certain method of heparinizing the eye is by the direct introduction of heparin.

292 Worthington Street (3).

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OPHTHALMIC MINIATURE

The use of the eye is to identify objects and to protect the body from external dangers, to deal with them as one sees fit. That is the reason it is placed in the uppermost portion of the organ, like a watcher in a garden.

The chief function of the eye is to recognize colors, the shape of objects, the details of bodies, and to determine what is large and what is small.

Memorandum Book of a Tenth-Century Oculist.

Translated by Casey A. Wood.

THE PRESERVATION OF RABBIT CORNEA FOLLOWING EXPOSURE TO THE CAPACITRON*

T. D. DUANE, M.D., AND O. S. LEE, M.D.†

Iowa City, Iowa

INTRODUCTION

One of the greatest handicaps to the more universal performance of the corneal transplant operation (circumscribed penetrating keratoplasty) is the unsatisfactory preservation of the donor tissue for prolonged periods. Many methods have been advocated and much has been written about the various techniques for corneal storage. However, the fact remains that with present methods the cornea cannot be preserved as suitable donor material for periods longer than 72 hours. A surgeon must have a close association with an eye bank or he cannot hope to perform this operation in his everyday ophthalmic practice.

What are the ideal conditions for storing the donor cornea? The answer cannot be given absolutely but the accumulated evidence indicates the following:

1. There should be a minimum interference with the physiologic status of the tissue.

2. Bacterial growth must be inhibited.

3. The tissue must retain its proper dimensions (that is, neither shrunken nor swollen) and the cellular architecture particularly of the epithelium and endothelium must not be altered.

Most methods of preservation attain one of these goals at the expense of the others. Thus, freezing and formalin prevent bacterial contamination but they grossly alter the cellular structure and physiologic functions. Storage in low-temperature Ringer's atmosphere permits bacterial contamination and corneal swelling. Perhaps no method will satisfy all the requirements for ideal storage, but it is apparent that the closer a given method approaches the ideal the more useful it will become for clinical practice.

It was with these factors in mind that we have attempted a new method of corneal preservation and our results are described in this report.

The principle of the Capacitron treatment is based on the bombardment of electrons into fresh tissue targets for ultrashort exposure periods.[1] In the treatment of such tissues as the cornea, the aim is to provide enough exposure time for the electrons to produce a biologic effect but too brief an exposure for the initiation of other and undesirable chemical side reactions. The Capacitron used delivers impulses of accelerated electrons at an energy of 2.2. Mev. at an intensity of 10,000 amperes during an exposure of about 1×10^{-6} seconds. Since this method has shown promise in the preservation of foodstuffs,[1] we hoped that it might preserve corneas also.

METHODS

Twenty-nine mature colored rabbits (58 eyes) were the source of corneas for these experiments, 9 of which were kept as controls. The animals were killed with intravenous air injections, the eyes were enucleated, and the entire corneas were removed.

A 4-mm. scleral collar was retained on some of the corneal specimens. As Cogan and his associates have demonstrated, the stromal limbus does not possess a protecting semipermeable membrane.[2] Thus we hoped a scleral collar would prevent hydration or dehydration at this portal.

The fresh corneas were immediately placed in ampules and were divided into

5 groups of 3 ampules each receiving 2, 4, or 6 impulses from the Capacitron. The media in the 5 groups of sealed ampules were: (1) Air; (2) air and 1 cc. of frozen saline (which was permitted to melt after exposure and was stored at room temperature); (3) air and 1 cc. saline (liquid); (4) nitrogen; (5) vacuum (15 mm. Hg). Opposite sides of every ampule received 50-

procedure in rabbits.[3] The details of the surgical techniques as well as the fate of the recipient cornea will be the subject of a future report by us.

Normal QO_2 for the rabbit cornea was assumed to be -0.55.[4]

All of the corneas in each ampule were used in the respiration studies, including the cornea from whose center a section was

TABLE 1

RESULTS OBTAINED IN CORNEAS EXPOSED TO THE CAPACITRON

Media	Impulses	No. of Corneas	Storage (days)	Appearance		Respiration (/Cornea)	Culture	Transplantation
				Gross	Microscopic			
Air	2	3	24	+++		0,0,0		0
Air	4	4	40	+++		0.0.0.+		++
Air	6	3*	48	+++	+	0,0		+
Air+frozen saline	2	3	52	+		0,0	No Gr.	0 to +
Air+frozen saline	4	4	53	+	0	0,0,0	No Gr.	0
Air+frozen saline	6	3*	24	+		0,0,+		
Air+saline	2	3	27	++		+,++,++++		0 to +
Air+saline	4	4	42	++	++	0,0,0		0 to +
Air+saline	6	3*	49	++	++	0,0		
Nitrogen	2	3	31	+++		0,0,0		0
Nitrogen	4	4	45	+++	+++	0,0,0		+
Nitrogen	6	3*	49	+++	+	0,+	No Gr.	++
Vacuum	2	3	33	+++		0,0,0		+
Vacuum	4	4	47	+++	+	0,0,0		++
Vacuum	6	2*	24	+++		0,0		
Control		3	0	++++	+++	++++		+
Control		3	0	++++	+++	++++		++
Control		3	0	++++	+++	++++		++++

* Scleral collars.
++++ = normal.

percent of the impulses. The ampules were all exposed at a distance of .17.5 centimeters from the aluminum window of the Capacitron.

Respiration studies were performed according to the standard Barcroft-Warburg technique. The microscopic paraffin sections were stained with hematoxylin and eosin. Beef broth was used for the culture studies. The corneal transplant surgery was performed under the handicap of our inexperience with the surgical difficulties of this

trephined to serve as a donor tissue but excluding the corneas which were placed in fixative in preparation for histologic studies. For the bacterial culture studies, a small wedge-shaped portion was aseptically removed from the periphery of a cornea and was incubated in beef broth.

RESULTS

The data are presented in Table 1.

a. *Gross appearance.* The fresh cornea when removed was used as a standard. Com-

pared to the fresh specimens, all of the Capacitron-treated corneas appeared to have thickened 25 to 50 percent. The transparency was diminished an estimated 33 percent. Only the corneas treated in frozen saline became an opaque milky white and swelled 100 to 200 percent of normal. All of the corneas had a rubbery consistency similar to that which results from formalin fixation.

b. *Microscopic appearance.* The specimens were sectioned in paraffin but the results were inconclusive since 90 to 100 percent of the epithelium was missing in all of the specimens, including the controls. The stroma was vacuolated (an artifact?). Descemet's membrane and the endothelium, in general, appeared normal. One of the treated corneas was placed in alcohol and was stained without passing through the usual course of fixatives. This tissue appeared to stain as corneas fixed by conventional methods.

c. *Respiration.* Six of the treated corneas showed respiration. Three of these were in the same ampule. The respiration varied from one-fourth normal to normal. Forty-one corneas showed no respiration.

d. *Culture.* None of the 3 specimens tested demonstrated any bacterial contamination. There was probably no contamination in the other ampules judged from their gross appearance and odor as compared with controls.

e. *Transplants.* Twelve of the treated corneas were used as donor material for corneal transplants to normal rabbit hosts. In one case the animal died during surgery. In another instance the lens was injured by the surgical procedure and the graft was extruded. Another developed secondary glaucoma postoperatively. Of the remainder, all corneal transplants healed satisfactorily, but

72 hours. No swelling appeared macroscopically. A control, normal, fresh cornea after submersion in water for 72 hours swelled some 400 percent (by volume), enough to change its shape from the normal hemisphere to a lenticularlike mass.

g. *Controls.* Eleven fresh corneas were used for controls. Two were placed in separate ampules, one containing air, the other saline. They became greatly altered in appearance after the third day and were obviously contaminated. The remaining 9 were directly employed in corneal transplants without previous storage. The successes increased with improvement in the technique until the last group of 3 remained as clear transplants.

DISCUSSION

The evidence indicates that in the corneas treated with the Capacitron there is probably a denaturation of the protein molecules. This denaturation is similar to that which occurs following other types of irradiation such as X-ray and ultraviolet-ray exposures. The change is not as vigorous as occurs in such chemical fixatives as formalin. The frozen saline group were probably altered more by the freezing than by the Capacitron irradiation.[5-6]

The fixation hypothesis is supported by the inhibition of the respiratory enzymes and by the absence of bacterial contamination, the latter due to a denaturation of the bacterial proteins. Furthermore, the normal staining which occurred in the treated cornea with no other fixation lends support to this impression. The absence of swelling in the 41 corneas immersed in the manometer flask fluids for periods up to 3 hours and the lack of swelling in the 1 cornea submerged for 72 hours indicates that the corneal proteins were denatured. One of the unique characteristics of the normal cornea

corneal transplantation are not surprising.[5-8] It is our impression that the discrepancy between the gross and microscopic appearances is due to the vagaries inherent in the sectioning of corneas embedded in paraffin, since it was noticed in the controls as well as the treated corneas. Sectioning of the isolated cornea for histologic examination usually results in an unsatisfactory specimen for examination. The presence of the scleral collar did not influence the response of the cornea in any of the tests.

The doses of irradiation used in these studies were high and the storage time was prolonged 10 to 25 times that which is the maximum with other techniques. It should be emphasized that the postulation of a fixation of tissue protein following exposure to the Capacitron is unproved. Therefore, the results reported should be considered as applicable only to the specific radiation conditions under which the samples were ex-

posed. It is possible that different results could be obtained with variations in the techniques.

SUMMARY

1. Rabbit corneas were stored at room temperature for periods up to 53 days in ampules containing various media following exposure to the penetrating electrons of the Capacitron.

2. Respiration and bacterial growth were inhibited.

3. The gross appearance was not greatly altered.

4. Corneal transplants performed with the treated corneas healed well but remained opaque.

5. The results are interpreted as probably representing a denaturation of the corneal proteins by the electrons from the Capacitron.

College of Medicine,
The State University of Iowa.

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SELF-STERILIZING OPHTHALMIC SOLUTIONS*

SAMUEL D. McPHERSON, JR., M.D., AND RONALD M. WOOD, B.Sc.

Baltimore, Maryland

The sterilization of ophthalmic solutions has always offered a perplexing problem to the ophthalmologist. Equally as difficult has been the problem of preserving the sterility of solutions once it has been achieved. Many methods have been proposed for the sterilization and preservation of solutions.

Gifford[1] advised the use of boric-acid buffers in ophthalmic solutions, stating that their use prevented the growth of yeast and fungi. Hasler[2] advocated the use of a mixture of nipagin and nipasol, esters of benzoic acid, to prevent the growth of mold and bacteria. Haffly and Jensen[3] proposed placing ophthalmic solutions in rubber-capped vials, autoclaving them, and removing the necessary amounts with a sterile hypodermic syringe. The commonest method in use at the present time consists simply of autoclaving solutions prior to their use and to repeat autoclaving at intervals of 2 weeks to 1 month.

All of these methods have certain limitations to their applicability. The use of boric-acid buffers prevents the growth of fungi and some bacteria, but does not kill bacteria once a solution is contaminated. The value of benzoic acid esters as preservatives has been disputed by Spengler and Kessler.[4] The storing of autoclaved solutions in rubber-capped vials and their subsequent removal with sterile hypodermic syringes is not feasible for a large institution in which many patients must be treated daily. Autoclaving achieves initial sterilization, but does not maintain it and, in addition, reduces the potency of many alkaloids by as much as one half.

The ideal method is to prepare solutions which are self-sterilizing. To produce ophthalmic solutions which have this quality, one must introduce some substance which (1) is bactericidal, (2) does not react chemically or physically with standard ophthalmic drugs, and (3) is nonirritating to the human eye.

Benzalkonium chloride satisfies most of these requirements. It is a mixture of high molecular, alkyl-dimethyl-benzyl-ammonium chlorides. It is freely soluble in water and has a pH at approximately the neutral point. It is a cationic detergent and is thus inactivated by anionic detergents—(soap).

The bactericidal powers of benzalkonium are well known. These have been investigated by Dunn,[5] Hoyt,[6] and Domagk.[7] It was found that benzalkonium is bactericidal to common pathogens in dilutions up to 1:35,000 at 37°C. Thompson, Isaacs, and Khorezo,[8] investigated a variety of antiseptics for their rapidity and completness of action and found that benzalkonium chloride in a concentration of 1:2,500 completely destroyed Staphylococcus aureus in less than one minute. Under similar conditions iodine, mercurochrome, silver nitrate, acriflavine, gentian violet, phenyl mercuric nitrate, argyrol, and merthiolate destroyed only a fraction of the organisms in five minutes. The authors concluded that benzalkonium surpassed by far the other disinfectants in its completeness and rapidity of action.

Benzalkonium chloride is compatible with practically all standard ophthalmic drugs. There are a few notable exceptions. These are argyrol, boric acid, silver nitrate, and sodium fluoresceinate. In addition, it is incompatible with nitrate and salicylate radicals.[9]

The effect of benzalkonium on human eyes has been investigated by O'Brien and Swan.[10] They found that concentrations of 1:2,500 and 1:2,000 caused diffuse superficial punctuate staining of corneas. This

disappeared when the drug was discontinued and did not recur when the drug was used in concentrations of 1:5,000 and 1:3,000. They advised the use of benzalkonium as a wetting agent with carbaminoyl choline to promote the absorption of the drug. Scobee[11] used benzalkonium in a concentration of 1:5,000 in the treatment of recurrent staphylococcal conjunctivitis and reported no untoward effects.

As a preliminary to the clinical use of benzalkonium chloride in ophthalmic solutions a series of experiments was performed to determine the survival time of common pathogenic bacteria in ophthalmic solutions prepared (1) in distilled water, (2) in dis-

All solutions except those containing benzalkonium were sterilized before the addition of the test organisms by autoclaving at 15 pounds pressure for 20 minutes. Solutions containing benzalkonium were not autoclaved.

The organisms used had been recently isolated from clinical material and grown in pure culture.

To 3 cc. of each drug solution under test was added 0.05 cc. (one drop) of an actively growing 24-hour broth culture of E. coli, B. pyocyaneus, and Staphylococcus aureus. Subcultures were taken at intervals of 2, 5, 10, 15, and 30 minutes and planted in trypticase soy broth using a standard

TABLE 1

SURVIVAL TIME OF ORGANISMS IN SOLUTIONS PREPARED IN STERILE DISTILLED WATER

	Coli (Minutes)				Pyocyaneus (Minutes)				Staphylococcus (Minutes)			
	2	5	15	30	2	5	15	30	2	5	15	30
Eucatropine Hydrochloride 5%	+	+	+	+	+	+	−	−	+	+	+	+
Cocaine Hydrochloride 4%	+	+	+	+	−	−	−	−	+	+	+	+
Pilocarpine Hydrochloride 2%	+	+	+	+	+	+	+	+	+	+	+	+
Atropine Sulfate 1%	+	+	+	+	+	+	+	+	+	+	+	+
Tetracaine Hydrochloride 5%	−	−	−	−	−	−	−	−	+	+	+	+
Scopolamine Hydrobromide ¼%	+	+	+	+	+	+	+	+	+	+	+	+
Eserine Sulfate ¼%	+	+	+	+	+	+	+	+	+	+	+	+
Homatropine Hydrobromide 2%	+	+	+	+	+	+	+	+	+	+	+	+
Distilled Water	+	+	+	+	+	+	+	+	+	+	+	+

tilled water with zephiran, and (3) in buffer solution with zephiran.

MATERIALS AND METHODS

The drugs used were obtained from the pharmacy in the powdered form and were prepared (1) in distilled water, (2) in distilled water containing benzalkonium chloride* (1:5,000), and (3) in a phosphate buffer solution of pH 7.2 recommended by White and Vincent[12] containing benzalkonium chloride (1:5,000). All glassware was thoroughly rinsed to remove any trace of soap prior to being used.

* The benzalkonium chloride used in these experiments is sold under the trade name Zephiran by the Winthrop Chemical Company, Inc.

1-mm. platinum loop. After an incubation period of 48 hours the subcultures were examined for evidence of growth and the results were recorded.

RESULTS

The first experiment consisted in contaminating sterile solutions of 8 commonly used ophthalmic drugs prepared in sterile water with E. coli, B. pyocyaneus, and Staphylococcus aureus. As a control, sterile distilled water was similarly contaminated. The results are given in Table 1. Organisms survived regularly for 30 minutes in most of the solutions tested. The coli and pyocyaneus bacilli failed to survive in tetracaine (0.5 percent). This was possibly due to the

TABLE 2

SURVIVAL TIME OF ORGANISMS IN SOLUTIONS PREPARED IN DISTILLED
WATER CONTAINING BENZALKONIUM 1:5,000

	Coli				Pyocyaneus				Staphylococcus			
	(Minutes)				(Minutes)				(Minutes)			
	2	5	10	15	2	5	10	15	2	5	10	15
Eucatropine Hydrochloride 5%	—	—	—	—	—	—	—	—	—	—	—	—
Cocaine Hydrochloride 4%	—	—	—	—	—	—	—	—	—	—	—	—
Pilocarpine Hydrochloride 2%	—	—	—	—	—	—	—	—	—	—	—	—
Atropine Sulfate 1%	—	—	—	—	—	—	—	—	—	—	—	—
Tetracaine Hydrochloride 5%	—	—	—	—	—	—	—	—	—	—	—	—
Scopolamine Hydrobromide ¼%	—	—	—	—	—	—	—	—	—	—	—	—
Eserine Sulfate ¼%	—	—	—	—	—	—	—	—	—	—	—	—
Homatropine Hydrobromide 2%	—	—	—	—	—	—	—	—	—	—	—	—
Benzalkonium 1:5,000	—	—	—	—	—	—	—	—	—	—	—	—

fact that the tetracaine used was a commercial preparation and contained acetone sodium bisulfite as a preservative.

The second experiment consisted in contaminating solutions of the same 8 drugs prepared in distilled water containing benzalkonium (1:5,000). The same three organisms were used and distilled water containing benzalkonium (1:5,000) was used as a control. The solutions used in this experiment were not autoclaved prior to contamination. The results are shown in Table 2. There was no growth in any solution including the control at 2, 5, 10, or 15 minutes.

The third experiment consisted in contaminating solutions of 7 drugs prepared in buffered solutions containing benzalkonium

(1:5,000). The purpose of this experiment was to determine if phosphate buffers in any way inhibited the bactericidal action of benzalkonium. The buffer solution alone and buffer solution containing benzalkonium (1:5,000) were used as controls. E. coli, B. pyocyaneus, and Staphylococcus aureus were again the organisms used. None of these solutions except the buffer alone were autoclaved prior to contamination. The results are shown in Table 3. All three organisms survived in buffer solutions without benzalkonium for a full 15 minutes. In the remainder of the solutions there was no growth in 2, 5, 10, or 15 minutes. It seems apparent from this that phosphate buffer solutions do not inhibit the bactericidal effects of benzalkonium.

TABLE 3

SURVIVAL TIME OF ORGANISMS IN SOLUTIONS PREPARED IN PHOSPHATE
BUFFERS CONTAINING BENZALKONIUM 1:6,000

	Coli				Pyocyaneus				Staphylococcus			
	(Minutes)				(Minutes)				(Minutes)			
	2	5	10	15	2	5	10	15	2	5	10	15
Eucatropine Hydrochloride 5%	—	—	—	—	—	—	—	—	—	—	—	—
Cocaine Hydrochloride 4%	—	—	—	—	—	—	—	—	—	—	—	—
Pilocarpine Hydrochloride 2%	—	—	—	—	—	—	—	—	—	—	—	—
Atropine Sulfate 1%	—	—	—	—	—	—	—	—	—	—	—	—
Tetracaine Hydrochloride 5%	—	—	—	—	—	—	—	—	—	—	—	—
Scopolamine Hydrobromide ¼%	—	—	—	—	—	—	—	—	—	—	—	—
Homatropine Hydrobromide 2%	—	—	—	—	—	—	—	—	—	—	—	—
Buffer and Benzalkonium 1:5,000	—	—	—	—	—	—	—	—	—	—	—	—
Buffer Alone	+	+	+	+	+	+	+	+	+	+	+	+

COMMENT

Solutions formerly used on the wards of the Wilmer Institute were prepared for the most part in Gifford's buffers. In addition, all solutions were autoclaved prior to being placed in use. Once in use these solutions were discarded after a period of two weeks. Cultures of these solutions show that an appreciable percentage of them exhibit some degree of bacterial contamination prior to being discarded. A series of solutions containing phosphate buffers and benzalkonium (1:5,000) was prepared and placed in use without prior sterilization. There were 27 such solutions. These were cultured 2 and 4 weeks after being placed in use and on both occasions all of the solutions were sterile. In addition, there was no instance in which the use of these solutions containing benzalkonium seemed to cause any undue local irritation or reaction.

It seems proper on the basis of these experimental and clinical findings to use benzalkonium chloride in ophthalmic solutions in order to make them self-sterilizing. The only exceptions are those solutions containing drugs with nitrate, salicylate, and fluoresceinate radicals. Benzalkonium chloride is compatible with most ophthalmic drugs and is nonirritating in concentrations necessary to achieve bactericidal effects.

Johns Hopkins Hospital (5).

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OPHTHALMIC MINIATURE

The fit time for couch of Cataracts

Couch Cataracts upon
 a day so faire,
That neither wind nor
 clouds disturbe the Ayre,
When spring with simples
 fils the Earth rich lap,
Or Autumne makes
 the tree put off his cap,
The Moone ith full,
 or in coniunction sly,
Or tracing Aries,
 or in Gemini.

Richard Banister, Mr. In Chyrurgery,
Oculist and Practitioner in Physicke.

PREVENTION OF INFECTION IN EYE SURGERY*

M. HAYWARD POST, JR., M.D.
Saint Louis, Missouri

Consideration of all the possibilities shows that infection in ophthalmic surgery takes place from:

Endogenous sources, such as (1) Systemic infection (lues, tuberculosis, septicemia, acute exanthemas, both in the active stage and during the incubation period, or even during convalescence). (2) Foci of infection (apical abscesses in the teeth, pyorrhea, and so forth; infected tonsils, accessory nasal sinus disease, and prostatitis). (3) Latent phacoanaphylaxis.

Exogenous sources, such as (1) Contamination residual in the conjunctiva, glands of the lids, lacrimal apparatus, and skin. (2) The hands and gloves of the surgeon, assistant, and nurses. (3) Droplet infection through the masks of the participants. (4) Dustborne organisms.

It is obviously impossible in a paper such as this to consider a problem of such magnitude in all its aspects. The discussion, therefore, will be limited to a consideration of methods for the prevention of infection resulting from contamination by the instruments used in intraocular operative procedures.

In any consideration of measures for the prevention of infection in eye surgery, it is obvious that the proper care and sterilization of the instruments used is of primary importance. Not only must the instruments be sterilized, but their sterility must be maintained up to the moment of their use in operation, and, at the same time, they must be kept in perfect condition, with edges and points sharp and free from oxidation.

METHODS OF STERILIZING INSTRUMENTS

Boiling in water is probably the oldest

known and has been investigated with the greatest amount of elaboration. It may be accepted as a proven fact that boiling instruments in sterile water does not affect the edges or produce rusting, provided no electrolytic action takes place. When injury does occur, it is the result of oxidation, or mechanical mishandling.

Lancaster[1] quotes Roscoe and Schoerlemmer[2] on this point. They say: "Iron only rusts in the presence of oxygen and liquid water containing either carbonic or some other volatile acid or metallic salt in solution," and "liability to rust is diminished in the presence of alkalies."

By careful experimentation, Lancaster found that polished steel plates showed faint spots after boiling for three hours in a 1-percent solution of bicarbonate of sodium and that, after five hours, well-marked oxidation was present. But in a footnote he states: "If the sterilizer is of such material that it is acted upon by the boiling soda, it is possible to get conditions favorable for tarnishing the instruments." He did find that a solution of potassium or sodium hydrate was even more satisfactory.

It is almost impossible, however, to find sterilizers in perfect condition. Furthermore, even when this requirement is met, if a number of instruments are boiled at the same time, electrolytic action may be set up between the various instruments, or, at times, even between the blade and the handle of the same instrument.

Foster, LeMay, and Johnstone,[3] of Gillette Industries, Ltd., noted that while boiling in water is a simple, detergent, complete, and rapid mode of sterilization, killing all spores in five minutes, if 2-percent Na_2CO_3 is added to the water, some knives are spoiled by only half a minute's boiling in it. They also find that other compounds, such as NH_4OH and Neutralin, used in dental sterilizers, produce

fewer deleterious changes, but that all such procedures have their limitations. They propose the use of a substance known as A.C.10 (surgical).

A.C.10 (surgical), "is the lightest of a series of anticorrosive products developed as the result of many thousands of experiments. It consists of 95 percent of a light petroleum oil and 5 percent of a complex of sodium salts of petroleum sulphonic acids (the inhibitor). Neither the oil, nor the inhibitor alone, is an effective corrosion preventive. To obtain optimum protection in a given set of conditions of exposure to corrosive attack, both the oil constituent and the mixture of sodium petroleum sulphonates must be carefully selected and mutually adjusted for compatibility."

They find that a cataract knife, if dipped for 15 seconds in neat A.C.10, can be boiled for 55 minutes without corrosion in a 2-percent w/v solution of Na_2CO_3 10 H_2O in water in which 2-percent v/v of A.C.10 has been emulsified, and that, if it is redipped in neat A.C.10 every 15 minutes, it can be boiled without corrosion indefinitely. It is obvious that boiling knives for sterilization is a rather complicated and delicate procedure.

Heating in dry air is satisfactory in many respects, but necessitates the use of special expensive apparatus and requires at least one-half hour exposure to temperatures from 150° to 160°C. Therefore, the same set of instruments cannot be used in successive operations without necessitating tedious delays.

Heating in mineral oil is quite satisfactory in many respects, but it is unpleasant to handle and difficult to remove from the instruments after sterilization is completed; moreover, the temperature must be watched to prevent the development of excessive heat, with the consequent loss of temper in the steel blades. If vegetable oils are used, fresh, corrosive, fatty acids and gummy polymerization and oxidation products result at each heating.

Exposure to formaldehyde gas is effective, but requires special and somewhat complicated apparatus. The gas is highly deleterious to aluminum.

CHEMICAL SOLUTIONS

The use of chemical solutions, therefore, appears to be the most desirable method, provided suitable ones that will effect proper sterilization without damaging the instruments can be found. Many proprietary solutions have been developed. Some of these contain formaldehyde, which is definitely deleterious to aluminum. Others depend upon mercury compounds for their bactericidal activity. Those containing this ingredient have a tendency to discolor rubber, attack aluminum, glass, and varnish, and, in aqueous solutions, cause rust in steel instruments.

While the effectiveness of these preparations within their limits is unquestioned, it is obvious that a preparation avoiding these limitations, and one that can be easily compounded by any pharmacist, is desirable.

In 1926-27, the late Dr. A. E. Ewing was boiling his knives in albolene but, dissatisfied with this procedure, was experimenting with the corrosive effects of various chemical solutions. From his studies, Dr. Ewing eventually evolved the following formula, which he believed would satisfactorily answer all requirements:

	Parts
Liquor cresolis compound	2.4
Liquid petrolatum	16.0
Commercial chloroform	120.0
Ethyl alcohol 95% qs. ad.	240.0

It was demonstrated that knives and scissors were not injured by this solution, even after immersion in it for many days.[4] Since those early studies, interest in this problem continued, chiefly with regard to the development of suitable chemical solutions which should contain only such ingredients as are available under ordinary conditions at every drug store. The formula originally suggested by Dr. Ewing did not

purport to kill spores and, due to its high volatility, the chloroform was rapidly lost. A second preparation with a doubled cresol content was studied, but the volatility of the chloroform continued to be an objection. A more potent solution, and one without the troublesome chloroform constituent, was sought. As a result, the following solution was studied:

	Parts
Cresol (U.S.P.)	2.0
Formaldehyde (U.S.P.)	2.0
Thymol (U.S.P.)	2.0
Ethyl alcohol 95%	94.0

The results of the work done with this preparation[5] made it apparent that, although this solution was highly bactericidal, aluminum handles repeatedly exposed to its action began to deteriorate from corrosion. Formaldehyde was known to be the offending ingredient.

In an effort to eliminate this agent, a solution, the formula for which is now known as No. 4, was studied by Mr. William Moor, technician to the department of ophthalmology, Washington University School of Medicine, and me. It may be written:

Liquor cresolis compound	8.0 cc.
Oil of lavender	2.0 cc.
Thymol crystals	2.0 gm.
Ethyl alcohol 95%	88.0 cc.

It was demonstrated by recorded experiments[6] that clean instruments contaminated by cultures of various types of organisms could be sterilized by immersion in this solution for a period of one-half minute. Four and one-half minutes were required, however, to sterilize similar instruments, previously soiled by blood and serum, when subjected to the same cultures, plus a heavy concentration of spore-bearing hay bacilli.

The contention that spore-bearing organisms were killed by this solution was rather bruskly waved aside by other observers, who group it among the phenoloids, whereas liquor cresolis compound—the formula for which is—

Cresol (U.S.P.)	500.00 cc.
Linseed oil	350.00 cc.
Potassium hydroxide	14.52 gm.
Sodium hydroxide	37.05 gm.
Aquae dest. qs.	1,000.00 cc.

might rather be classified as a detergent, a detergent being considered as an agent acting as a go-between, enabling soaps to unite with and dissolve solid particles of matter; the cresol component, in this instance, acting upon the soap formed through the union of linseed oil with potassium and sodium hydroxide.

EXPERIMENTS IN STERILIZATION

In an effort to answer the challenge and to evaluate properly the potency of the preparation to the common spores of the hay bacillus, further experiments have recently been carried out. While it is well understood that the viability of spores varies greatly, and it is impossible to say that all spores can be killed in four minutes, the vast majority of those at all likely to be encountered in the operating room have been demonstrated not to survive such an exposure.

A number of old Graefe knives were totally immersed in a suspension of a mixture of vegetable B. subtilis and B. subtilis spores. Microscopic smears taken from this suspension indicated that the proportions were roughly 20 spores to each actively growing bacillus. The knives were allowed to rest in this culture for about five minutes, then all picked up together and placed in solution No. 4.

At intervals, as indicated in Table 1, a knife was picked from the solution, was rinsed by dipping in the indicated bath three times, and was given a single shake to remove excess moisture. The blade was then slid over the surface of an agar slant hard enough to make an indentation, and forced into the agar depths. Finally, it was plunged into a tube of broth. The agar was tryptose (2 percent), dextrose (0.5 percent), and agar (2 percent). The broth was tryptose (2 percent) and dextrose (0.5 percent). The

pH of each was 7.2. In Table 1, it may clearly be seen that, in all four experiments reported, spores were killed in less than four minutes.

This solution No. 4 has now been in use by the department of ophthalmology of Washington University School of Medicine in all eye surgery since about February 1, 1941. It has also been in frequent use at the Saint Louis City Hospital and St. Luke's

cent, occurred between that time and the use of the instruments in operation. It was demonstrated that the major part of this contamination took place through the medium of dust-borne organisms settling in the water bath in which the germicidal solution was washed from the instruments, upon the towels for drying them, and directly upon the instruments themselves, as they lay upon the table awaiting use.

TABLE 1

RESULTS OBTAINED IN STERILIZATION TESTS*

	15 secs.	30 secs.	45 secs.	1 min.	1½ min.	2 min.	3 min.	4 min.	5 min.
Solution No. 4. No Rinse									
Agar	++	+	+	+	+	+	−	−	−
Broth	++	++	++	++	++	++	+	−	−
Solution No. 4. Saline Rinse									
Agar	++	++	+	+	+	+	−	−	−
Broth	++	++	++	++	++	++	−	−	−
Solution No. 4. Saline Rinse Plus Aqueous Zephiran (1:3,000)									
Agar	+	+	+	+	+	−	−	−	−
Broth	++	++	++	++	++	++	−	−	−
Solution No. 4. Saline Rinse Plus Aqueous Zephiran (1:3,000) Plus Sodium Nitrate (0.5 percent)									
Agar	+	+	+	+	−	−	−	−	−
Broth	++	++	++	++	++	−	−	−	−

* Growth is indicated by plus sign, very heavy growth by double plus sign, and absence of growth after 96 hours by minus sign.

Hospital, Saint Louis, since about that time.

During the summer of 1944, and especially the month of September, several infections occurred in the eyes of patients operated upon for cataract in the McMillan Hospital of Washington University School of Medicine. It seemed desirable, therefore, to re-check the test previously made, this time under operating room conditions. It also seemed advisable, while studying the action of the germicide, to conduct other experiments in order to determine where contamination might be taking place, if it was proved that the sterilizing solution was acting in a satisfactory manner.

From these studies,[7] it developed that complete sterilization was present immediately after removal of the instruments from solution No. 4, but that a very high degree of contamination, an average of 36.22 per-

It is obvious that many of the organisms causing such a high degree of contamination must have been nonpathogenic, or no eyes would have survived intraocular surgery. It is, nevertheless, also obvious that such a high degree of contamination is highly undesirable and undoubtedly leads to infection in a large percentage of those cases where infection does take place. In fact, those cases in which eyes were lost from purulent infection showed invaders similar to those grown on agar plates exposed in the operating room on subsequent occasions.

AIR STERILIZATION

A means was sought, therefore, to eliminate, as far as possible, this source of contamination. In general, two methods of attack against such organisms are available: Air sterilization, or instrument sterilization

at the moment of use in operation. The first of these may be accomplished by sterile lamps, or by the infusion of various bactericidal solutions into the air through the medium of vaporizers; the second, by dipping the point of the instrument into boiling water or sterilizing solutions of sufficient potency, at concentrations noninjurious to the eye being operated upon.

Sterile lamps have been developed extensively and are in use commercially on a rather comprehensive scale. The lamps may be used with the rays directed upon the field of operation or in the duct of air conditioners supplying air to the closed room. The first arrangement is obviously impossible in the case of an eye operation; the second requires elaborate air conditioning of the entire operating room unit. Matthew Luckisch, director of Lighting Research Laboratory, General Electric Company, at Nela Park, Cleveland, has given considerable space in his recent book, *Applications of Germicidal, Erythemal, and Infrared Energy*, to a discussion of this problem, with many diagrams illustrating various ways in which germicidal lamps may be used.

Spraying the air with various bactericidal solutions gives promise of becoming a very practical and satisfactory method, under certain conditions. Dr. O. H. Robertson, of the University of Chicago, working with propylene and, more extensively, with triethylene glycol vapor, has shown that 1 cc. of this substance in 10,000 cubic feet of air is lethal to pneumococci, streptococci, and influenza virus previously injected into the air, and that, in this concentration, it cannot be detected and is noninjurious to individuals, even after long exposure to its effects. Air sterilization can be greatly improved by oiling the blankets and sheets.[8]

All observers have attributed much of the air pollution to the disturbance of dust upon the floors. It is, therefore, desirable that some method to hold that dust be instituted. Pale paraffin oil is satisfactory, but becomes slippery on tile floors. A solution of urea (5 percent), ninol (3 percent), and rocall (0.9 percent) may be substituted, but must be renewed every few days.

DIPPING OF INSTRUMENTS

Since all of these methods are expensive and difficult to carry out, the second method, dipping the instrument to be introduced into the eye in boiling water for 2½ seconds immediately before use, and later, into aqueous zephiran (1:3,000) for the same length of time, has been under investigation for the past two years. Nothing original is claimed for the use of boiling water in this manner, as it has been used for many years, but apparently no previous experiments have been carried out to determine its efficacy. The best practical test appears to be to what extent the contamination of numerous instruments, selected at random from the postoperative tables following cataract and other intraocular surgery, can be reduced by this method.

Investigation showed that 77.77 percent of the instruments tested when taken from these tables without the use of such procedures showed contamination of broth culture tubes inoculated by them. By the use of boiling water, it was possible to reduce this percentage to 14.28 percent. It was found, however, that boiling water was difficult to handle and increased the humidity of the atmosphere about the operating table. A sterilizing solution, therefore, was sought.

USE OF ZEPHIRAN

Zephiran, one of the approximately 2,000 known detergents, seemed well suited to this procedure. Belonging to the anion-active group of detergents, its action upon the ocular tissues is well understood. These experiments showed that an exposure of 2½ seconds to a 1:3,000 aqueous solution of this preparation reduced the contamination to 6.66 percent, a considerably lower figure than that obtained with boiling water.

This procedure has been in use since February 1, 1944, in all intraocular operations conducted in the operating rooms of McMillan Hospital, under the direction of the Eye Service of the Washington University School of Medicine. Since its introduction, 742 cataract operations had been done up to January 1, 1947, and 326 other intraocular procedures, with only one instance of purulent infection, a percentage of 0.09, and a figure which appears to justify the use of this sterilizing procedure in all intraocular operations.

Experiments conducted on four rabbits' eyes have shown, however, that shortly after the injection of aqueous solutions of zephiran (1:500, 1:1,000, and 1:3,000) into the anterior chamber there occurs a nebulous opacity of the corneal endothelium that tends to clear up in from 3 to 5 weeks. Atrophy of the iris, most marked in the region of the injection, appears in from 2 to 3 weeks and persists indefinitely. Synechias do not result from this atrophy.

It would appear wise, therefore, not to allow zephiran solutions to enter the anterior chamber more than necessary, recognizing, however, that the circumstances of these experiments greatly exaggerate any occurring in actual operative practice. Even after the accidental use of a solution of zephiran (1:300) for one month in the McMillan Clinic, no untoward ocular reactions were noted, but some rusting of the instruments was observed. It seemed best, therefore, to add sodium nitrate solution (0.5 percent) to the zephiran, in keeping with the recommendations of the manufacturers of this product, in order to introduce a further safeguard against rusting, the nitrite taking up any free oxygen that might be present in the solution.

ZEPHIRAN BATH

This use of zephiran has proved so satisfactory that it seemed wise to substitute a solution of zephiran (1:3,000) for the water bath, which has been shown to be a frequent source of contamination. Experiments were conducted to determine whether such a solution would remain sterile after considerable periods of exposure to the air in shallow uncovered trays. Five minims of this solution were removed from a tray so exposed, at intervals for a period of five hours, and dropped into culture tubes containing sterile broth. In no instance did contamination result.

To reinforce the findings of this procedure, five instruments were cultured which had just been sterilized by immersion for five minutes in germicide No. 4 and then washed off in the zephiran bath. The first group was in the bath for 30 minutes; the second for 90 minutes. As was to be expected, in both instances the cultures remained sterile.

In practice, the zephiran bath gradually becomes cloudy from the carryover of solution No. 4 by the instruments being sterilized. It has become customary in our operating rooms to discard the solution at the end of the operating day, or sooner if turbidity becomes excessive.

CONCLUSION

In conclusion, the care and preservation of instruments between operations should be mentioned. Obviously, they should be removed from the operating table as soon as possible after the operation has been concluded, carefully washed in soap and water, and dried on soft towels. For sharp instruments, a small cotton pledget is probably the most innocuous material for this procedure.

After the washing and drying have been completed, one of a number of bland oils may be used in order to leave a slight film on the blades. Solution No. 4 may be used in this manner, although slight brownish stains may occasionally be observed after a considerable length of time has elapsed. If desired, these instruments can be left immersed in solution No. 4 for an indefinite period of time, certainly many years, with entire safety.

It has been noted that rusting of instru-

ments when not in use occurs much less frequently in the clinics of India, due to the generally high alkaline content of the air in that climate. It is undoubtedly true that a dry, slightly alkaline air is beneficial. Certainly, moisture and acidity should be carefull avoided. This may be accomplished by introducing silica gel and lime desiccators into the cabinets where the instruments are kept.

520 Metropolitan Building (3).

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OCULAR COMPLICATIONS OF TEMPORAL ARTERITIS*

CARROLL SMITH, M.D., AND PHILLIP B. GREENE, M.D.
Spokane, Washington

Fifteen years ago, Horton, Magath, and Brown[1] published the original description of temporal arteritis. Since that time, including the four cases herein presented, more than 40 cases have been reported, almost 50 percent of which have shown visual disturbances. As with many new diseases, the rarity of temporal arteritis is more apparent than real, and its recognition by ophthalmologists will occur with increasing frequency. Certainly this disease should be borne in mind when an elderly patient suffers an occlusion of the central retinal artery or its branches, particularly if there is a history of head and scalp pains, painful nodules along the course of the temporal arteries, and absence of pulsation.

Within a period of a few days, we saw two cases of temporal arteritis. The first patient suffered complete, bilateral loss of vision, and the second, a loss of vision in one eye with partial recovery in the other.

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CASE REPORTS

CASE 1

History. An emaciated white woman, aged 70 years, was first seen on March 18, 1946. She was referred by her physician for visual disturbances in the right eye of several days' duration, followed by complete loss for five days. She had been ill for several months, had aged rapidly, and a diagnosis of influenza and anemia, possibly primary, had been made.

Eye examination. On examination, the pupil of the right eye was moderately dilated and fixed to light. The consensual reflex was present. The media were clear and the fundus examination was notable for its lack of findings. The veins showed a moderate dilation and a Grade-II sclerosis of the arteries was noted. The disc was normal and no edema of the retina was present. There were two small hemorrhages along the course of small vessels just above and below the temporal aspect of the disc.

The fundus of the left eye showed the

same grade of sclerosis but nothing else re-markable. Vision in this eye was 20/30, with correction, being limited by a few cortical lens opacities.

Because of the sudden onset and lack of findings, a retrobulbar vascular accident was assumed, and the patient was reassured as to the status of the left eye.

On March 26th, however, 18 days after the onset of symptoms in the right eye, visual disturbances were noted in the left eye, and the patient was hospitalized. A fundus examination on March 27th showed nothing abnormal, but the next morning all light perception was gone from this eye also. The fundus showed a moderate (1 diopter) edema of the disc and peripapillary area. The caliber of the arteries was not changed, and no segmentation of the blood column was observed. There was one small hemorrhage just above and temporal to the disc. There was no color change in the macula.

The edema faded rapidly in the course of the next few days, and the fundus of each eye showed nothing except a slight pallor of the disc. Now, a year later, both discs are very pale and the patient is well but completely blind. .

Diagnosis. The diagnosis of temporal arteritis was not made at once. Repeated consultations with internists and a neurologist were of no help. Finally, in the course of questioning the patient, the history of nodules along the forehead and severe head and scalp pains six weeks before onset of eye symptoms was obtained. Complete absence of pulsation of both temporal arteries was noted.

The original physician was contacted and his report of earlier symptoms and findings of cachexia, anorexia, moderate fever, and lancinating pains of the face, jaw, scalp, and occiput were enough to establish the diagnosis.

The history and course were so typical that no section was taken from a temporal artery.

CASE 2

History. A man, aged 68 years, whom I had refracted four years previously, came to me on March 26, 1946, with the history that he had not been well during the past winter. He had been treated by his family physician several times for influenza attacks. Recovery from each attack had been slow and seemed to take longer each time. For the past few weeks he had been under treatment for anemia, the hemoglobin count having been down to 60.

The day before the present visit, he had discovered that he could not see with his left eye. Vision in the right eye with correction was 20/40−2; in the left eye, hand movements only. Four years earlier, at the time of refraction, vision had been 20/15−3, with correction, O.U., and no pathologic condition of the eyes had been present.

Ophthalmoscopic examination. Findings in the right eye were negative. In the left eye, there was a slight swelling of the disc and a moderate amount of grayish edema of the macular area. The visual loss was out of all proportion to the fundus findings.

Course. A week later the patient was seen again. Vision in the right eye had failed two days previously. It was 20/200. The left vision had improved slightly and he was able to count fingers at three feet. The right disc was moderately swollen and there were a few grayish spots in the right macula.

Since Case 1 had been presented at the monthly meeting of the local medical society, when the second patient was next seen, he was questioned regarding pains in the temporal areas. It was then learned that he had had pains in both temporal areas over a period of several weeks. He was then seen by Dr. Mark Anthony, by Dr. David Hartin, by Dr. Andrew de Roetth, and by both of us.

The temporal arteries were hard and nodular. Pulsation could not be felt on either side. Vision in the right eye was light perception only. The disc borders were oblit-

erated and at least one diopter of swelling of the disc was noted. Upon pressing the eye, the veins became smaller and upon releasing the pressure, the blood backed up in the veins in segmented clumps and then slowly progressed centrally.

Vision in the left eye had improved to 20/60, with correction, and the swelling of the disc had disappeared.

Pathologic report. The patient was then hospitalized and a section of the left temporal artery was removed. There was no bleeding, so the artery was not ligated. The pathologist's report was: "Microscope shows the lumen to be practically obliterated and filled with organized thrombus in which there is marked cellular infiltration. There is also marked cellular infiltration into the muscular coat. The infiltrate is of lymphocytes, giant cells, and a few polymorphonuclear cells. There is some attempt at recanalization of the vessel."

Pathologic diagnosis. Mesarteritis and endarteritis of the temporal artery.

Treatment. The Wassermann reaction was negative. The patient was put on erythroltetranitrate when he was hospitalized (0.25 gr., every 8 hours, for 6 doses, then 0.5 gr., every 8 hours). He was kept on that for a week, and then the dose was reduced to 0.25 gr. every 8 hours, and was continued for another two weeks. It is, however, questionable about the beneficial effects of the vasodilator drug.

Results. This patient has been seen every few weeks since the onset of the trouble. He has faint light perception in the right eye, and vision in the left eye has continued to improve. It was 20/25, with correction, on April 1, 1947.

There is marked excavation and atrophy of both discs. Tension has been taken frequently and has never been above normal. Fields were taken several times. Those of the left eye showed gradual concentric contraction. In September, the left field was limited to 35 degrees except temporally,

which was 45 degrees. In February, the left lower temporal field was reduced to 10 degrees, with slight reduction of other areas. When last seen on April 1, 1947, it was unchanged.

Two additional cases have been seen since this paper was submitted for publication.

CASE 3

History. Mrs. B., aged 81 years, was seen on August 24, 1948, in the Sacred Heart Hospital, at the request of her family physician. She had been admitted to the hospital several days previously for treatment of a skin eruption that followed administration of a sulfa drug given for symptoms of influenza and pains in the sides of her head. She said that vision in the left eye had been poor for the past two weeks.

Eye examination showed normal pupillary reactions and normal tension. Vision was: R.E., 20/100; with correction, 20/40; L.E., hand movements. The lens, media, fundus, and disc of the right eye were normal. In the left eye, the veins were tortuous and engorged, and there was segmentation of the lower temporal branch. Two small hemorrhages were located just below the disc. The disc outlines were blurred and the arteries were small. The temporal arteries were hard and tender and did not pulsate. Blood pressure was 190/90 mm. Hg. Blood and urine examinations were negative. The patient was put on erythroltetranitrate.

Course. On September 2nd, vision in the right eye failed. Examination of this eye revealed an intraocular picture similar to that of the left eye. The patient was slightly irrational at times. A piece of the right temporal artery was removed. There was no bleeding so ligation was not necessary.

Pathologic report. "The internal coat is absent and has been replaced with fibrous tissue. Marked increase in fibrous tissue is present throughout the muscularis, with an infiltration of lymphocytes and endothelial

leukocytes in the muscular coat."

Pathologic diagnosis. Obliterative endarteritis.

Outcome. The irrational periods recurred occasionally until the patient's discharge from the hospital on September 29th. She had become blind by the time she left the hospital. On October 12th, she died of coronary occlusion.

CASE 4

History. A woman, aged 70 years, had been ill for six months, during which time she had lost 40 pounds in weight. She suffered from pain in the scalp, behind the ears, and in both temporal areas. There were palpable, tender nodules along the course of both temporal arteries. No pulsation was present in either artery.

Eye examination showed the right eye to be normal with the exception of Grade II arteriosclerosis. In the left eye, there was obstruction of the nasal branches of the central artery. The temporal artery was still carrying a diminished flow of blood. There was nasal retinal edema. No hemorrhages were present. Vision was finger counting at six inches.

No further details of this case can be reported, since the patient was lost to follow up.

COMMENT

It is not the intention of this paper to enter into a general discussion of temporal arteritis. Several recent papers have covered the subject well. It seems probable that the name should be revised.[2,3] Ocular findings alone give evidence of a more widespread affection.

We are chiefly concerned in drawing attention to ocular complications and in bringing the disease to the attention of ophthalmologists.

In this connection we should like to point out the somewhat unusual discrepancy between visual loss and lack of objective findings. This point has also been emphasized by Johnson, Harley, and Horton.[4] Some cases (our second case, for example) show a frank obstruction of the central artery, but several (as in our first case) give the impression that an interruption of the vascular nutrient branches to the optic nerve has been the chief factor in the visual loss. The cavernous atrophy and excavation of our second case would lend credence to this.

It seems more probable, however, that the interruption of the blood flow comes on gradually over a period of some hours or days, and thus the dramatic changes of an embolus or thrombosis with ischemic edema, cherry-red spot, and so forth do not occur. However, in our first case there was no evidence that the arterial supply to the retina was ever interrupted. It is conceivable that it was slowed enough, however, so that a prolonged partial anoxemia produced the same effect as a complete block. Perhaps both factors (the central retinal artery and optic-nerve vessels) are concerned at the same time.

The cavernous atrophy and excavation of the disc in the second case is interesting. The recent tendency[5] to regard these pseudoglaucomas as a result of arteriosclerotic vascular obstruction is supported by the evidence in this case.

Mention has been made of an anastomosis between the anterior deep temporal artery with the lacrimal branch of the ophthalmic artery.[4] It is more likely, in view of the recent trend to regard this disease as more widespread, that the ophthalmic artery is involved directly by the disease or from central vessels. This is an obscure disease and many questions remain unanswered.

755 Paulsen Building (8).

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DISCUSSION

DR. ANDREW F. DE ROETTH (Spokane, Washington): I was privileged to examine both of these patients. Dr. Smith and Dr. Greene did good service to our cause by bringing up this subject. As far as I can learn, only two papers dealing with eye symptoms in temporal arteritis have been published in ophthalmic periodicals. This in spite of the fact that in half of the more than 40 cases of temporal arteritis so far published there was involvement of the retinal artery in one or both eyes.

This paper shows wise moderation in not touching upon the controversial or unclarified problems of this disease, one of which is the etiology. The inflammatory symptoms, the fever, and the focal infections point to an infectious cause, although investigations by several authors have failed to find the infectious agent. However, I want to remind you of the etiology of iritis in which the cause is probably more often than not a toxin; not a microörganism.

The histopathology of this disease, even in the clear-cut cases, resembles periarteritis nodosa and thromboangiitis obliterans. There are borderline cases that can scarcely be differentiated from the latter disease. It could be that, as Dick and Freeman suggest, the histopathologic picture of temporal arteritis is due to a certain unknown damage superimposed on the senile artery.

Another problem is the selective localization of the disease. However, the localization is not at all so selective as it seemed to be after the first publications. The same changes were found by Cooke and his associates not only in the temporal, but also in the radial, femoral, coronary, retinal, and other arteries. If this is the situation, one may assume that occasionally the retinal artery might be involved without involvement of the temporal artery.

The third problem is that of therapy which, due to our ignorance of the etiology of this disease, cannot be specific. Assuming an infection, however, one should try the new drugs of chemotherapy, as well as the antibiotics. Vasodilators are indicated. Fortunately, Nature is kind, and the involvement of the retinal artery is not an early symptom. There is hope, therefore, that by combating the infectious cause this artery will not become involved.

In connection with the authors' second patient, the question of pseudoglaucoma could also be discussed. This patient had a typical deep cupping 8 months following the onset of the disease. I have observed a patient who had the same deep cupping, with typical glaucomatous fields and tormenting temporal headaches but with patent temporal arteries and no increased intraocular pressure. There was no X-ray evidence of intracranial lesion during 8 months of continuous observation. It seems that typical glaucomatous excavation can be produced by a vascular lesion without increased intraocular pressure.

DR. E. B. BOLDREY (San Francisco, California): The authors have mentioned that they wish to bring the ophthalmic aspects of this disease to the attention of ophthalmologists. I think that it is extremely for-

tunate that they have brought the disease to the attention of neurologic surgeons as well.

These patients come in with a complaint of pain in the temporal region or in some other area of distribution of the external carotid artery. The temporal region is the most common, of course, and hence is the source of the syndrome's name.

We have been interested in the relationship of this disease to various other diseases mentioned—generalized arteriosclerosis, Buerger's disease, and other senile vascular diseases. Also, we have been interested in its relationship to the use of tobacco.

Another factor of interest to us is the relationship, as it appears in the patient who is seen early, of this disease to migraine. Migraine, of course, is regarded as related to contraction or spasm in the distribution of the external carotid artery. It occurs in the younger age groups. Temporal arteritis, on the other hand, occurs in older age groups, but it also implicates the branches of the external carotid artery.

In both instances, pain is the presenting symptom. We have interpreted this pain as being due to irritation of somatic fibers related to the sympathetic and coming along the adventitia of the blood vessels. The proof of that relationship, of course, has been the relief of pain in a considerable number of instances after the temporal artery or other affected branch has been cut.

We have also been interested in the possible connection between this type of disease and the arteriosclerotic senility seen in advanced age, which is related to arteriosclerosis of the internal carotid artery and its branches.

As you are aware, in the treatment of a carotid aneurysm one can tie off the internal carotid artery in the neck and also clip it inside the cranium distal to the point where the ophthalmic artery comes off, without greatly endangering vision in that eye.

In a cadaver, one can tie off both internal carotids in the neck and in the cranium, presumably trapping the ophthalmic artery, tie off one external carotid, then inject material into the other external carotid and fill the isolated internal carotid on the opposite side through the only connection it possesses, that of the ophthalmic. This shows the extent of the anastomotic relationship between the ophthalmic artery and the external, as well as the internal, carotid.

The fact that the ophthalmic artery has now been shown to be implicated in temporal arteritis, a disease that has so widely affected the external carotid, is further evidence of its clinical, as well as its anatomic connections, with both the external and internal branches of the carotid artery.

OPHTHALMIC MINIATURE

Our only chance for restoring sight, when the retina has been injured by concussion is in keeping the organ quiet, in taking blood from the neighbourhood by cupping or leeches, and in the general treatment called antiphlogistic.

Sir William Lawrence, *A Treatise on the Diseases of the Eye*, 1833.

CHRONIC SERPIGINOUS ULCER OF THE CORNEA (MOOREN'S ULCER)*

ETIOLOGIC AND THERAPEUTIC CONSIDERATIONS

JAY G. LINN, JR., M.D.

Pittsburgh, Pennsylvania

Chronic serpiginous or rodent ulcer of the cornea was first recognized as a clinical entity by Mooren[1] in 1867. Nettleship[2] wrote an excellent summary of the subject in 1902. He found 62 cases reported in the literature and added 11 cases of his own. The number of cases reported at the present time has not been determined but is probably over 150. Very little has been added to the knowledge of this corneal disease since Nettleship's original paper.

Numerous additional methods of treatment have been reported as successful in isolated cases, but a consistently effective treatment has not yet been established. This report includes a discussion of the clinical features, an analysis and evaluation of the various therapeutic measures, and the report of a case in which etiologic studies were made.

ETIOLOGY

Numerous factors have been mentioned in the etiology of chronic serpiginous ulcer. Andrade[3] isolated a diplobacillus, and Rodigina[4] isolated an organism resembling zur Nedden's bacillus. Both investigators reported a reproduction of the ulcer in the rabbit eye. Attempts to confirm this work have been unsuccessful.

Duke-Elder[5] and Berens[6] consider it to be a disease of elderly persons, but case reports include all ages. One patient reported by Taylor[7] was three years of age. Age and general health are certainly not important.

Koeppe[8] suggested a tubercular etiology and reported two cures with tuberculin injections. De Berardinis[9] and de Schweinitz[10] saw the ulcer develop following a corneal foreign body. Other writers have related the disease to metabolic disorders and malnutrition,[11] trophic disturbances involving the trigeminal nerve,[12] deficiency of vitamin B_1,[13] and numerous other factors.

The ulcer has been bilateral in about one fourth of the cases, sometimes several years passing before the second eye is involved.

No virus studies have been reported on chronic serpiginous ulcer. This ulcer, however, displays many characteristics of a virus disease. It is a chronic progressive lesion which shows remissions and exacerbations. It does not respond to the various chemical and antibiotic agents now available.* Rivers,[14] in a recent paper, made particular note of the fact that the majority of virus diseases do not respond to these agents. The histologic studies performed have revealed predominantly a round-cell infiltration of the involved cornea. Dean[15] inoculated a guinea pig intraperitoneally with scrapings from an active ulcer. Sections revealed multiple lesions resembling tubercles grossly, but the histologic structure was not that of a tubercle. This could possibly have represented pock-formation of the virus. The frequent occurrence of corneal anesthesia in these cases may indicate a neurotrophic factor of virus origin. A virus is certainly the most likely cause of chronic serpiginous ulcer.

CLINICAL PICTURE

The ulcer may occur at any age, although it is uncommon before puberty. It begins as a narrow grayish infiltration near the limbus which, in a few weeks, breaks down to form a marginal ulcer. Multiple limbal infiltrations

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* Streptomycin and tyrothricin have not been tried.

may be present which ulcerate and extend marginally to coalesce. At this stage they may resemble simple marginal ulcers.

It spreads slowly, penetrating about one third of the depth of the cornea. There is an advancing margin which undermines the superficial corneal layers, producing a gray infiltrated overhanging edge of half-dead corneal tissue with an intact epithelium. The exact depth of undermining is only realized by probing, and the full extent of corneal involvement is not appreciated until this overhanging edge is removed. Behind this active margin, healing takes place from the periphery with the development of new vessels and an ingrowth of epithelium.

Mayou[16] has noted that there is no tendency toward fibrous tissue formation and the healed cornea is about one-half the original thickness. Only the active margin stains with fluorescein. The ulcer spreads around the limbus, toward the center of the cornea, and sometimes into the sclera (Parsons[17]).

Progress is slow but not uniform, and one portion of the margin may be actively advancing while another portion is inactive. The uninvolved cornea remains clear but, unless progress is checked, the entire cornea is affected after a period of 3 to 9 months. A series of small secondary ulcers may appear in the already healed cornea. Perforation has been reported in several cases[18-21] following which the ulcer may heal.

Injection of the bulbar conjunctiva is very mild considering the severity of the process. Hypopyon does not occur unless there is secondary infection. A mild iritis is common.

Pain is a variable symptom. When present, it is very severe and is usually accompanied by lacrimation and photophobia. The pain is more often noted when the ulcer is actively advancing. In spite of the severe pain sometimes present, the congestion remains mild.

During the active stages, ptosis is usual but disappears after healing. The opacity of the healed cornea may clear so that the iris again becomes visible, but vision does not improve.

PATHOLOGY

Microscopic studies of chronic serpiginous ulcer have been made in several cases, the most complete description being reported by Feingold.[19] The healed cornea, previously damaged by the ulcer, is infiltrated predominantly with lymphocytes, although a few plasma cells and an occasional giant cell may also be found. It is generally a diffuse infiltration but nodules may form. Bowman's membrane is destroyed. The area contains numerous small blood vessels with a perivascular collection of lymphocytes. The epithelium over this area is thicker, being composed of 7 to 10 layers rather than the usual 5 to 6 layers.

The active margin of the ulcer contains polymorphonuclear leukocytes and occasionally a few eosinophils. Here the cornea is increased in thickness. Bowman's membrane is intact to the edge of overhanging corneal tissue. This overhanging edge is made up of epithelium, Bowman's membrane, and superficial stromal lamellae undergoing necrosis.

The deep corneal lamellae are almost normal except for some deep vascularization. The granulation tissue may extend into sclera with loss of scleral substance.

TREATMENT

The treatment of this corneal disease remains an unsolved problem. The rarity of the disease prevents any single person from obtaining sufficient experience to evaluate properly the various therapeutic methods and to establish a consistently effective routine. Numerous methods of treatment reported as producing cures have subsequently failed in other cases. Some writers claim a cure with a specific drug, although in conjunction with the drug, they had used other therapeutic measures which previous authors had claimed to be effective.

Fifty-three cases in which cures are reported have been collected. A summary of these cases is presented in Table 1.

TABLE 1

REPORTED CURES OF CHRONIC SERPIGINOUS ULCER

Therapy	Author	No. of Cases
I. Cauterization (with or without curettage)		
A. Chemical agents		
1. Used successively pure carbolic acid, formalin, and electrocautery	Shannon[22]	1
2. Successively, tincture of iodine, carbolic acid, and nitric acid	Stevens[23]	1
3. Nitric acid, 5 applications	Jackson[24]	1
4. 20% carbolic acid	Dufour[25]	2
5. Curettage and trichloracetic acid	Risley[26]	1
B. Physical Agents		
1. Galvanocautery	Stephenson[27]	1
2. Galvanocautery	Frank[28]	1
3. Galvanocautery	Cronquist[29]	2
4. Galvanocautery	Krey[30]	2
5. Paquelin's cautery	Krey[30]	1
6. Electrocautery	Fisher[31]	1
7. Cautery and excision of overhanging edge of cornea	H. Gifford[32]	1
8. Cautery (type not mentioned)	Ellett[33]	1
II. Paracentesis or Delimiting Keratotomy		
1. Paracentesis (repeated 5 days, 14 days)	Fuchs[34]	2
2. Paracentesis (repeated 21 days)	Mayou[16]	1
3. Delimiting keratotomy (repeated 8 days, 10 days)	S. Gifford[35]	2
4. Delimiting keratotomy	Thygeson[36]	3
III. Conjunctival Flap over Ulcer		
1. Flap and galvanocautery	F. W. Dean[16]	1
2. Flap and trichloracetic acid	S. Gifford[35]	1
3. Flap and sulfanilimide	Blaess[37]	1
4. Flap alone	A. C. Dean[38]	1
5. Flap and ulcer "scraped"	Tyrell[39]	1
6. Total hooding of cornea	Kreiker[40] (Kettesy)	3
IV. Chemotherapeutic and Antibiotic Agents		
1. Cyanide of mercury (1:1,500) by subconjunctival injection (2 cc.)	E. L. Jones[41]	1
2. Bichloride of mercury (1:2,000) by subconjunctival injection	Andrade[3]	2
3. Aqua formalinata (0.3:1,000 or 0.5:1,000) as an eye bath or hot fomentations	Hidaka[42]	1
4. Zinc ionization	H. L. Jones[43]	4
5. Daily application of silver nitrate (1.5%) for 3 months	Haab[44]	1
6. Mercuric perchloride by subconjunctival injection	Augerias[45]	1
7. Tincture of iodine application	Koller[46]	1
V. Radiation		
1. Beta radiation unscreened 45 to 50 minutes	Ward[47]	3
VI. Miscellaneous		
1. Excised ulcerated area and replaced with corneal tissue from rabbit	de Berardinis[9]	1
2. Liver extract, daily injection, and Metri cautery 80 to 85° F.	Cantillon[48]	2
3. Cauterized with trichloracetic acid, high vitamin diet, and cod-liver oil locally	Townsend[49]	1
4. Vitamin B_1 injections	Suurkula[13]	1
5. Tuberculin injections	Koeppe[8]	2
Total Number of Cases		53

Some forms of treatment mentioned as effective against Mooren's ulcer are not included in this list because definite cases were not cited. Schepens[50] suggested beta rays or one-third to one-fiftieth erythema dose of X rays. Nettleship[2] performed an optical iridectomy on some cases and used a cautery in others. Fisher[51] reported favorable results with thyroid extract (1 gr., 3 times daily).

Although cauterization has apparently cured more cases than any other method, it has been reported ineffective in the greatest number of patients. Failure with paracentesis or delimiting keratotomy has occurred in several instances. Thygeson[36] found the sulfonamides and penicillin to be ineffective. Streptomycin and tyrothricin have apparently not been used. No failures have

been recorded with radiation or conjunctival flap.

CASE REPORT

T. B., a Negress, aged 17 years, was first seen in the university eye clinic July 22, 1947, complaining of a "spot" on the right eye which had been present for 4 months. It began as a constant burning sensation in the right eye accompanied

hemoglobin, 80 percent; W.B.C., 10,500 (with 66-percent neutrophils, 33-percent lymphocytes, and 1-percent eosinophils). The urine was normal. Sedimentation rate was 3 mm. in 60 minutes. The Wassermann and Kahn tests were negative. The Frei test was negative. X-ray examination of the chest and teeth were negative.

Treatment was begun with instillation of 0.5-percent atropine sulfate solution twice daily and

JUL. 22   AUG. 9   AUG. 25   AUG. 26

SEPT. 11   SEPT. 13   OCT. 31
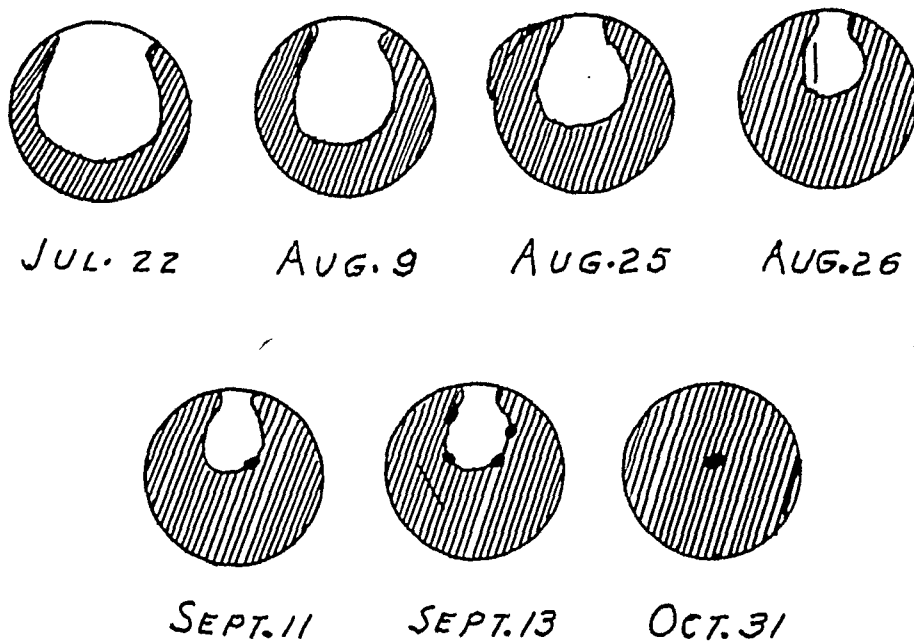
Fig. 1 (Linn). Diagram of the progress of the ulcer. The marked difference from August 25th to August 26th indicates the amount of undermining which became apparent only after the overhanging edge was removed.

by severe headaches. She was treated in another clinic for 1 month with no improvement. She was then seen by a private physician for 2 months who cauterized the "spot" twice a week with medicines. The pain stopped spontaneously 2 weeks prior to her first visit to the eye clinic.

On initial examination vision was: R.E., 20/50; L.E., 20/20. The cornea contained a large ulcerated area extending marginally from the 1- to the 11-o'clock positions (fig. 1, July 22). The edge of the ulcer was elevated, undermined, and stained with fluorescein. Corneal sensation was normal. The right upper lid was ptosed. Conjunctival injection was mild. Atropine sulfate (1-percent solution) and sulfathiazol ointment were prescribed, pending admission to the hospital.

The patient was admitted to the Eye and Ear Hospital on August 9, 1947, on the service of Dr. S. D. Evans. The ulcer had advanced since seen in the clinic (fig. 1, August 9).

Physical examination was negative except for the patient being slightly underweight. Culture and smear of the right eye were negative for bacteria. The blood count was: R.B.C., 4,080,000;

penicillin solution (1,000 units per cc.) by iontophoresis with a corneal bath twice daily. The eye was patched with penicillin ointment between treatments. The patient was also given multivitamin capsules (ABdol with vitamin C) twice daily.

One week later (August 16) no improvement was evident. Penicillin was discontinued. A subconjunctival injection of 1 cc. of 5-percent sodium sulfacetamide solution was performed and repeated in 3 days. A 30-percent sodium sulfacetamide solution was instilled every two hours during the day. A daily injection of liver extract (Lederle) was begun at the same time and continued for 5 weeks.

A week later (August 24) it was noted that the ulcer was progressing, and the patient began to have pain in the eye. Sodium sulfacetamide was discontinued. Sulfanilamide was begun, and a blood level, varying between 4 mg. percent and 7 mg. percent, was maintained. Sulfanilamide ointment was used locally.

On August 26, 1947, the ulcer was curetted and the curettings transferred to 1 cc. of sterile physiologic saline solution for use in animal studies.

The overhanging edge of cornea was excised and also saved. The excision of this overhanging edge revealed more extensive corneal destruction than had previously been recognized, as well as an extension of the ulcer into the sclera at the 10-o'clock position (fig. 1, August 25 and August 26). A muscle hook heated in an alcohol flame was applied to the active ulcer margin. A delimiting keratotomy was performed in advance of the temporal margin which appeared more active at this time.

The keratotomy incision was reopened daily for 14 days at which time it was allowed to heal over because the cornea did not take a fluorescein stain in any area, and showed no apparent activity. In the meantime, sulfanilamide had been discontinued because of a drug reaction manifested by generalized urticaria, fever, and lymphadenopathy.

Fig. 2 (Linn). Appearance of the eye on August 11, 1947.

Two days after allowing the keratotomy incision to close, a pinpoint area of the ulcer margin had broken down (fig. 1, September 11). This area was curetted and cauterized with trichloracetic acid. In two more days several active areas had appeared (fig. 1, September 13).

Paracentesis was performed at this time in a previously involved corneal area because there was so little normal corneal tissue remaining. This incision was reopened daily for 27 days.

The patient was discharged from the hospital on September 28th and she returned for daily treatments as an out patient. Active areas remained throughout the entire period. These were curetted on several occasions and cauterized with trichloracetic acid.

On October 10, 1947, the paracentesis was allowed to heal because no improvement was noted. Local cod-liver oil and atropine were used. The disease spread to involve the entire cornea, a single active central area remaining (fig. 1, October 31). On November 14th, a tissue culture was inoculated directly with curettings from this central area.

On January 14, 1948, there was no apparent activity of the lesion but the central corneal

Fig. 3 (Linn). Appearance of the eye on January 28, 1948.

area was still not covered with epithelium. A few drops of the patient's own blood were instilled into the conjunctival sac and a patch was applied as used by Grossman[52] in the treatment of other corneal lesions. This was repeated daily for 18 days with complete healing of the cornea. At this time the opacity of the cornea obscured any observation of the iris.

On March 23, 1948, the cornea was noted to be less opaque and iris stroma was visible above and below. The patient had no ptosis for the first time since the original examination.

ETIOLOGIC STUDIES

Since it was felt that a virus is the most likely cause of chronic serpiginous ulcer, the attempt was made to culture a virus from this patient. Lesions have been reproduced by others in the rabbit[3, 4] and the guinea pig.[15] It was for this reason that these animals, along with chick embryos, were used in these studies.

An abraded rabbit cornea and two chick embryos (4 days) were inoculated with a saline suspension of curettings. The eggs were inoculated directly over the embryos. After incubation for 11 days, no gross lesions of the embryos were apparent. At this time, they were emulsified, and a suspension of this material was injected intraperitoneally in guinea pigs, intracerebrally in mice, and subconjunctivally in rabbits. No lesion was observed in any animal.

Corneal tissue excised from the ulcer margin which had been frozen for 3 weeks was then transferred intraperitoneally in a guinea pig and buried subconjunctivally ad-

jacent to the limbus in a rabbit. Again no lesion was produced.

Curettings from the remaining active ulcer area late in the disease were transferred directly to a 4-day old tissue culture of embryonic mouse brain. Five days later, a second tissue culture was inoculated from the first. These tissue cultures were used in 7 and 10 days to inoculate abraded rabbit cornea near the limbus, a small amount being injected subconjunctivally adjacent to the abrasion. They were also used to inject guinea pigs intraperitoneally. No lesions appeared in the rabbits and the guinea-pig peritoneum was normal to gross and histologic examination 6 weeks later.

Assuming a virus is the etiologic agent in Mooren's ulcer, several explanations can be presented to explain these negative studies. The initial curettings, procured during the very active stage of the ulcer, were diluted with saline and not used for inoculation for a period of at least 1 hour. At this time the virus concentration may have been so low as to be nonpathogenic. The chorio-allantoic membranes of the chick embryos were discarded. Viruses in general grow better on these membranes than on the embryo itself.

The inoculation of the tissue cultures was performed at the bedside, but at this time, the activity of the lesion was slight and no virus may have been present.

Sanders,[53] in discussing the cultivation of viruses, noted the difficulty of culturing viruses of more common eye diseases such as trachoma and inclusion blenorrhea. The ideal medium for culturing viruses affecting the eye has apparently not been discovered.

COMMENT

Although resolution occurred in the case reported, it is not considered to be a cure. Spontaneous resolution following complete involvement of the cornea has been previously reported. The whole blood used in this case is considered to have been important in stimulation of corneal epithelization.

Experimental studies to support this conclusion were recently reported by Newell.[54] It may prove effective against the active ulcer in the future, but in this patient was used after the disease process had become inactive.

The treatment used included: penicillin, sodium sulfacetamide, sulfanilamide, liver extract, vitamins, delimiting keratotomy, cauterization, and whole blood. Of this group, cauterization, liver extract, delimiting keratotomy, and vitamin B_1 have been previously reported as curative.

The greater majority of reported cures were in early cases. The more consistently effective therapeutic measures fail in far-advanced cases. It is, therefore, recommended that an untried new method of treatment not be used except in an early case. Even then it should be replaced by another method if no improvement results in two weeks.

The most effective procedures apparently are beta radiation, delimiting keratotomy combined with cauterization, and a conjunctival flap operation. These procedures should probably be used in the order given. If a delimiting keratotomy is effective, it will be apparent after reopening in about 14 days. A conjunctival flap should not be delayed much after that period.

Therapeutic measures worthy of further consideration are convalescent serum and whole blood locally. Streptomycin or tyrothricin may be tried.

SUMMARY

1. A brief discussion of the clinical and pathologic features of chronic serpiginous ulcer (Mooren's ulcer) is presented.

2. An analysis of 53 reported cures of this corneal disease is made. From this analysis it is concluded that beta radiation, delimiting keratotomy, and a conjunctival flap operation are the most effective therapeutic measures.

3. A case is reported which was treated without success. Several methods of treat-

ment were used in this patient which had been previously reported successful. Resolution of the disease occurred after the cornea was completely involved.

4. An unsuccessful attempt was made to demonstrate a virus as the etiologic agent.

500 Penn Avenue (22).

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OPHTHALMIC MINIATURE

A prescription for a collyrium to sharpen and strengthen vision is made of equal parts of sagapen gum, opopanax, rock salt, verdigris, white pepper, asafoetida, balsam oil, ox gall, long pepper and ginger—10 drugs in all. These are thoroughly triturated with fennel water and applied to the eyes.

Also, if a little opopanax resin is mixed with sweet basil water and rubbed on the eyes it clears vision; so does the juice of half a boiled green, unripe pomegranate, to which half its bulk of honey is added. Expose the mixture to the sun for 20 days, after which it will be ready for use.

Memorandum Book of a Tenth-Century Oculist.

Translated by Casey A. Wood.

NEISSERIA CATARRHALIS ENDOPHTHALMITIS*

REPORT OF A CASE WITH COMPLETE RECOVERY

ISADORE GIVNER, M.D.
New York

The case to be reported is singular in that an endophthalmitis produced by the Neisseria catarrhalis followed an intraocular operation on an apparently clean case and that a successful recovery followed penicillin therapy.

CASE REPORT

History. J. R., aged 24 years, an unmarried white woman, had known of her diabetes for 2½ years. She has been on 90 units of insulin daily. Five months before presenting herself for examination she noticed blurring of vision in her left eye. For the past week the right eye had become hazy.

Eye examination on September 4, 1947, showed mature cataracts in both eyes with vision: O.D., counting fingers; O.S., light perception. Good light perception in both eyes. The remainder of her ocular and general examination was negative including sac irrigation, bacteriologic studies of the conjunctiva, and sensitivity tests for lens antigen.

On September 18th a small conjunctival flap was laid down. A keratome section was made, iridectomy performed, and the anterior capsule of the left lens was removed. The lens was irrigated out completely, the iris roots were replaced, and the conjunctiva was reunited with interrupted silk sutures. Atropine (1 percent) was instilled and both eyes patched.

On September 20th, at the first dressing, the left upper lid was swollen and red. The bulbar conjunctiva was chemotic and the anterior chamber filled with stringy pus. The

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* From the Ophthalmological Service of Dr. Raymond E. Meek, New York Eye and Ear Infirmary.

diagnosis of endophthalmitis was obvious and the patient was taken to the operating room where the conjunctival sutures were removed. A culture was taken from the anterior chamber which was then irrigated with penicillin (2,000 units per cc.). Much stringy pus remained after the irrigation. The culture was later reported as Neisseria catarrhalis. No fermentation of the Gram-negative diplococcus occurred in dextrose, maltose, or lactose.

Treatment. Each day thereafter pads of cotton soaked in penicillin (20,000 units per cc.) were placed in the lower cul-de-sac for 30 minutes and systemic penicillin and sulfadiazine were kept up for one week.

From the time of the first dressing after the irrigation, marked improvement occurred until on October 11th the entire anterior chamber was free of discharge and the eye was white with no ciliary or conjunctival congestion.

The pupillary area was filled with a thin membrane and a small infiltration was present in the substantia propria of the cornea just below the pupillary area extending about 2 mm. in length and 1 mm. in width. The tension was normal and light perception and projection were good. Atropine (1 percent) and neosynephrin (10 percent) was continued until October 25th.

Result. On April 13, 1948, a Wheeler discission was done horizontally at right angles to the lines of tension in the pupillary membrane. On May 7th, with a + 14.0D. sph., vision in the left eye was 20/20; with a + 2.5D. addition for near she could read J1.

Culture. Animal (rabbit and cat) experimentations with the culture of Neisseria catarrhalis produced a violent endophthalmitis after anterior-chamber inoculation. This was not at all controlled or favorably affected by streptomycin irrigations.

Discussion. Since seeing this case, I have had a written report from an out-of-town colleague who has seen three cases of en-

dophthalmitis produced by the Neisseria catarrhalis after cataract extraction. Since this organism has a common habitat in the nose it behooves all of us to be sure our masks cover our nostrils. This is offered as a theoretic precaution only, as I have not been able to inoculate successfully a blood agar plate by breathing on it at either 4, 8, or 10 inches.

In reviewing the literature, only one other author* has reported on an intraocular infection by the Neisseria catarrhalis. The cultural studies as given in the two reported cases of this author are inadequate but suggest that the offending organism probably was the Neisseria catarrhalis. One case followed an injury by a missile of glass and another was metastatic in a patient with bronchitis.

SUMMARY

A case is reported of a Neisseria catarrhalis endophthalmitis after a cataract extraction. This organism has not been recorded previously as the cause of a postoperative endophthalmitis. The inflammation was successfully controlled by a penicillin irrigation of the anterior chamber followed by daily pledget applications of penicillin, systemic penicillin, and sulfadiazine systemically.

108 East 66th Street (21).

COLOBOMA OF THE OPTIC NERVE

CHARLES E. BIKLE, M.D., AND
JESSE M. LEVITT, M.D.
Brooklyn, New York

The atypical appearance of coloboma of the optic nerve associated with pseudoptosis, total paralysis of the superior rectus muscle, microphthalmos, absence of the macula, and defective growth of the orbit makes the following case worthy of record.

* Salvati, G.: Panophthalmitis caused by Micrococcus catarrhalis: Two cases. Lettura Oftal., 5: 146 (Mar.) 1928.

History. R. D., an 11-year-old boy, was brought to the eye clinic of the Brooklyn Eye and Ear Hospital, service of Dr. E. C. Place, in October, 1947. The mother stated that she first became aware of the abnormality of the right eye when the patient was 9 months old. "Crossing" and narrowness of the palpebral fissure were then noted. The mother did not have any

Fig. 1 (Bikle and Levitt). Note the microphthalmos and narrow palpebral fissure of the right eye.

illness during pregnancy. The patient had two sisters, aged 16 months and 3½ years, and two brothers, aged 5 years and 7 years. The eyes of all the other siblings were examined and found to be entirely normal.

Eye examination. The vision of the patient's right eye was limited to counting fingers at a 6-inch distance, eccentrically in upper nasal and lower temporal fields. The vision of the left eye was 20/15+3. The left eye was normal in all respects.

The palpebral fissure of the right eye was 3 mm. smaller than that of the left eye and the right eyeball was markedly smaller than the left, creating the appearance of a ptosis of the upper lid (fig. 1). The corneas were of equal size.

The eyes were straight in the primary

position. There was complete inability to rotate the right globe up and temporally, and there was a tendency to overshoot the right eye in the down and temporal position and the left eye in the up and nasal position of gaze.

The irides were essentially of the same color. The pupils were round. The right pupil was smaller than the left and reacted sluggishly to light. There was a faint webbed opacity attached to the posterior capsule in the nasal half of the lens, which was otherwise normal. The vitreous chamber was clear.

There was no semblance of a normal optic nerve or macular area in the fundus. At the normal nerve site there was a five-sided depressed area slightly larger in extent than that of a normal nerve, with a faint pink hue and slight irregularity of tissue margin above (fig. 2). The depression was devoid of vessels. Surrounding it there was a narrow slate-colored zone and then a broader white zone. With the binocular ophthalmoscope the appearance resembled somewhat a doughnut, the hole being the irregular depression and the ring the slate-colored and white zones which were elevated and roundish.

The main retinal vessels, which were dis-

Fig. 3 (Bikle and Levitt). X-ray picture of orbits showing smallness of right orbit.

tributed peripherally fairly normally, coursed around the ring and disappeared just before reaching the edges of the depression. The macula was not differentiated. In its normal place, there was a diffuse honey-combing which was spread over a broad area. The peripheral fundus background had a fairly normal color. Scattered throughout the fundus there were variously sized spots of chorioretinitis of the atrophic type and dense deposits of pigment.

Radiologic study. Aside from the ocular abnormality the patient was healthy and normally developed. Blood Wassermann was negative. A radiologic study of the skull, orbits, and paranasal sinuses revealed that the skull vault was normal in form, thickness, and structure. The convolutional markings were not increased in depth or number. There was no diastasis or premature synostosis. There were no intracranial calcifications and no pathologic changes were apparent in the base of the skull, including the sella.

The optic foramina were normal in size and form. The right orbit was slightly smaller in all its dimensions than the left. The measurements of the right orbit were 3.8 by 3.9 cm. as compared to the left orbit which measured 4.1 by 4 cm.

The frontal sinuses were rudimentary.

Fig. 2 (Bikle and Levitt). Right fundus showing atypical coloboma of the optic nerve.

The ethmoids of both sides and both antra were clear. The left sphenoidal sinus was small and clear. The right was of moderate size and slightly cloudy. There was a large mass of soft tissue density high in the nasopharynx, probably adenoid tissue.

1 Nevins Street (17).
991 Ocean Avenue (26).

DEMONSTRATION OF TRACHOMA INCLUSIONS*

A PRACTICAL AND RAPID STAINING TECHNIQUE

V. O. EARECKSON, JR., LT. (JG), (MC), U.S.N.R.
Camp Lejeune, North Carolina

This paper is written with the intention of bringing to the busy ophthalmologist a rapid staining technique for the demonstration of trachoma inclusions. This method is not only rapid but simple both in technique and in the reagents necessary. The need for a short cut in a busy practice was forcibly brought to my attention by two cases which I recently saw.

One was the case of a 49-year-old white woman, a native North Carolinian, who has not been out of eastern North Carolina for several years. In September, 1947, she began having pain, photophobia, and redness of the left eye. She immediately sought the aid of a practitioner who treated her for a simple conjunctivitis.

After several weeks of treatment she was referred to an ophthalmologist who made the diagnosis of uveitis, which apparently was quite correct. This was treated for several months and, in January, she was told that the uveitis had cleared but that she had another condition.

The attending physician made many tests,

all of which cost valuable time and money, but at the end of a month of X-ray studies, laboratory tests, and consultation, the diagnosis was still undetermined.

Being a United States Navy dependent, she sought aid at this hospital. Upon seeing her eye, one could not but notice a pannus which had grown down at least 3 mm. upon the cornea. The typical cobblestones of trachomatous conjunctivas were present on both upper and lower lids and also involved the caruncle. Conjunctival scrapings done at this time revealed the typical inclusions of trachoma.

The second case is that of a 23-year-old marine who stated that in December, 1946, upon returning from maneuvers in the Caribbean he first noticed pain, redness, and blurring of vision in the right eye. He was admitted to the dispensary at his activity under the diagnosis of corneal ulcer and was treated with penicillin, hot compresses, and atropine.

He did not improve, so was transferred to a naval hospital where he was treated similarly with the exception that the ulcer was repeatedly cauterized with trichloracetic acid. It is noted in his previous write-up that he had recurrent ulcers at various points on the cornea.

He showed no improvement under this treatment and it was felt advisable to transfer him to another hospital. Here he was treated off and on with sulfadiazine in small doses, penicillin, atropine, hot compresses, typhoid vaccine, sterile-milk injections, X-ray therapy, and radium. He had numerous consultations and was found by the urologist to have chronic prostatitis. The diagnosis was then made of nummular keratitis secondary to chronic prostatitis. He was massaged and given more sulfa and penicillin but to no avail.

After eight months in the hospital the cornea finally cleared enough to send the man back to duty, and it was felt that if the prostate condition would remain quiescent the eye would not flare up.

At this time his vision was 20/40 and he had an opacity in the center of the cornea about 4 mm. in diameter. He states that his eye was still red and still felt irritated. The eye did remain rather quiescent until April 9, 1948, when he was hospitalized because of acute laryngitis. At this time the same symptoms returned and a large ulcer was noted in the center of the cornea. He was then referred to me for consultation.

Upon examining the eye, there was seen an ulcer, 3 mm. in diameter, in the center of the cornea encircled by a large area of opacification which extended through the stroma. There was marked engorgement of all the blood vessels of the eye and quite a great deal of pain. At the upper margin of the limbus there was noted a small pannus growing down upon the cornea (this condition had been discovered previously but it was felt that it was consistent with the changes of nummular keratitis). Vision at this time was limited to hand motion at three feet. Scrapings of the conjunctiva at this time revealed the epithelial cells to be loaded with inclusions typical of trachoma.

TECHNIQUES OF STAINING

After the scraping has been made and spread upon a clean glass slide it is allowed to fix by drying in the air. Then the slide is flooded by Wright's stain and allowed to stand the prescribed time for that particular solution, following which it is neutralized with distilled water. At the end of this neutralizing period it is washed with tap water and allowed to dry. It is then ready to examine under oil. The entire time for this procedure in our laboratory is 7½ minutes —3½ minutes for the Wright's stain and 4 minutes for the buffered mixture. However, this time varies with the solution of Wright's stain used.

This staining technique seems to me to be a boon both to the physician and to the anxious patient, since it is easily carried out in the office and may be included as a routine procedure in practice.

If one were to compare the results of this method with those of the Giemsa stain, it would be found that the inclusions stain blue in both methods but the Wright's stain gives a lighter blue. It would also be found that the nuclei of the epithelial cells stain a rather definite purple which is in contrast to the nuclei poorly stained with Giemsa stain. The time element is the big factor. Since Giemsa stain takes 24 to 48 hours and, in addition, is very sensitive to pH changes, it is not practical as an office test. On the other hand, the Wright's stain technique takes from 7 to 10 minutes and is as simple as a differential blood-smear stain.

The technique of demonstrating the inclusions in these cases has also been used in several cases of inclusion blenorrhea and seems to give ideal results in both.

SUMMARY

1. Two cases of trachoma are presented which were relatively far advanced. The loss of vision, time, and money could have been prevented by examining the conjunctival scrapings of these patients earlier.

2. A rapid staining technique is described for the benefit of the busy ophthalmologist. It can be done in the same manner as a differential blood smear.

3. A comparison is drawn between the Giemsa stain and the Wright's stain.

United States Naval Hospital.

THE BILATERAL SLAB-OFF*

R. L. SCHMIDTKE, M.D.
Saint Paul, Minnesota

The use of a unilateral "slab-off" for the equalization of the prismatic effect in cases of anisometropia is not new to the ophthal-

mologist and optician, but, to my knowledge, the use of a bilateral "slab-off" for the elimination of the prismatic effect in presbyopic patients who wear a moderately high myopic correction (myopia of about 5 to 10 diopters) has never been reported in the literature.

Several years ago a patient reported for a refraction and during the interview he complained that, since getting his first bi-
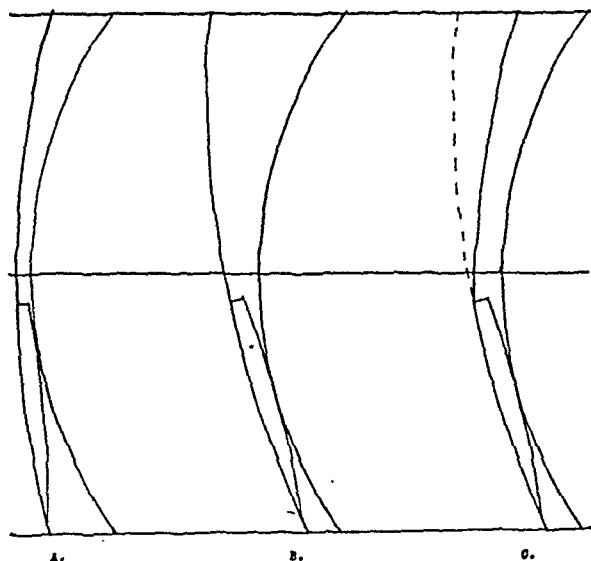
Fig. 1 (Schmidtke). The principle of grinding a bilateral "slab-off."

focals, he had been uncomfortable because, as he stated, he had a feeling of looking around the lower edge of his glasses.

During the refraction it occurred to me that this patient's symptoms were due to the prismatic effect produced by his moderately high myopic correction when using his presbyopic add for near vision. In an effort to make this patient more comfortable a flat-top bifocal segment combined with a bilateral "slab-off" was incorporated in his final prescription.

After wearing these glasses for more than a year, this patient reports that he has never had such a comfortable pair of glasses. Since then, I have prescribed this type of lens for a number of myopic patients, all of whom report greater eye comfort.

Without encroaching too much upon the optician's field I will briefly discuss the principle of grinding such a lens (fig. 1).

(A) is a diagrammatic cross section of the conventional myopic lens incorporating a flat-top type bifocal segment.

(B) is a diagrammatic cross section of this same lens into which a prism of appropriate strength and base up has been incorporated so that the optical center has been shifted from a point 2-mm. above the segment to 4-mm. below the top of the segment, thus superimposing the optical center of the distance lens over the optical center of the bifocal segment. Such a lens would be fine for close work but could not be tolerated for distant vision.

(C) is a diagrammatic cross section of the finished lens. Grinding off the prism above the top of the segment produces a new optical center for the distant part of the lens, 2-mm. above the segment, without disturbing the optical set-up for near vision, thus giving the wearer a pair of ophthalmic lenses with two optical centers—one for distant and one for near vision.

If properly made, ophthalmic lenses in which a "slab-off" has been incorporated are no more unattractive than conventional bifocals of the same power.

In cases of high myopia (myopia of 10 diopters or more) requiring a presbyopic near add, this type of lens has no advantage over the "double-myo" lens.

441 Lowry Medical Arts Building (2).

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW YORK SOCIETY
FOR CLINICAL
OPHTHALMOLOGY

May 3, 1948

DR. DANIEL KRAVITZ, *president*

BIOMICROSCOPY WITH POLARIZED LIGHT

DR. GEORGES KLEEFELD discussed this subject during the instruction period.

PRESENT STATUS OF DIABETIC RETINOPATHY

DR. GEORGE ANDERSON said that diabetic retinopathy represents universal retinal vascular disease rather than arterial degeneration alone. Rupture of fragile capillary micro-aneurysmal dilatations has been described. Small, round, deep hemorrhages are probably the most characteristic feature of this specific retinopathy especially in the absence of systemic hypertension.

The duration of the diabetes rather than the age of the patient is the definitive factor. Juvenile diabetics of long duration (15 years) are especially susceptible. Only 8 percent of 200 of Priscilla White's juvenile diabetics between the ages of 20 and 39 years, who had had the disease for 15 years or more, escaped vascular degeneration (85 percent of these had retinal sclerosis; 80 percent, retinal hemorrhages).

In this series, freedom from evidence of vascular degeneration occurred only in those patients who had been well controlled. Careful analysis points to the fallacy of the argument that control of the diabetes makes little or no difference. It is almost impossible to attain 100-percent steady chemical control of the diabetes in the juvenile who is an unstable, ever-changing, growing individual. A discrepancy from complete control is countenanced by most clinicians as inevitable. As shown by postmortem statistics of Root and

the clinical results of Boyd and Jackson, control of the diabetes, difficult as it may be, pays dividends in the postponing of vascular degeneration.

In clinics where the philosophy is at variance with control, the incidence of retinitis is reported as 100 percent in juvenile cases of long duration, whatever be the degree of control. This is as would be expected when correlated with the results of those practicing meticulous control of hyperglycemia and glycosuria.

It is probable that retinopathy will not undergo substantial reduction until a smoother, automatically acting insulin, in complete homeostatic relationship with the organisms, makes total 24-hour control of the diabetes possible without sharp flings from hyper to hypoglycemia and without intermittent phases of excessive fat mobilization. These fluctuations probably exist to some extent in the best controlled diabetic under the best methods presently available.

The mildest diabetic, one with a "touch," frequently suffers from the most severe retinopathy. He is usually the neglected diabetic whose underlying disease is discovered by his alert ophthalmologist.

Effective treatment of diabetic retinopathy is essentially prophylactic and must take place in the early stages of the disease. It represents the most meticulous control of the hyperglycemia that is possible. The youthful and the adult diabetic in early stages of the disease should be treated vigorously by diet and insulin. The obese adult with beginning diabetes should have consistent, unrelenting weight reduction to improve insulin efficiency and carbohydrate metabolism. This vigorous treatment should not be applied to the elderly diabetic with advanced retinopathy.

When retinopathy has developed in the

late diabetic, the diabetic state must be sacrificed to the welfare of the eyes in order to avoid vascular catastrophe. A balanced diet, relatively high in protein for repair and maintenance of damaged tissues, a diet not calculated to reduce weight except most slowly and cautiously, and a diet that does not increase individual insulin sensitivity gives the best results.

Relative or absolute hyperglycemia must be cautiously avoided, since it causes, through compensatory adrenal response, rupture of fine fragile vessels and results in blindness. Meticulous chemical (sugar) control in these advanced patients becomes, therefore, meddlesome therapy.

At present, it would seem that few diabetics are well enough controlled to be promised freedom from eye complications. After 15 years of the disease, whatever be the age of the patient, the process is, at best, only delayed.

The evidence that diabetic retinopathy, as well as the underlying diabetes, is caused by a third and unknown condition is meager. It is likely that when the ideal, automatically acting insulin is discovered the incidence of diabetic retinopathy will approach that of a cross-section of the population for the same age grouping.

Discussion. Dr. Isadore Givner said that Dr. Anderson's emphasis on the importance of better diabetic control in slowing the development of diabetic retinopathy is most important. This has been the experience of others, including Rabinowich who stated that better dietary control may forestall retinal changes.

Joslin has emphasized, however, that the mechanism by which lack of control can affect the retinal vessels which induce hemorrhages is still a mystery. Yet here lies the crux of the situation for, if this factor could be established, methods of treatment might vary accordingly. Some say it is the hyperglycemia itself. This idea was championed by Graefe who stated that without increase in blood sugar no sign of diabetes would occur. Others believe it is the intermediate products of metabolic change dependent upon impaired protein metabolism, hypercholesterol, and liver dysfunction.

Priscilla White called attention to Smith's work with menotoxin and suggested a like toxin acting in diabetes as a vascular poison. Acting on this suggestion, Dr. Givner said that he arranged with Dr. David Macht of Baltimore to study blood sera in patients with diabetes that had marked vitreous hemorrhages and advanced capillary fragility. A case of this type recently studied, however, showed no toxin as studied with this phytopharmacologic method.

Statistics, such as quoted from Priscilla White's patients, cannot be evaluated properly unless one knows the duration of the diabetes. Duration of the disease has been emphasized by Dolger and others as more important than the severity of the disease or the control in the incidence of retinal pathology. Comparison of the figures given in Priscilla White's series of 850 eyes with Waite and Beethan's combined series of juvenile diabetics (where only 1.7 percent of the cases showed retinal hemorrhages) shows a marked discrepancy which can be explained only on the basis of the duration of the disease in White's cases.

In spite of Waite and Beethan's dictum that the only danger from insulin, insofar as retinal hemorrhages were concerned, lay in withholding it, Dr. Givner said he was inclined to agree with Dr. Anderson. He described a recent case in which an immediate acute attack of glaucoma was precipitated by the substitution of globin insulin, with its explosive action, for the protamine zinc that the patient had been taking with no ill effects.

In conclusion he emphasized Dr. Anderson's statement that, although diabetics show a greater incidence of increased capillary fragility at each decade than nondiabetic controls, a fragility which is especially marked in cases of diabetic retinopathy, the

present therapeutic approach (vitamin C, rutin, and high protein intake) is not a specific bulwark against vascular damage. We must continue our search for more effective treatment.

Viruses in relation to orbital neoplasms

Dr. Alson E. Braley said that the possibility of viruses causing neoplasms is a reasonably old hypothesis. The first of these investigations was carried out by Borral and others in France. The infectious etiology of neoplasms must meet rigid specifications in order to explain many facts.

Dr. Braley said that in November, 1947, Mrs. Alexander and he reported on a virus obtained from a patient with a neoplasticlike lesion in the orbit. The differential diagnosis of this tumor was rather difficult to make. The possibility of exophthalmos associated with a thyrotropic hormone may have been an exciting factor. After many biopsies the diagnosis of pseudotumor of the orbit was made. This virus may be one of the causes of pseudotumor of the orbit.

There does not seem to be any relationship between this virus and the etiology of Hodgkin's disease or lymphoma, even though a great deal of the existing pathologic processes found in the tumors produced by this virus are similar to lymphomas and Hodgkin's disease.

The association of hormonal disturbances such as have been reported by Weinstein, and Aprunt and McDearman, may have some influence on the development of these neoplasms.

Operation for blepharoptosis

Dr. Charles Littwin said that there have been about 80 procedures described for the correction of blepharoptosis, and he wished to present (with motion pictures) a report on the Trainor operation, which he felt was simple in its performance and efficient in its results.

He said that blepharoptosis is an abnormal drooping of the upper lid and may be divided into pseudoptosis and true ptosis. The former may be caused by an abnormal widening of the palpebral fissure on one side, thus producing an apparent ptosis on the other; or it may be due to disease or increased weight of the lid on the side of the ptosis, such as occurs with edema, elephantiasis, relaxed skin, prolapsed orbital fat, blepharochalasis, trachoma, tumors, endophthalmos, spasm of the orbicularis muscle, and neurofibromatosis.

True ptosis results from inadequate lifting power of the levator palpebrae muscle and is caused by an abnormality of the levator muscle or its nerve supply. It may be congenital, acquired, or hereditary in origin; unilateral or bilateral, partial or complete.

Dr. Littwin said that there are three main types of operations usually employed for the cure of ptosis: (1) Suspension of the upper lid from the brow, thus utilizing the action of the frontalis muscle for the lifting of the lid; (2) attachment of the upper lid to the superior rectus, thereby replacing the action of the levator by the lifting power of the superior rectus; (3) enhancement of the normal action of the levator by advancing, tucking, or resecting this muscle.

A successful operation for ptosis should meet the following requirements: (1) The curve of the margin of the upper lid should overlap the cornea equally on the two sides, covering the upper port of the cornea where the lashes are normally open; (2) the margin of the lid should be a smooth curve and similar in the two eyes, with no tendency to form a notch or Gothic arch or to invert the lashes when the lid is widely open; (3) the superior palpebral crease should correspond on the two sides; (4) the eye should be capable of being widely opened and of shutting completely, both in forceful closure and in sleep; (5) normal winking should be possible; (6) the vertical distance between the eyebrow and the margin of the upper

lid should normally be the same in the two eyes; (7) the upper lid of each eye should move synchronously with the globe in all directions of gaze; (8) diplopia or disturbing heterophoria should be absent.

It is doubtful whether any operation for ptosis ever completely achieved all these requirements, especially in a case of unilateral, complete, congenital ptosis. Certainly, the frontalis type of operation does not give this degree of perfection because the upper lid can be raised only by raising the brow. The superior rectus operation nearly always weakens this muscle, producing hypotropia and leaves the lower part of the cornea exposed in sleep. Adequate resection of the levator muscle in cases of complete congenital ptosis often produces lagophthalmos in downward gaze. Therefore, in any case of complete congenital ptosis the surgeon must decide which of these criteria are the most important and which should be ignored.

It is important to make an accurate diagnosis and then to choose an operation that will produce the best possible results in each case. In the case reported, Dr. Littwin said he chose the Trainor operation because there was everything to gain and nothing to lose. The upper rectus was not weakened as in the Motais operation and, if success were not obtained, the tarsal hammock could be undone, and the condition would be no worse than it was originally.

The technique of the Trainor operation consists of using a strip of the upper boarder of the tarsus as a hammock to support the upper lid by sliding it under the insertion of the superior rectus. The steps involved are:

1. Anesthesia. Four or five drops of 0.5-percent pontocaine are instilled into the conjunctival sac. (a) The lid is everted. The needle is thrust under the loose conjunctiva, just beyond the border of the tarsus and the solution is injected until the whole retro-tarsal fold balloons out. (b) The lid is righted, and without withdrawing the needle the point is pushed to the skin side and more

solution is injected to slightly balloon out the skin. Both surfaces of the entire lid thickness are completely anesthetized. An injection is also made in the belly of the superior rectus through the conjunctiva.

2. The lid is everted and held with fixation forceps. A cut is made in the upper border through the entire thickness about 2-mm. wide, and a strip of tarsus covered with conjunctiva, but not skin, about 15-mm. long is freed, leaving it attached to the inner end.

3. The superior rectus is grasped and a tunnel is made through Tenon's capsule under the muscle by means of a scissors point.

4. The strip of tarsus is then passed under the superior rectus, either with mosquito forceps or suture.

5. The free end of the strip is now attached to its original position with one or more sutures which are bitten deep in both tarsal body and strip.

6. A protective dressing, consisting of a broad strip of adhesive, is attached to the cheek, and the lower lid is raised so as to cover the cornea. Maintaining this traction upward, a piece of gauze is used to cover the upper lid and eyebrow. The adhesive is then attached to the forehead.

ECZEMATOUS KERATITIS AND ARIBOFLAVINOSIS

DR. H. J. STERN AND DR. J. LANDAU presented the paper on this subject, which was published in the AMERICAN JOURNAL OF OPHTHALMOLOGY, volume 31, page 1619, December, 1948.

Bernard Kronenberg.
Recording Secretary.

CHICAGO OPHTHALMOLOGICAL SOCIETY

February 16, 1948

Dr. Beulah Cushman, *president*

Scientific program

Beta irradiation of the eye

Dr. William F. Hughes, Jr., presented the paper on this subject which was published in the American Journal of Ophthalmology, volume 32, page 351, March, 1949. A brief abstract follows.

Beta particles of radon represent a concentrated source of irradiation which is largely absorbed within the first 2 mm. of tissue and is therefore useful in the treatment of superficial conditions of the lid, the conjunctiva, cornea, and sclera.

The effective use of beta irradiation in ophthalmology depends upon an exact knowledge of the differential between the sensitivity of normal tissues and the pathologic tissues to be destroyed.

In general, lymphoid tissues (the follicles in vernal conjunctivitis), the epithelial growths (papillomas), and vascular endothelium (in corneal vascularization) form the most sensitive tissues which can be destroyed by beta irradiation without undue injury to the normal ocular structures.

Evaluation of loss of central vision and central scotomas

Dr. Helen Holt presented a paper on this subject. The discussion concerned the group of patients whose chief symptom was blurring or reduction of central vision with no history of associated ocular symptoms or known general illness which might have a bearing on the problem. The importance of an accurate history, evaluation of visual acuity with analysis of the manner in which the letters are read, age of the patient, and exact refraction was stressed. Central fields

were plotted on a tangent screen at a distance of 1,000 mm.

The central scotomas were grouped as positive and negative scotomas. The first type was considered as largely due to macular lesions, such as pathologic conditions of the macula, macular degeneration, macular hole, and infectious processes. The second type was due to lesions of the conducting neuron, the result of inflammatory, mechanical, vascular, or toxic processes, vitamin deficiencies, or hereditary degenerative conditions. Case histories illustrative of the various conditions with central field and fundus photographs were presented.

Discussion. Dr. Derrick Vail felt that Dr. Holt had presented a splendid dissertation on a subject which tends to be neglected in the modern practice of ophthalmology. Perhaps not as many of us take fields as should. Dr. Holt has pointed out the importance of this procedure, which can be time consuming but also rewarding for both patient and ophthalmologist. Particularly interesting is her discussion of patients "spotting" from one letter to another, particularly the subtle changes one may pick up unconsciously in testing the patient's distant vision. For some time he had noted that patients with negative scotoma can read charts better when the chart is not illuminated. These patients with a relative central scotoma will see the letters better than when the chart is lighted; whereas, in positive scotoma, such as central angiospasm, they will read 20/20 with the lighted chart and with the unlighted chart 20/50. Has Dr. Holt noted that?

Antistine in ophthalmology

Dr. Paul Hurwitz presented this subject. An abstract of the paper, which was published in the American Journal of Ophthalmology, volume 31, page 1409, November, 1948, follows.

The antihistaminic chemical drugs and their action were briefly reviewed and 50 cases of ocular allergy and their response,

symptomatically and therapeutically, to the new antihistaminic ophthalmic solution were presented. Antistine ophthalmic solution (Ciba) was advocated for use in the symptomatic relief of patients with extraocular allergy.

Discussion. Dr. Louis Bothman said that when he read Dr. Hurwitz's paper he feared that he was rather too enthusiastic. The report of 84-percent good results is pretty high. His own experience with these drugs in allergic conditions was not sufficient to permit definite conclusions. With pyribenzamine in solution, the patients complained of burning and he was reluctant to use it because of the irritating effect. Dr. Hurwitz's observation that the astringent effect reduced the injection was one of the outstanding findings, and relief from itching was the principal result. Dr. Hurwitz also noted improvement in folliculosis, but he had found no change in folliculosis with any of the antihistamine drugs, although there was some relief from itching and tearing.

The patients with marked injection seemed to get more relief with privine hydrochloride. With 0.1-percent solution they get sensitivity, and say it gives relief for 4 to 6 hours. He had seen no allergic manifestations with the use of privine. It constricts the blood vessels and acts almost immediately. He hoped to give antistine a more extensive trial to see what it would do.

With pyribenzamine in ointment and solutions, some patients had relief from itching, but some complained of burning and refused to continue its use. About all that can be hoped for is symptomatic relief, and apparently no drug will affect the folliculosis.

Dr. Hurwitz mentioned that he had not obtained results in cases of vernal catarrh. He, himself, had seen one boy who had granulations so severe that they produced severe keratitis. After two courses of radium the involved conjunctiva was removed, and the fornix conjunctiva was transplanted to the upper lid. Then follicles began to appear in the transplanted conjunctiva. After a period of 8 to 10 months of desensitization (during which radium and other treatment had been of no value), the granulations began to shrink and the conjunctiva in one eye became smooth. Even in this very severe form the condition is reversible. Whether this result was because of treatment of the mold sensitivity was not clear. This work should be continued, and this and other drugs should be used in the effort to relieve the patients.

Dr. Stefan Van Wein asked whether Dr. Hurwitz had noted any exacerbation of manifestations in the eye during the allergic tests.

Dr. Paul Hurwitz (in closing) said that possibly his percentages were a little high, as Dr. Bothman said. Individuals doing investigative work are sometimes carried away by their own enthusiasm. However, the director of the Ciba Laboratories has said that scattered reports from different areas of the country showed a 77 percent improvement in ocular allergic conditions with the use of antistine opthalmic solution.

With regard to the burning effect of antistine, it has been noted that it is not as severe as with pyribenzamine solution. It is usually fleeting. Only one patient refused to use the solution because of the burning; a small group complained but continued to use it. The majority of patients came back for more of the solution. This indicates that they prefer the burning to the itching that is present in ocular allergies.

In reply to Dr. Van Wein, he had noted no exacerbation of the ocular lesions during the skin tests.

CLINICAL MEETING

(Presented by staff members, Department of Ophthalmology, University of Chicago.)

CONGENITAL ECTOPIC PUPILS

Dr. Ryerson presented R. F., a 32-year-old white man, who came to the eye clinic

of The University of Chicago, July 23, 1947, with the complaint of inflammation of the right eye for the preceding two weeks. He gave the history of having had an operation on his left eye seven years previously in hopes of improving his vision. His uncorrected vision was: R.E., 20/100; L.E., 4/200. Examination revealed bilateral ectopic pupils. The right pupil measured 2 by 3 mm. and was displaced nasally. The left pupil measured 1.5 by 2.5 mm. and was displaced superiorly. There was a 1.5 by 3.0 mm. artificial pupil slightly below the axis of the left eye. The right eye was mildly inflamed and there was a 2+ aqueous ray.

The iritis responded well to atropine and conservative therapy. Because of his poor dental hygiene, he was referred to the dental clinic. He was treated for severe pyorrhea and several carious teeth were extracted.

The diagnostic tests were: Kahn, negative; urinalysis, negative: W.B.C., Hgb., and R.B.C., normal. Chest microfilm, negative. Old tuberculin skin test negative.

After the iritis in the right eye had cleared up a manifest refraction yielded the following correction: R.E., −0.62D. sph. $\subset$ +2.5D. cyl. ax. 135° gave the patient 20/40 vision. It was not possible to improve the vision of the left eye. The patient habitually squinted to see clearly and preferred this to a glass prescription. He was successfully employed as a painter.

Gonioscopic examination revealed many peripheral anterior synechias, especially inferiorly. The lenses did not appear to be ectopic.

B. F., aged 15 years, a sister of the patient, presented herself primarily for our benefit. Her uncorrected vision was: R.E., 20/100; L.E., 5/200. Her right pupil was displaced toward the 10-o'clock position and the left pupil toward the 12-o'clock position. The pupils dilated poorly with homatropine, paradrine, and neosynephrin. It was not possible to improve her vision on a manifest refraction.

Slitlamp examination revealed bilateral cataractous lenses consisting mainly of peripheral punctate opacities. In the left eye, there was a beautiful display of zonular fibers. There was a slight irregularity of the equatorial portion of the left lens.

The original patient (R. F.) has children, aged 3 and 5 years, who have no apparent ocular defects.

NUCLEAR APLASIA AND MARCUS GUNN PHENOMENON

DR. STEPHEN J. ALEXANDER presented the case of J. C., a 4½-year-old white boy of Polish parentage, who was first seen at the University of Chicago Clinics, January 12, 1948. The mother of the child stated that since birth the right eye seemed smaller, it did not move, and the upper lid drooped.

Past history. No serious infectious diseases, no injuries or other defects were present. The patient was the third child born. Pregnancy, labor, and delivery were normal.

Family history. The father and paternal grandfather have some type of neuromuscular anomaly. The mother has a questionable left ptosis and a high exophoria. One older sister is living and well; one younger sister is living and well; one older sister died shortly after birth of "enlarged thymies."

Physical examination. Vision was: R.E., 10/30, not correctible; L.E., 10/20, with correction, 10/30. The facies were asymmetrical, the left side of face was most prominent. The right palpebral fissure was narrower than the left. Examination of the extraocular muscles revealed a right ptosis, partial paralysis of the right third nerve, complete paralysis of the right fourth and sixth nerves, and a Marcus Gunn jaw-winking phenomenon.

On convergence the right eye turned in less than 10 degrees and there was no movement in any other direction of gaze. The pupils reacted normally. The anterior segments and fundi were normal.

The patient is wearing the following pre-

scription: R.E., −0.75D. sph. ⊃ +3.25D. cyl. ax. 105°; L.E., −0.25D. sph. ⊃ +2.25D. cyl. ax. 92°.

Dr. Douglas N. Buchanan of the department of neuro-pediatrics confirmed the above diagnosis.

SARCOID UVEITIS

DR. A. W. FELDMAN presented Mrs. B., a 59-year-old white woman, who first came to the eye clinic of The University of Chicago with a number of minor complaints and the significant complaint of moving black spots. Her past history revealed that she had been discovered to have diabetes one year previously. Her corrected vision was: R.E., 20/40; L.E., 20/25. The eye was somewhat injected but the patient had a mild bilateral conjunctivitis at the time. The media of the right eye were slightly hazy. Slitlamp examination of the eye revealed numerous mutton-fat keratitic precipitates and a 1+ aqueous ray. The patient was started on 5-percent homatropine and later switched to atropine. On one occasion, a few small perivascular exudates were seen near the macula.

The patient had all her mandibular teeth extracted on the recommendation of the dental clinic because of a nonsuppurative periodontitis. The metabolism clinic has easily controlled her diabetes with moderate dosage of insulin and diet.

Because of a peculiar dilatation of the vessels of the nose, the patient was referred to dermatology. A tentative diagnosis of lupus pernio was made. This was later confirmed, as a biopsy of the nose revealed sarcoidosis. The dermatologists instituted calciferol therapy (high vitamin D). Shortly thereafter, the nose became quite painful and a crusted lesion developed. This cleared up when the calciferol was stopped. X-ray studies of the hands and feet and of the chest did not reveal evidence of sarcoidosis.

The vision of the right eye dropped to hand movements at two feet and at times the eye was quite painful. Atropine therapy had to be discontinued because the patient became sensitive to atropine. A secondary cataract developed and there was some deep vascularization of the cornea. The left eye remained essentially normal.

The following diagnostic and laboratory tests were performed: Old tuberculin, 1:10,000 and 1:1,000, negative; W.B.C., 10,800; Hgb., 16.2 gm.; R.B.C., 5.28 million; sedimentation, 27 mm.; urine, usually negative; highest fasting blood sugar, 115 mg. percent; serum calcium, av. 10 mg. percent; serum phosphorus, 3.8 mg. percent; alkaline phosphatase, 2.4 units. Plasma proteins: Albumin, 4.70 mg. percent; globulin, 2.54; A/G ratio, 1.85. Petechial count, 11 (Thompson).

This case is somewhat unusual from the following standpoints: (1) Although the general pathologic processes associated with sarcoid uveitis are spotty, they are usually located in the lungs and lymph glands. The lesion responsible for diagnosis in this case was located in the skin; (2) sarcoid uveitis is usually painless, but in this case there was considerable associated pain, although there was no evidence of secondary glaucoma; (3) sarcoid uveitis is bilateral in the majority of cases but was unilateral in this case.

SALZMANN'S CORNEAL NODULAR DYSTROPHY

DR. P. G. WOLFF presented Mr. J. A. H., a 58-year-old machinist, who was first seen in the eye clinic of The University of Chicago on February 21, 1944, complaining of sudden loss of vision in the left eye, following the extraction of 10 teeth, about 6 weeks previously. Aided vision was: R.E., 3/200; L.E., 20/30, not improved by a 1-mm. pinhole. A thrombosis of a branch of the left superior temporal retinal vein was found. This gradually resolved and four months later vision of the left eye had improved to 20/20+.

A rather vague history of the cause of the poor vision in the right eye was the best that could be obtained. First, at the age of 8 years this eye was very irritated and painful at irregular intervals. No doctor was consulted

and this spontaneously ceased about two years later without any recurrence of either pain or other annoyances. By the age of 15 years vision in the right eye was already noticeably decreasing and it has continued its unrelenting, slow, steady decline ever since. All eye doctors that he had seen advised that there was nothing to be done.

The patient did not believe that any of his seven siblings, his parents, or other relatives had had any "eye trouble." There was no history of consanguinity.

General physical examination revealed a moderate hypertension, mild generalized osteo-arthritis, and a fused left hip. There were conflicting opinions as to the nature of the etiology of the last-mentioned condition, but the Crile Clinic in Cleveland told him it was "acid fast" about 30 years ago. In addition, X-ray examination revealed old healed apical lung lesions. Old tuberculin, in 1/1,000 dilutions, gave a negative skin test. Repeated blood findings, including the Kahn test, and urinalyses were negative.

Objective examination of the left eye was negative except for some thinning of the left cornea without any opacifications in the inferior temporal region and for moderately advanced arteriosclerotic vessel changes in the retina.

The right eye never showed evidence of irritation or infection during observation. The right cornea was of normal size and shape, measuring 11 by 10 mm., and, except for the elevation of the nodules, was of normal curvature. Its sensitivity was reduced about 50 percent.

The pathologic changes were in a horizontally oval pattern, extending the breadth of the cornea and measuring 5 mm. in the vertical diameter. This pattern consisted of 5 elevated, blue white, structureless, opaque nodules, clearly showing that they had been formed by the union of previously existing small nodules, all lying in the superficial stroma.

The posterior one half of the cornea was normal. This cornea had never taken a fluorescein stain. All about its margin and passing over the limbus could be seen many fine superficial blood vessels on their way to the nodules. The central and the peripheral superior and inferior portions show a diffuse superficial gray clouding through which the underlying structures could be seen to be of normal appearance. The pupil reacted promptly.

With the slitlamp there could be found no regular obstruction of the dystrophic nodules, although their centers were uniformly more elevated and white than the surrounding periphery. They were observed to extend forward some one-half the normal thickness of the cornea. The corneal nerves were observed as normal. One pupillary nodule prevented a fundus study but repeated peripheral and Bjerrum fields of this eye revealed nothing abnormal.

While under observation for the past four years, there has never been any irritation or inflammation in the right eye; there has been neither apparent advancement or the disease nor any evidence of involution. To date, no evidence of involvement of the left cornea can be seen.

Richard C. Gamble,
Secretary.

LOS ANGELES OPHTHALMOLOGICAL SOCIETY

February 5, 1948

Dr. Orwyn Ellis, *chairman*

SYMPOSIUM ON ORBITAL IMPLANTS

Dr. Clarence Albaugh stressed the criteria of a good implant.

1. Adequate blood supply to prevent slipping of the muscles from their attachment to the implant.

2. Avoidance of pressure on the conjunctiva.

3. Protection of the cul-de-sac.

4. Even weight distribution between the

muscles and the lower lid by a floating-type appliance over the implant. These criteria were satisfied by a new type of basket implant as devised by Dr. Albaugh. A motion picture clearly demonstrated these points.

DR. ORWYN ELLIS described his covered implant which has been used successfully by a number of men. The implant consists of a lucite ball with an anterior ring. In 80 cases in which the implant has been used for over 10 months there was only one instance of extrusion. Dr. Ellis stated that since Tenon's capsule and the conjunctiva are fused to the sclera for 1 mm. to 2 mm. around the limbus, removal of the globe cannot be replaced with more than an 18-mm. sphere. He demonstrated his implant by the use of slides.

DR. GEORGE KILGORE of San Diego (by invitation) reported on the work at Dibble Hospital during the war. He found that the Cutler basket implant gave poor results, perhaps from faulty technique, and that it was frequently extruded. It was given up because of the atrophy above and behind the implant, and the Cutler doorknob implant was used. Good results were seen in some cases with the doorknob type but extrusion also occurred. He described three cases in which the doorknob implants were used.

1. The medial rectus pulled from its attachment postoperatively and could not be reattached, so it was removed and a basket implant was substituted.

2. A doorknob implant was placed successfully for two weeks and then the medial rectus pulled loose. A basket type was tried but was extruded because of infection but was later successfully placed.

3. Ideal movement was noted but the eye chattered when the patient read because the pin was too loose in the implant. Convergence was good as well as the vertical and lateral movements.

The important points to consider, according to Dr. Kilgore, are:

1. An additional pursestring suture through Tenon's capsule and the conjunctiva to take the strain off the muscles and allow them to heal well.

2. The medial rectus will tear loose if the good eye is uncovered too soon.

3. Penicillin and sulfa drugs should be used to keep down any infection and allow better healing.

4. Lag of movement seen with the basket type can be prevented by the doorknob implant.

DR. GEORGE LANDEGGER stated that the most important thing in an implant was permanency and that an implant covered with conjunctiva was best. Good movement in the extremes of rotation were not necessary. The larger size implants were favored since some of Tenon's capsule was gained from that stripped off the muscles. He favored the Ellis implant, having used it successfully in 7 cases. In one case, however, the implant was extruded from an inflamed orbit.

DR. GILBERT STRUBLE said that the buried implant always has a lag in movement and cannot make the excellent appearance of the Cutler and Ruedemann types. He used the 24-mm. size, earlier type Ruedemann implant in over 20 cases but all were failures since strabismus developed in all the patients when the backs of the prosthesis moved postoperatively. Sensitivity to the acrylic of the implant caused great thickening of Tenon's capsule and eventual extrusion of the eye.

The more recent mesh-type Ruedemann implant had not been observed by Dr. Struble. He had to remove three of the Cutler ball and ring implants because of recurrent cellulitis, and these were successfully replaced with glass balls. He felt that the Cutler basket implant gave a poor appearance because of the depression of the sulcus of the upper lid. Bone balls were condemned since draining sinuses were produced and the fragments of bone were so hard to remove.

Dr. Struble has gone back to using the old type of transplants since he felt there was a violation of general surgical principles in trying to attach muscles to nonviable tissue. The ideal volume size to be replaced by the implant was 18 to 19 mm. The muscles were not drawn over the implant since they were of no added help. A pressure bandage was applied for a week.

Dr. George Zugsmith favored an implant of the Ellis type which has complete covering of the implant by the conjunctiva. He felt that eviscerations with scleral implants gave the best results and believed that this was the best operation in all cases except sympathetic ophthalmitis, tumors, and in old and debilitated patients where an implant wouldn't be used anyway.

Mr. Ted Kaiser (by invitation) discussed prostheses as related to the type of implant. He said the implant will not move more than the cul-de-sac and that subse-

quent shrinkage which occurs after surgery accounts for the limitations. The appearance was best in eviscerations with scleral implants. Some basket implants pull the conjunctiva forward into the basket and thus foreshorten the socket and give a poor fit. Sewing up the posterior rent in Tenon's capsule after enucleation, as advocated by Dr. Rodman Irvine, has given good support since it brought the implant farther forward.

Dr. Abraham also emphasized the value of a large cul-de-sac to allow full movement of the implant and thus explained why eviscerations seemed to have better movement.

Dr. Loutfallah stressed the technique of a careful enucleation and the use of the obliques to hold the eye forward. He mentioned the new AO implant which combines the Cutler and Ruedemann principles.

Daniel B. Esterly,
Secretary.

Ophthalmic Miniature

I am very sincerely solicitious for the preservation or curing of Mr. Langton's sight, and am glad that the chirurgeon at Coventry gives him so much hope. Mr. Sharpe is of opinion that the tedious maturation of the cataract is a vulgar error, and that it may be removed as soon as it is formed. This notion deserves to be considered; I doubt whether it be universally true; but if it be true in some cases, and those cases can be distinguished, it may save a long and uncomfortable delay.

Boswell's Johnson, letter to Bennet Langton, October 18, 1760.

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THE NEWLY BLINDED

The ophthalmologist's responsibility to his newly blinded patient should not cease at the termination of his professional services. The losing battle to save sight is a hard and difficult one, encompassed by physical and emotional distress on the part of the patient and much soul-searching, mental anguish on the part of the surgeon, who dies a little every time one of his patients becomes hopelessly blind. There is little comfort here in the words of Hippocrates, "The art is long, life is short, experiment perilous, decision difficult."

The honest struggle to do everything possible and to see to it that everything possible is done for the patient usually ends up with the patient being grateful to his physician for his care, even if futile, and the latter filled with respect and admiration for the patient's fortitude in adversity. The terrible fight has engendered a mutual regard and friendship that deserves cultivation.

Many new and good things in the training of the newly blinded came out of the experience of the last war, especially from the program established by the Army at Old Farms, Avon, Connecticut. These new techniques

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and methods of approach to the problem have been carried on and applied to the civilian needs, not as yet, however, to the fullest possible extent. The keynote of the modern philosophy in this field is that of instilling and fostering self respect in the afflicted individual. The training is long, often seemingly brutal, generally agonizing, frequently affected by setbacks, but to be successful always honest and frank. Experience has shown that the sooner the newly blinded person starts on learning how to be blind the better. ·

In a recent pamphlet, *The Newly Blinded*, printed for distribution by the Seeing Eye, Inc., Morristown, New Jersey, there is this statement that sums up the situation. "If newly blinded men and women are approached and looked upon as normal human beings; if they are given sympathetic understanding rather than maudlin sentimentality; if an effort is made to assure them that they still have their rightful place in the family and the community; and if they are encouraged to lead active lives in spite of blindness; then a true service will have been rendered not only to them but to their families and to the Nation."

The ophthalmologist is the last line of defense against blindness. He should be the first line of offense against the depression and gloom that envelop it. His fitness for this task depends upon his training and wisdom. It is his stern duty to exert his capacity as wise physician, friend, and counsellor. It is an integral part of his responsibility to his patient. It is not to be yielded up until the blind person is properly guided into the new career and terrifying experience of blind living in a seeing world.

In order properly to discharge this responsibility, the ophthalmologist should know much about the new techniques. He should know to what proper agencies in his community he can direct his charge. Most of these agencies are good and noble, others less so. He should be familiar with the Talking Book, the Braille watch, the writing guides,

the Seeing Dog, and all of the other auxiliary things and services that splendid and generous people have made available.

A small but most important aid in this first approach is the pamphlet, *The Newly Blinded*, already referred to. It is brief and austere, worthy of the beauty of its philosophy of help and of its great service to the patient and his family. The paragraphs on orientation, walking, personal appearance, table etiquette, smoking, Braille, the Talking Book, watches, handwriting, typewriter, recreation, theatre and movies, family, and employment are short but adequate. They were written by blind men out of their experience.

The Seeing Eye, Inc., of Morristown, New Jersey, will supply physicians and the personnel of hospitals with copies of this manual upon request. Each ophthalmologist should have a few on hand against the need.

Derrick Vail.

PONTOCAINE ALLERGY: TECHNIQUE OF INSTILLATION

On page 263 of the February issue of the JOURNAL, Thomas W. Cowan reports a striking case of allergy to pontocaine, manifested by redness, swelling, and itching of the skin of the lids after removal of a chalazion. The patient subsequently gave a rather violent reaction to a patch test on the arm.

The author's description of the technique of anesthesia in this case suggests certain comments on the customary routine employed for instillations not only of pontocaine but of other drugs. From observation of instillation as practiced in a number of hospitals, clinics, and offices, by surgeons and nurses, I am disposed to believe that this apparently minor field of daily technique may be open to general improvement.

Allergic reactions do not always depend upon the amount of offending substance involved. But sometimes they do, and it is better not to employ more of a drug than is necessary for the effect desired. It is also to be noted that the cornea and conjunctiva

sometimes appear to be less sensitive to a given drug than is the surrounding skin. This is true of atropine, which may produce an annoying skin reaction but much less disturbance of the conjunctiva. However, some of this apparent difference in sensibility may be credited to the fact that the tears are constantly active in removal of instilled drugs, while the skin has no such protection.

The eye itself is capable of absorbing only a very small quantity of the instilled solution, from the thin film of the drug which spreads over the conjunctiva and cornea. Moreover, under ordinary circumstances, out of the much larger quantity ordinarily dropped on to the eye at one application, only the amount of a single small drop remains in contact with the eyeball, the remainder being promptly spilled over the lid margin.

(It may be worth while to mention here, especially as bearing on the mixing of small quantities of dilutions, that the drop from a medicine dropper whose tip has an inside caliber of 2 mm. is not a minim but only about three fifths of a minim.)

Thus, of the "two or three drops" (rather frequently much more) dropped upon the eye by an assistant or nurse, most of the drug stays on the skin of the face, without surgical benefit, but always capable of irritating the skin. For ordinary purposes, no more than one drop of 0.5 percent pontocaine is necessary, if properly instilled. This is plenty for removal of a superficial foreign body from the cornea, although rather more is sometimes required for a foreign body close to the limbus. The cornea is usually insensitive as soon as the burning experienced by the patient from the instillation has ceased. The greatest efficiency is obtainable by laying the last joint of the left thumb flat on the upper lid and brow while the patient looks down, sliding the lid and brow up on to the forehead, with gentle but uniform pressure, and then placing the single drop on the sclera above the cornea—not allowing the drop to fall from a rather considerable height.

In using instilled pontocaine as a preliminary to infiltration, I have not found it necessary to make more than one such preliminary instillation. In advising the mother how to instill atropine in a young child, prior to refractive estimation. I emphasize that at each instillation only sufficient solution to make a single drop should be drawn into the dropper.

Some evidence of allergy to pontocaine has been experienced by me on a few occasions after repeated use of 0.5-percent solution of pontocaine, in connection with the permission rarely given to a workman to employ such a solution in carrying on important work after burn from a welding arc, or other minor injury. Special interest attaches to Cowan's case, on account of the severe reaction and the apparent complete lack of previous use of the drug.

W. H. Crisp.

SURGICAL TREATMENT OF HETEROTROPIA

The best method of surgical treatment for noncomitant heterotropia has long been a subject of controversy. As has happened in so many other controversies, two schools of thought have arisen. One school favors a direct attack on the paretic muscle by the performance of one of the strengthening operations. The opposite school prefers an attack on the direct antagonist of the paretic muscle by some one of the so-called weakening operations.

The latter school owed its existence almost solely to the frequent and often rather remarkable "recoveries" of paretic muscles when the opposition of their direct antagonist was purposely decreased.

The explanation generally accepted has been that a paretic muscle, when antagonized by a normal muscle, never had the chance to regain normal tonus even after the original cause of the paresis had ceased to exist; presumably the once paretic muscle was put on such a stretch due to partially unopposed ac-

tion of the antagonist that it failed to function normally while the antagonist meanwhile became spastic and thus continued its dominant role even after the cause for the paresis had disappeared. Proponents of the "weakening operation" could thus point to a fairly satisfactory percentage of surgical "cures." Their explanation for these satisfactory results was always suspect and lacking in real proof.

Those favoring a direct attack on a paretic muscle objected to any weakening operation on quite logical grounds. The mere fact that one muscle is weak is a poor excuse for weakening another and trying to strike a balance in the degree of weakness, as it were. The school favoring the strengthening operation for paretic muscles can also point to a respectable percentage of surgical "cures."

Both schools explained their failures by saying that the paretic muscle was just "too weak." The "weakening" school believed that the paretic muscle was too weak to regain any tonus and then resorted to some "strengthening" operation as a second procedure. Those in the "strengthening" school state that it is perfectly obvious that shortening a completely paretic muscle will not enhance its effect in the slightest except, perhaps, as an anchor.

There the discussion comes to an end with no satisfactory decision in favor of either side.

It must be said that the "strengthening" school apparently had a better explanation for their failures than did the "weakening" school. Since each school is able to present a fair percentage of successful cases, it would be highly significant if the failures could be explained on some logical grounds. It would seem that perhaps the failures of one school may be the successes of the other and vice versa. If cases could be properly classified prior to surgery, then the proper mode of attack—strengthening or weakening—would be clear and the general batting average of both schools might rise to far more satisfactory and impressive heights.

Some light is thrown on the subject by always using the phrase "apparently paretic" instead of just "paretic." The idea of apparent paresis rather than real paresis opens a new line of thought. What would cause a muscle to appear to be paretic when actually it is not—or at least was not originally?

If one muscle appears to be paretic and yet is found upon investigation to be normal, attention is then logically turned to the antagonist. The muscles of each eye work in antagonistic pairs. When the agonist contracts, the antagonist must relax and vice versa, according to Sherrington. Most of our thought has been directed at only one half of this problem; namely, that of contraction. If a muscle contracted properly, it was considered to be normal; if not, it was subnormal and therefore paretic.

The other phase—that of relaxation—has seldom been considered except in the same breath with "spasm." Spasm is a nice idea on paper, but even Duane had doubts about it as an individual entity.

Thinking through the relaxation phase of the problem, anyone will readily admit that, if an antagonist is prevented from proper relaxation by any reason whatsoever, the agonist will be prevented from securing the maximum effect from its contraction and will, therefore, appear to be weak or paretic. This would account for an appearance of paresis where no paresis, in the true sense of the word, exists. The important question, then, becomes: "What will prevent a muscle from proper relaxation when its antagonist contracts?"

Recent studies have suggested that many apparently insignificant anatomic anomalies associated with the ocular muscles or their fascial connections, while not preventing in any way the contraction of those muscles or enhancing their mechanical advantage at all, will nevertheless often serve to prevent adequate relaxation of those same muscles during the contraction of their antagonists. This can be easily proved by anyone willing to try the forced duction test.

For example, there is left esotropia and the left lateral rectus appears to be paretic; if, under general anesthesia, one attempts forced abduction of the left eye by depressing a muscle hook in the lateral conjunctival fornix, any resistance to this forced duction can be felt easily via the muscle hook and may even produce noticeable retraction of that eye. If there is only paresis and nothing else, there should be no resistance to forced abduction; there is no such resistance in normal eyes.

On the other hand, any cause acting to prevent adequate relaxation of the medial rectus will serve to produce resistance to the forced abduction. When such resistance to the forced duction test is encountered, surgical exploration of the offending medial rectus will quickly reveal whether the obstacle to adequate relaxation is due to contracture and perhaps fibrosis of the muscle alone or to some anatomic anomaly or to a combination of both.

Frequently, in young patients the muscle in question will be found to be normally elastic and forced abduction of the eye becomes free and easy only when the associated anatomic anomalies are sectioned. Once adequate relaxation is assured in the medial rectus, the lateral rectus can then contract fully and is obviously no longer paretic.

Here is an explanation for the successes of the "weakening" school and for the sometimes remarkable "recovery of tonus" of a "paretic" muscle.

If these same anomalies are not sought, found, and sectioned, they also explain the failures of the "strengthening" school; no matter how much "strengthening" one performs on an apparently paretic muscle, if the fault lies in its antagonist, the "strengthening" procedure is going to be of little or no avail.

It is perfectly logical to attempt to strengthen a truly paretic muscle. It is com-pletely illogical to direct our fire at a muscle that is "apparently paretic" when in truth the fault lies in the antagonist.

What has been called the "weakening" school is in reality not that at all. It should more accurately be called the school of "removing obstructions to proper relaxation." Removal of such obstacles on an antagonist allows an agonist to contract fully and efficiently and thus to appear to gain strength. The weakening school is really a strengthening school after all. The weakening school gained a majority of their successes in cases of "apparent paresis" while the strengthening school gained theirs in "true paresis."

When secondary changes of contracture and fibrosis have occurred as a result of inadequate relaxation over long periods of time, the two schools step on common ground although many adherents of both refuse to admit it. It would seem that the two schools arose because of a lack of knowledge of the true situation.

As more and more facts are brought to light, it is inevitable that the two schools will lose their identity and merge into a single group of those who are treating causes rather than effects. There are definite indications for the "strengthening" operations and equally definite indications for the so-called "weakening" operations. Neither procedure alone will result in 100 percent of cures and there is no reason to expect that they should.

Richard G. Scobee.

BOOK REVIEWS

GENERAL CYTOLOGY. By E. D. P. De Robertis, W. W. Nowinski, and Francisco A. Saez. Philadelphia and London, W. B. Saunders Company, 1948. 345 pages, 143 figures, and index. Price, $5.50.

This book relates knowledge concerning the composition of the cell and, in particular, that knowledge which results from the

application of modern physical methods such as polarization optics, X-ray diffraction, the ultramiscroscope, and the electron microscope.

The authors are De Robertis, whose microphotographic records of the path of the poliomyelitis virus along the nerve fibers, made in the department of biology at the Massachusetts Institute of Technology, have been widely publicized; Nowinski of the department of anatomy at the University of Texas Medical School; and Saez of the Institute of Montevideo.

From the first chapter, which presents the history of cytologic knowledge from the discovery of the cell to the new theories of interpretation of cellular structure, through the final chapter, which is on the differentiation, senescence, and death of the cell, the reader is aware that here is a book written by up-to-date authorities in the field of cytology.

Since it is impossible in a short review to discuss the entire text of a volume such as this, I should like to single out Chapter XI, "Visible Manifestations of Cellular Activity," as the one that may well arouse an unusual amount of interest.

In this chapter, ameboid motion is discussed as well as the property of chemotaxis which has great importance in the defense mechanisms of the organism and especially in inflammation, certain substances attracting or repelling cells and so influencing their motion.

Advances in the study of the ultrastructure of the cilia and flagella, and the resultant motion, are reviewed. With polarization optics the cilia and the flagella show a positive intrinsic and form birefringence, which leads to the belief that they are composed of submicroscopic fibrillas orientated along the length of the axis. Direct evidences of this ultrastructure have been obtained with the electron microscope.

Analysis of movement has been facilitated greatly by ultrarapid cinematomicrography which permits one to follow the various phases in the contraction of a cilium and to calculate the duration of each cycle. One recent theory of the mechanism of ciliary movement is on the basis of changes in water content, the two sides of a cilium being believed to differ in their capacity to absorb water in such a way that the increase in the number of water molecules on one side would cause the cilium to curve toward the opposite side.

The visible manifestations of the nutrition of the cell—as phagocytosis, inclusions, or paraplasm—are included in this chapter together with the cytomorphologic aspects of cellular secretion and techniques to study the process of secretion by vital observation (biomicroscopy). In addition, there are fascinating diagrams of the processes of secretion in thyroid and parathyroid glands on which De Robertis has done much original work.

One has but to thumb through this book to understand why it has aroused an unusual amount of interest. It contains a great number of electron micrographs and examples of other forms of microscopy and X-ray diffraction, which are among the finest such pictures ever published.

Interesting and stimulating to anyone who has ever examined a slide under a microscope, the book is particularly excellent for students of medicine and for pathologists, but actually valuable for all who, for the purposes of teaching or investigation, wish to have a general and inspired view of the modern aspects and present-day orientation of cytology.

S. Rodman Irvine.

MANUAL FOR THE OBJECTIVE EXAMINATION OF THE OCULAR MUSCLE BALANCE. By Beulah Cushman, M.D. Ann Arbor, Michigan, Edwards Brothers, Inc., 1949.

Lithoprinted, 72 pages, references. On sale at the University Bookstore, 434 East Huron Street, Chicago 11, Illinois. Price, $2.50.

Teachers and students of ophthalmology have long needed a manual of objective examination of the ocular muscle balance. Dr. Cushman has done a good job of it. There are 16 short chapters beginning with the examination of the ocular muscle balance and finishing with suggestions for the surgical correction of squint.

The chapters on amblyopia and its treatment, the near point of convergence, convergence excess and insufficiency, divergence excess and insufficiency, and the value of orthoptics are particularly noteworthy.

Thirty-six cases, chosen from Dr. Cushman's extensive experience, are described in outline detail at the end of the manual and are most instructive. The manual is not intended to supplant the more extensive treatises. It supplements them with an economy of words that is most helpful. It is recommended most heartily.

Derrick Vail.

Toxoplasmosis. A clinical, serological, and histopathological study with special reference to the eye manifestations. By C. D. Binkhorst, M.D. Leiden, Stenfert Kroese, 1948. 163 pages, 14 figures, 3 colored plates, bibliography. Price: Paper bound, $3.00; cloth bound, $3.75. (This book may be purchased from the publishers, Breestraat 14, Leiden, Holland.)

Toxoplasma in human tissues has been observed in nearly every country in the world since Laveran discovered toxoplasma protozoa in animals in 1900. In 1911, Jankû of Prague found protozoa in the eye of a hydrocephalic infant. In 1939, Wolf, Cowen, and Paige isolated protozoa from the brain of a child, aged 31 days. Sabin, in 1937, published a work on toxoplasma and since then has been one of the chief workers in this field.

As one of the agents responsible for granulomatous disease in the eye, notably chorioretinitis, toxoplasma has become of grave importance in the determination of the etiology of this disease. Unfortunately, the diagnostic tests that have so far been evolved are either untrustworthy, time consuming, and expensive, or are too difficult for the ordinary laboratory to undertake. The future promises a good deal, however, along this line.

The monograph by Binkhorst is well written and of value. The first part consists of a review of the literature, the epidemiology and properties of the etiologic agent, the diagnosis, ocular manifestations, and treatment. The second part consists of a description of the author's own cases (20) and his observations.

Two of his cases were examined histopathologically. In Case 1, there was a bilateral, chronic, necrotizing retinopathy, with toxoplasma in one of the eyes; the choroid was almost normal. In Case 2, there was one small retinal granuloma.

The question is discussed as to whether the ophthalmoscopic picture is characteristic of toxoplasmosis. Inactive fundus lesions are probably not to be distinguished from chorioretinal atrophy by other causes.

This contribution to our kowledge of toxoplasmosis in ocular disease is timely and welcome, and will help in putting this condition on a firmer basis in the consideration of its importance in chorioretinitis.

Derrick Vail.

ABSTRACT DEPARTMENT

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1
ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Ballantyne, A. J. The nerve fibre pattern of the human retina. Tr. Ophth. Soc. U. Kingdom 66:179-190, 1946.

The author reviews earlier work of others and describes the nerve fiber layer of the macular area and temporally. He presents an answer to the unsolved problems of what happens to the fibers of the papillomacular bundle at the margin of the macula and temporally to it and the extent and structure of the raphe. In his investigation the unstained retina was spread face upwards on a glass slide and mounted in glycerin. The composite picture showed that as the radial bundles pass from the disc they gradually spread out more thinly, exchanging fibers from one to the other and showing occasional interspaces. As the nerve fiber bundles approach the periphery they spread apart and the interspaces are wider and are occupied by the feet of Müller's supporting fibers. The raphe is an area from one-half to two millimeters wide within which the nerve fiber bundles assume the form of a network, the meshes of which are so irregular as to give no indication of the direction or destination of the fibers. The findings explain the form of some retinal lesions but do not reveal the relations of the nerve fibers to the ganglion cell and to other elements of the central area of the retina, nor do they provide an anatomical basis for the phenomenon of the nasal step. (10 figures.)   Beulah Cushman.

Loewenstein, A. Glomus cells in the human choroid. Nature 163:69, Jan. 8, 1949.

Large round or polyhedric cells of 10 to 20μ. in diameter are found in the periphery of some chorodial arteries in the posterior pole of many human eyes. They have clear protoplasm, and their nuclei are stained an even dark purple with hematoxylin without visible chromosomes or nucleoli. These so-called glomus or epitheloid muscle cells occur in groups in the media and adventitia of arteries in hypertension and other circulatory disturbance. They serve as cushions by filling the lumen of arteriovenous anastomoses and by shrinking or swelling they may open or close the arteries and veins. They make possible a short circuit from artery

to vein in many normal and morbid processes. It is also conceivable that they are contractile and, constricting certain vessels, help to regulate the choroidal blood circulation and intraocular pressure.　　　　　　　　R. Grunfeld.

Wolff, Eugene. **The mucocutaneous junction of the lid margin and the distribution of the tear fluid.** Tr. Ophth. Soc. U. Kingdom 66:291-307, 1946.

The author describes the junction between the skin and conjunctiva as a sharp line on a level with the posterior margin of the openings of the Meibomian glands, just where the lid margin is no longer wetted by the tears. This is confirmed microscopically. The eleiden and keratin layers of the skin end quite sharply and give place to several layers of nonkeratinized squamous epithelium. The number of layers of squamous cells are gradually reduced till at the subtarsal fold the superficial cells become columnar and cubical. In this region goblet cells begin to appear. The oily secretion of the Meibomian glands tends to limit the lacrimal fluid and acts as a low wall round the whole tear reservoir and directs the tears towards the puncta.

A strip of lacrimal fluid is found at the posterior margin of the upper and lower eyelids and the inferior marginal strip runs up on the cornea for a millimeter or so because of surface tension. It is prevented from overflowing by the secretion of the Meibomian glands. A tear lake was found at the outer canthus and the author emphasizes its importance because the lacrimal fluid from the upper conjunctiva may reach the lower conjunctival cul-de-sac through it. The puncta dip into the strips of fluid at the posterior lid margin and in this manner the lacrimal secretion reaches the efferent passages rather than by drainage from the lacus lacrimalis.

　　　　　　　　Beulah Cushman.

2
GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Dean Guelbenzu, Manuel. **Simple and effective therapy of ocular burns.** Arch. Soc. oftal. hispano-am. 8:1004-1015, Oct., 1948.

Because good results followed treatment of burns of the skin with powdered sodium bicarbonate, the author used it in burns about the eye and found it very satisfactory. He then tried an ointment of sodium bicarbonate in ocular burns, and found its effect very agreeable in acid burns, and of value in caustic burns. In the caustic burns he uses a 4-percent solution of ammonium chloride for the first two or three days, after which sodium bicarbonate was substituted. To explain its favorable action he refers briefly to the work on the physiology of inflammatory processes, by Elkinton, Wolff and Lee, Menkin, Schade, and Fenn and Evans. These investigators demonstrated that the increased permeability incident to an inflammation causes an invasion of the tissues by plasma and its proteins, with a consequent compression of the vessels, and cellular asphyxia. The inflammatory exudate upsets the local acid base equilibrium, with a shift toward acidity; the local anoxia leads to an accumulation of lactic acid, which rises from 19 to 240 percent. Associated with the local acidosis is a marked reduction in the bicarbonate and sodium anions, and an increase of potassium ions. The phagocytic activity requires an alkaline medium and is arrested in a medium with a pH of 5.5. The processes of cicatrization also require an alkaline medium, and are retarded in an acid medium. The beneficial effect of sodium bicarbonate is therefore attributed to its alkalinization of the tissues and normalization of the acid base equilibrium, to its effect on absorbtion of tissue fluids and local an-

oxia, and to its soothing local action on the inflamed tissue. (1 table.)

Ray K. Daily.

Friedenwald, J. S., Buschke, W., Crowell, J., and Hollaender, A. **Effects of ultraviolet irradiation on the corneal epithelium. II. Exposure to monochromatic radiation.** J. Cell. and Comp. Physiol. 32:161-174, Oct., 1948.

Experiments on the corneal epithelium of the rat are reported. In this paper the effects of monochromatic ultraviolet radiation of various lengths are noted. In a previous paper (1945) the results of an investigation of the cellular changes following the use of unscreened cold quartz mercury vapor arc were described. The stimulation of mitosis of the corneal epithelium in the cold quartz experiments of 1948 was found to be due to the gas, possibly ozone, that surrounded the generator. When ozone was removed from the exposed area by suction an inhibition of mitosis resulted. Mitosis inhibition, nuclear fragmentation, and loss of tissue cohesion in the corneal epithelium was observed after exposure to monochromatic ultraviolet radiation and sensitivity curves are described. F. M. Crage.

3
VEGETATIVE PHYSIOLOGY, BIO-CHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Bakker, A. **Carbonic anhydrase and cataracta lentis.** Brit. J. Ophth., 32:910-912, Dec., 1948.

The author discusses the enzyme equilibrium of the lens. By lens culture he has studied the enzyme carbonic anhydrase. As the aqueous does not contain this enzyme, it seems probable that the lens produces its own carbonic anhydrase. The normal lens contains a high amount, lenses with some opacity have considerably less, and mature cataracts none. It was found that the concentration of car-bonic anhydrase decreased with an increase in cataractous changes.

Orwyn H. Ellis.

von Brücke, H., Hellauer, H. F., and Umrath, K. **The relationship between the acetylcholine and aneurin content and the innervation of the cornea.** Ophthalmologica 117:19-35, Jan., 1949.

In 1938 von Brücke discovered the high acetylcholine content of the cornea which became greatly reduced after postganglionic section of the ophthalmic nerve. Now it is found that the epithelium contains nearly all the acetylcholine present in the cornea. After postganglionic section of the ophthalmic nerve, the acetylcholine content increases slightly during the first few hours and then starts to drop; if no keratitis sets in, it drops to about one-half normal. If a neuroparalytic keratitis follows, it varies inversely with the severity of the keratitis. The vitamin B_1 content of the cornea closely parallels the fluctuations in the acetylcholine content. Preganglionic section of the fifth nerve affects the acetylcholine and aneurin content of the cornea only slightly. Cocaine or pontocaine, applied topically, lower the acetylcholine content of the cornea. Topical application of acetylcholine in aqueous solution appears to be beneficial in neuroparalytic keratitis in man. The part played by acetylcholine in the metabolism of the cornea is not definitely known. Peter C. Kronfeld.

Duke-Elder, S., and Davson, H. **Studies on the intra-ocular fluids.** Brit. J. Ophth. 33:21-38, Jan., 1949.

In the cat and rabbit, the glucose concentrations in the aqueous humor and vitreous body are lower than would be expected on the basis of a simple diffusion equilibrium with the plasma. Experiments indicate that this deficit of glucose is due to the metabolism of both the lens

and the retina. The possible physiologic significance is discussed and the importance of including the vitreous body in any study of intraocular dynamics is stressed. Morris Kaplan.

Giardini, A. **The glucose content in normal and in diabetic persons.** Boll. d'ocul. 27:585-599, Sept., 1948.

Ninety-eight sugar determinations were performed in specimens of lacrymal fluid taken from 43 individuals with normal glucose metabolism and from 21 diabetics. The Hagedorn-Jensen method was used in spite of the fact that it measures not glucose alone but reducing substances. The results are shown in four tables. Normal tears had a glucose content of 0.02 to 0.28 percent; three subjects had reducing substances in their lacrimal fluid. Repeated examination on the same individual may reveal very different values. One of the diabetics had no reducing substances in his tears, the others 0.04 and 1.20 percent. The author did not succeed in obtaining phenylglucosazone crystals from the lacrimal specimens. Further research with the Nelson-Szomogyi method is contemplated. (Bibliography.) K. W. Ascher.

Grandjean, E., and Zwahlen, P. **Alterations of the ocular tension and of the retinal arterial pressure at high altitudes.** Helv. Physiol. et Pharm. Acta. 6:560-566, 1948.

During a stay at Jungfraujoch (3450 m.) the ocular tension and the brachial and retinal arterial pressure of five healthy subjects were measured daily. The tension dropped after several days at a high altitude which the authors attribute to a general dehydration of the organism. Whereas the brachial arterial pressure dropped at high altitude the retinal arterial pressure rose, which in the opinion of the authors is due to a peripheral vasodilation of the retinal vessels. This elevation seemingly reflects a parallel circulatory alteration of the cerebral vessels. R. Grunfeld.

Guimarães, Laertes. **Antibiotics in ophthalmology.** Arq. brasil. de oftal. 11:173-198, 1948.

This sixteen-page review of the literature regarding penicillin, tyrothricin, and streptomycin, to which is added a nine-page bibliography, should be of value to readers of the Portuguese language.
W. H. Crisp.

Herrmann, Heinz. **Effect of antihistamines on loss of adhesiveness of corneal epithelium after injection of histamine.** Proc. Soc. Exper. Biol. and Med. 69:506-507, Dec., 1948.

Histamine, injected into excised cornea, caused a marked decrease of epithelial adhesiveness. It effected the detachment of the upper layers of the epithelium from the basal ones. The corneas were incubated for 12 to 15 hours at 28 to 30°C. and the adhesiveness of the epithelium was tested with a simple scraper. It was possible to estimate adhesiveness approximately. If antihistamine was injected together with histamine, the anti-histamine protected the epithelium. Several antihistamines are compared quantitatively. R. Grunfeld.

Hoang-Xuan-Man, and Bailliart, J. **Benzyl-imidazol (priscol) in ophthalmology.** Ann. d'ocul. 181:702-723, Nov., 1948.

This drug is a sympatheticotonic peripheral vasodilator of low toxicity which has been employed during the past ten years in Raynaud's disease, angiitis obliterans, diabetic gangrene, arterial hypertension and other vascular degenerative diseases. It is used in tablets of 25 mg. for oral use, and in ampules of 10 mg. for retrobular injection. In 30 of 40 patients with macular senile and precapillary degenerations improvement

followed one to four injections. Either retrobulbar or oral administration may be employed, but their combined use is apparently more effective. In numerous other ocular degenerative vascular diseases the authors report improvement following the use of priscol.

Chas. A. Bahn.

Laborne Tavares, Cazimiro. **Antibiotics in ophthalmology.** Rev. brasil. de oftal. 7:53-67, Dec., 1948.

Penicillin, tyrothricin, streptomycin, chloromycetin, garlecin, and to some extent aureomycin are discussed as to forms of administration, and as to organisms against which they are respectively available. As far as possible, preliminary laboratory examination should be utilized to determine the responsible microörganism. Further clinical experimentation is desirable. (References.) W. H. Crisp.

Leopold, I. H., and Steele, W. H. **Choice of sulfonamide drugs for local use.** Arch. Ophth. 39:563-578, May, 1948.

Most striking of all factors that influence intraocular penetration of locally applied sulfonamide drugs is the state of the cornea. A great increase in penetration occurs when the cornea is inflamed and partially denuded. Theoretically, it is desirable to have a preparation of the same pH as the tears. If an ointment is desired an ideal vehicle is one that retards epithelial regeneration minimally, is of the oil-in-water type to enchance penetration, and maintain an alkaline pH as an aid in dissociation of the drug, and does not disappear too quickly from the conjunctival sac. Penetration is more rapid from solutions than from ointments. The sodium salt of sufacetimide (now available in 30 percent concentration) is the drug of choice, because of its low pH and great penetration. Sulfadiazine and sulfapyridine are next best.

Ralph W. Danielson.

McGraw, J. L. **Infection of the cornea due to herpes simplex.** Arch. Ophth. 40: 531-552, Nov., 1948.

After a general discussion of the nature of the virus and a review of the literature on treatment of herpes simplex, the authors describe their investigations. Penicillin is ineffective in combating the virus of herpes simplex in mice and in vitro. Streptomycin in high concentration seems to have a slight inhibitory effect on the virus in vivo. Tyrothricin in dilution of 33 mg. per hundred cc. has an unfavorable effect on herpetic infection of the eye of the rabbit. Hyperimmune serum and intravenous use of sodium iodide is ineffective. The local application of 3.5-percent iodine and 70-percent alcohol to herpes-infected eyes of rabbits delays healing and results in greater scarring. Anode iontophoresis of 0.25-percent zinc sulfate is contraindicated in dendritic kertitis in the rabbit but cauterization of dendritic ulcers with 20-percent zinc sulfate is of definite value.

Ralph W. Danielson.

Tschirren, B., and Wiesinger, K. **Investigations concerning the time element of the consensual pupillary reflexes at a high altitude.** Helv. Physiol. et Pharm. Acta 6:554-559, 1948.

The consensual pupillary reflexes of seven healthy men were examined at altitudes 550 m., 800 m., and 3450 m. above sea level. The average latent period is the same as in low altitudes and the average constriction time is considerably smaller in high altitudes. The daily average value of latent period and constriction time diminishes at the beginning of stay at high altitudes but increases after the fifth day. R. Grunfeld.

Verdaguer, J., and Sielacznik, A. **Use of chamico. (A Datura stramonium.)** Arch. chilenos de oft. 4:457-464, 1947.

This plant is a common weed among

the cultivated crops of Chile. Its pharmaceutical and toxic properties do not differ essentially from those of the Jimson weed of the United States. The author tabulates the results of tests upon the eyes of 550 patients with 12 mydriatics, including chamico, atropine, scopolamine, and homatropine. (References.)   W. H. Crisp.

Wiesinger, K., and Plüss, H. R. The size of the pupils in high altitudes. Part I. Examination with a photographic method. Helv. Physiol. et Pharm. Acta 6:528-539, 1948.

The size of the pupil of six persons was measured with a photographic method three times daily on 21 consecutive days at 800 and 3450 m. altitude. The diameter became gradually smaller at 800 m. and at an altitude of 3450 m. the pupils became extremely miotic between the third and fifth day and thereafter they gradually enlarged. The oscillations of the pupils, 1 to 2 minutes after illumination change, were smaller at 3450 m. than in the valley.

R. Grunfeld.

Wiesinger K., and Werner H. The size of the pupils in high altitudes. Part II. Examinations with a double-image pupillometer. Helv. Physiol. et Pharm. Acta 6:540-553, 1948.

The size of the pupils of ten persons was measured twice daily at 560 m. for 9 days, at 3450 m. for 9 days, and at 800 m. for 5 days. The apparatus used for the measurement of the horizontal pupillary diameter consisted of a double refracting Wollaston quartz prism. It was found that at high altitudes the pupils are constricted, the difference of size of the pupillary area in the morning and evening pupil is diminished and the oscillatory pupillary changes are smaller. Fatigue accentuates these findings. As the persons became adapted to the high

altitude, the altitude miosis disappeared altogether.   R. Grunfeld.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Barraquer Cerero, Tomás. Contact lenses and binocular vision. Arch. Soc. oftal. hispano-am. 8:981-987, Oct., 1948.

Barraquer reports the appearance of convergent strabismus in a high myope, for whom contact lenses were prescribed for cosmetic purposes. The patient wore minus nine spheres in each eye, which corrected the vision of the left eye to normal, and that of the right eye to 6/10. The right eye had a high degree of myopic astigmatism, the correction of which brought its vision to normal. The patient did not have binocular single vision, and used the left eye for monocular fixation. With normal vision in each eye the patient had simultaneous perception, but no fusion, and the right eye turned in. With orthoptic training binocular vision was developed, and the patient was enabled to wear the contact lenses with comfort.

Ray K. Daily.

Birren, J. E., Bick, M. W., and Fox, C. Age changes in the light threshold of the dark adapted eye. J. Gerontology 3:267-271, Oct., 1948.

Minimum light thresholds determined with the Hecht Shlaer adaptometer on 130 men between the ages of 18 and 83 years showed a significant decline in the subjects over 60 years of age and the most marked changes in those over 70. There was a larger range of individual difference in the older group. The technique is described in detail. The pupils of all subects over 40 were dilated with 5-percent euphthalmine in order to eliminate miosis. When violet light and white were both used there were similar changes found. There was no significant difference in dark adaptation between

subjects who lived in institutions and those who lived at home (2 tables).

Herman C. Weinberg.

Bischler, V. **Binocular triplopia.** Ophthalmologica 116:254-255, Oct.-Nov., 1948.

Postoperative triplopia is a bizarre visual phenomenon resulting from the simultaneous manifestation of anomalous and normal retinal correspondence in certain recently operated cases of squint, first described by Javal in 1864. With the recent developments in the field of binocular sensory co-operation in strabismus, triplopia has become well known. The author describes a typical case. Despite accurate surgical correction of the squint, triplopia has persisted for over a year, the anomalous correspondence maintaining its supremacy. Persistence of the two correspondences may be due to an actual obstacle to fusion which in the author's case was present in the form of a cyclophoria. Peter C. Kronfeld.

Campbell, D. A. **Primary amblyopia.** Tr. Ophth. Soc. U. Kingdom 66:413-428, 1946.

The author separates primary amblyopia from secondary amblyopia which is due to toxic, neurological, psychological and nutritional causes. An error of refraction, particularly anisometropia or bilateral hyperopia, is frequently the primary factor in the onset of suppressive amblyopia. Suppression follows a disturbance of the normal balance of position of the two eyes. The treatment of primary amblyopia should be begun as early as the age of six months by the use of atropine and glasses. Before the age of five years much less time was required to improve the vision than after that age. Longer periods of occlusion were necessary for those patients with vision of 6/60 or less. (5 tables.)

Beulah Cushman.

Cibis, P. **Contribution to the pathology of the adaptation of definite retinal areas. Part II.** Arch. f. Ophth. 148:216-257, 1948.

The author presents the theoretical background for the data he published in Arch. f. Ophth. 148:1-92, 1947 (abstract Am. J. Ophth. 31:638, 1948). The reader interested in the explanation of visual phenomena by photochemical processes will consult the iriginal paper. (235 references.) Ernst Schmerl.

Dartnall, H. J. A. **Visual purple and the photopic luminosity curve.** Brit. J. Ophth. 32:793-811, Nov., 1948.

The hypothesis that visual purple is the mediator of photopic luminosity sensations as well as of scotopic is investigated. Two main assumptions are made in developing the hypothesis. The first of these is that the production of visual purple from its precursors is a rapid process in comparison with regeneration from its photoproducts; the second, that the influence of absorption by the photoproducts on the light absorbed by visual purple is equal to that obtaining in a homogenous mixture of the substances.

It is shown that the effect of the accumulation of photoproducts (indicator yellow) in a retina exposed to light, is to move the position of maximum light absorption by visual purple towards the longer wavelengths. This process is not indefinitely prolonged. As the amount of indicator yellow accumulates the light absorbed curve of visual purple rapidly approximates to a limiting position having a maximum at about 550 mu. When this limiting curve is corrected for absorption by the ocular media and by the macular pigment, the resulting curve closely approximates to the photopic luminosity curve.

Apart from accounting for the Purkinje shift in a quantitative manner the hypothesis provides a basis for the explanation of a number of other visual phe-

nomena, notably the reduced sensitivity of photopic vision and the dependence of the rate of dark adaptation upon the previous light history of the retina.

Author's summary.

Evans, P. J. Amblyopia. Tr. Ophth. Soc. U. Kingdom, 66:397-412, 1946.

The amblyopia of congenital nystagmus is due to the movements of the eyes and the duration of fixation is the essential criterion of the level of visual acuity. The suppression is physiologic and not associated with the production of the impaired acuity, but is an essential adaptation to an altered visual mechanism. "Fusion" has little significance in the physiology of binocular vision. The grades of binocular vision are in fact grades of physiologic suppression in a center apart from the striate cortex. Suppression is a normal constant process. These grades account in progressive measures for normal vision, retinal rivalry, the suppression of alternating squint, congenital nystagmus, and amblyopia ex anopsia. (4 tables, 1 figure.)

Beulah Cushman.

Györffy, I., and Kahán, A. Hypersensitivity against contact-lenses. Orvosok Lapja 42:1337, Oct. 17, 1948.

Antistin-privin prolongs the time of tolerating contact lenses. This is ascribed to the hindering of the effects of histamine set free from the irritated cornea and conjunctiva. Gyula Lugossy.

Hamburger, F. A. The refraction of persons with normal vision. Klin. Monatsbl. f. Augenh. 113:261-266, 1948.

Organically normal eyes may vary in vision as a result of refraction, clarity of media, size of image, the size of cones, and better function of the individual cone. A statistical study of the refraction and vision of the normal eyes of 433 persons, 18 to 22 years of age, is presented. The vision varied from 6/4 to 6/7. An eye with 6/4 vision may have a 3/4-diopter astigmatism, whereas others with 6/8 may have only a small hyperopic error. Only 367 of the 866 eyes had spheric refraction alone. Almost a third had astigmatism of 0.50 diopters or more. A slight hyperopia is usual. Strict emetropia is the exception and such eyes have a myopia for blue light.

Max Hirschfelder.

Jonkers, G. H. Dark-adaptation measurements by two different methods. Ophthalmologica 116:350-356, Dec., 1948.

Recording of the corneoretinal potentials due to the opticokinetic nystagmus elicited by horizontally moving pattern of low light intensity can be used for objective adaptometry. In subjective adaptometry the appearance or disappearance of the light stimulus may be used as the criterion. The latter method was developed by Lohmann and seems to give the most accurate values although differences between the two methods are insignificant. Peter C. Kronfeld.

Kettesy, A. Pigment-anomaloscopy: a new procedure for testing the coloursense. Brit. J. Ophth. 33:47-54, Jan., 1949.

The author has devised an anomaloscope in which one can utilize pigment colors as well as spectral colors. The new instrument consists of a view box containing two cylinders around which are placed detachable papers bearing triangles or parallelograms of any color or shade of color. The subject looks through a slit and shifts the rotating cylinders on their axes until he feels that the colors match. (4 figures.) Morris Kaplan.

Kettesy, A. The stabilisation of the refraction and its role in the formation of ametropia. Brit, J. Ophth.33:39-47, Jan., 1949.

Steiger's doctrine of the origin of refraction is enlarged with the conception of stabilisation. The latter is the cessation of the growing of the eye, its term varies with individuals, and it is an inherited quality. The cause of the higher degrees of myopia is interpreted as retarded stabilisation. The two weak points of Steiger's doctrine, the excess and the asymmetry of the variation-curve, are explained by the biological peculiarities of stabilisation. Near work has nothing to do with the development of individual myopia, therefore restrictions in the near work of the young myopic patient are unnecessary.

Morris Kaplan.

Knüsel, O. **Contact lenses.** Ophthalmologica 116:225, Oct.-Nov., 1948.

The author's instrument for taking the exact measurements of the anterior segment consists of multiple levers on a central tube that contains the fixation point. By placing the tips of these levers against the sclera a tracing of the shape of the anterior segment is obtained which should permit the fitting of contact lenses without taking a mold.

Peter C. Kronfeld.

McKellen, G. D. **Conical contact lenses.** Brit. J. Ophth. 33:120-127, Feb., 1949.

The surface of a conical contact lens must rest on an area sufficiently behind the limbus to avoid pressure far enough from the edge of the lens to prevent the edge from digging into the eye, and it must rest on an area narrow enough to allow change to a new area as the eye moves. The fluorescein test is used to determine the correct angle of cone and the radius of the optic. The band of contact should be 2 or 3 millimeters behind the limbus and give corneal clearance when the eye is in the primary position. Most eyes can be satisfactorily fitted in considerably less time than is required

for other types. The veiling problem does not seem to be appreciably changed.

Orwyn H. Ellis.

Nordenson, J. W. **On the measure of the stereoscopic acuity of vision.** Brit. J. Ophth. 32:913-914, Dec., 1948.

In a discussion of the measure of stereoscopic vision for adoption of international standards the author reviews the previous reports and states that it seems appropriate to choose for this measure the stereoscopic radius of the examined person. This radius is the quotient of the pupillary distance and the stereoscopic angle of distinction.   Orwyn H. Ellis.

Pascal, J. I. **Role of corneal variability in contact lenses.** Ophthalmologica 116: 318-321, Dec., 1948.

Differences in corneal curvature account for the well-known phenomenon that eyes with widely different amounts of ametropia are corrected with the same contact lens.   Peter C. Kronfeld.

Pirenne, M. H. **Independent light detectors in the peripheral retina.** J. Physiol. 107:471, Sept. 30, 1948.

In 1945 the author observed that in the periphery the retina possibly was made up of a mosaic of units, each about two degrees in diameter, which, under near-threshold conditions of stimulation, behave as independent light-detectors. When a dim light is flashed over a wide field, only a few detectors among many might be stimulated. Despite this, such a field is not a discretely spotted pattern.

Using dim, constant light flashes (0.03 sec.) as a stimulus in a dark-adapted subject, a field of known area was uniformly illuminated and the light-detection reactions noted to test the above theory. Light detection reactions were noted as correct, incorrect, or absent after repeated light flash stimuli were tried in each case.   Francis M. Crage.

Posternak, J. **The visual field at high altitude.** Helv. Physiol. et Pharm. Acta 6:524-527, 1948.

The visual fields of six persons were measured for white, yellow, red, and blue at an altitude of 550 m. at Lausanne, and during a ten day stay at the Jungfraujoch, altitude 3450 m. The visual field for white showed no change during the stay at the high altitude. The visual fields for color were not conclusive.

R. Grunfeld.

Posternak, J. **Visual adaptation to darkness at Jungfraujoch.** Helv. Physiol. et Pharm. Acta. 6:516-523, 1948.

The authors measured the accommodation to darkness of six persons with a calibrated Engelkind and Harting adaptometer. Measurements were taken first in Lausanne at an altitude of 550 m., then during the course of a ten day stay at the Jungfraujoch, altitude of 3450 m., and then again in Lausanne. The stay at the higher altitude produced a lowering of the threshold which the author attributes not to an acceleration of adaptation but to an increased visual sensitivity.

R. Grunfeld.

Quinn, L. H. **Effect of insulin hypoglycemia on the ciliary muscle.** Arch. Ophth. 39:587-594, May, 1948.

Retinoscopic examinations were made before and during therapeutic insulin hypoglycemia. Paredrine hydrobromide ophthalmic, homatropine hydrobromide and atropine sulfate were used to dilate the pupils. Definite stimulation of the ciliary muscle was found in some eyes when paredrine was used as a mydriatic. This was most pronounced in the youngest patients and was greatest during deep insulin hypoglycemia. Homatropine partially abolished the stimulation of the ciliary muscle, and atropine did so almost completely. The fact that the refractive change which occurs during insulin hypoglycemia can be abolished by atropine cycloplegia indicates that it is due to stimulation of the parasympathetic nervous system. This observation is in agreement with other signs of stimulation of the parasympathetic system, namely, pinpoint pupil, slow heart rate, salivation and increased gastric secretion and motility.

Ralph W. Danielson.

Ríos Sasiain, Manuel. **The influence of monochromatic aberration on nocturnal myopia.** Arch. Soc. oftal. hispano-am. 8:925-938, Sept., 1948.

The object of this investigation was to determine the effect of spherical aberration on nocturnal myopia. In general, nocturnal myopia is accounted for to a small extent by Purkinje's shift from photopic to scotopic vision, and to a greater extent by changes in the crystalline lens. The effect of pupillary dilatation uncovers the marginal zones of the lens, and that brings about spherical aberration. Earlier investigations on the effect of the size of the pupil on the spherical aberration of the eye are reviewed, and the author's experimental armamentarium is described in detail. The charted and graphic data show that the eye is an overcorrected optic system in which the marginal zones of its refracting surfaces have a greater radius and a lesser curvature. The spherical aberration of the incident marginal rays is neutralized by the diminished curvature of the peripheral zones. Under physiologic conditions the eye has no spherical aberration; it therefore can not be a factor in the phenomenon of nocturnal myopia. Nocturnal myopia is greater with small than with large pupils.

Ray K. Daily.

Romero, Eduardo. **Neutral astigmatism.** Arch. Soc. oftal. hispano-am. 8:918-924, Sept., 1948.

Romero contends that all simple cylinders in the trial case should be replaced by crossed cylinders, because each simple cylinder exerts a spherical effect of one-half the strength of the cylinder. In crossed cylinders the spherical component is neutralized, and the effect on the refraction is only in one meridian, which he designates as neutral astigmatism.

Ray K. Daily.

Rubiño, A., and Pereyra, L. **The eye and the diencephalon.** Riv. oto-neuro-oftal. 23:69-84, March-April, 1948.

Extensive studies lead the writers to conclude that the daily life sense variations are a part of the metabolic and neuro-vegetative manifestation of the mesodiencephalic day-night rythm. (5 figures, 38 references.)

Melchiore Lombardo.

Sloan, L. L., and Wollach, L. **Comparison of tests for red-green color deficiency.** J. Aviation Med. 19:447-455, Dec., 1948.

The pseudo-isochromatic plates, anomaloscopic, the Rabkin test are evaluated. (2 figures, 7 tables). Irwin E. Gaynon.

Speiser, S. **The influence of the size of the pupil upon the critical flicker frequency.** Ophthalmologica 116:357-370, Dec., 1948.

The phenomenon of flicker is reviewed with special reference to its use as a clinical method of studying retinal function. Dilation of the pupil raises the critical flicker frequency while constriction of the pupil lowers it. These effects are due to variations in the amount of incident light and not to any action of the drugs upon the retina.

Peter C. Kronfeld.

Wagenaar, J. W. **So-called color stereoscopy.** Ophthalmologica 117:74-81, Feb., 1949.

Several phenomena of so-called color stereoscopy, that is, pseudo-plastic effects of flat color-containing patterns, are reviewed. Verhoeff described the optical illusion that the portions of a red line on a black and white background seem to be respectively nearer or farther away and he attributed the phenomenon to the effects of chromatic aberration and eccentricity of the lens system. Loewenstein and Donald observed the following phenomenon and believe that some psychologic factors at present unknown play a great part in producing it. When certain colored patterns are viewed against colored backgrounds for some time, the backgrounds change from surface colors to colored spaces in which the pattern seems to float. The phenomenon was found to be independent of color and almost as striking monocularly as binocularly. Wagenaar explains these and similar phenomena as partly optical, resultant from the superimposition of image and after image in oscillating fixation, and partly psychologic in terms of concepts of "Gestalt" psychology. Peter C. Kronfeld.

5
DIAGNOSIS AND THERAPY

Alcalá López, Antonio. **A dark room lamp.** Arch. Soc. oftal. hispano-am. 8: 946-948, Sept., 1948.

Alcalá describes an inexpensive arrangement consisting of 100 candle-power light globe in a dark housing with a small opening on each side. One serves as a source of illumination for ophthalmoscopy and has attached to it a holder for filters. A blue filter introduced into the holder provides a blue light for the examination of fluorescein-stained corneal defects. The other opening is connected to a tin tube capped with a holder for a condensing lens to focus the light on the cornea for removal of foreign bodies. The lamp is attached to the wall by an adjustable bracket. (1 figure.) Ray K. Daily.

Alcalá López, Antonio. **A model for a box of optotypes.** Arch. Soc. oftal. hispano-am. 8:901-906, Sept., 1948.

Alcalá López designed a new optotype box, with the special objective of discovering simulators, malingerers who hope to escape military service, as well as those who attempt to conceal their visual impairment. The instrument consists of an illuminated box, with a rotating chart on which one letter at a time is exposed. The chart contains letters, Landolt's rings, green and red letters for use with red and green spectacles and targets for estimation of heterophoria. The optotypes are printed on both sides of the paper and can be used directly at 5 meters or reflected in a mirror at 2½ meters. (4 figures.)

Ray K. Daily.

Arentsen, Juan. **Injection of air into the anterior chamber.** Arch. chilenos de oft. 4:485-490, 1947.

The author recommends careful consideration of this detail of technique, as described by Barraquer (Arch. Soc. oftal. hispano-am. April, 1946, abst. Am. J. Ophth., 1947, p. 348) for protection against contact of the iris with the operative wound, and for release of the vitreous from the operative wound in cases complicated by loss of vitreous. The author also speaks very favorably of the measure as applied to filling of the anterior chamber after suture of penetrating corneal wounds.   W. H. Crisp.

Bangerter, A. **Surgical experiences.** Ophthalmologica 116:214-216, Oct.-Nov., 1948.

To dilate the pupil before the intracapsular cataract extraction the author routinely uses homatropine. If this proves insufficient, he injects a small amount of cocaine and epinephrine subconjunctivally. He uses one Liégard suture and makes two basal iridectomies, one on each side of the suture. He administers eserine immediately after the delivery of the lens. The patient sits up in bed during the first 24 hours after the operation. Old age or acute dacryocystitis do not contraindicate a dacryocystorhinostomy. Bangerter advocates von Blaskovics' resection and advancement of the levator for most forms of ptosis. The sutures are tied over a metal strip which acts as a splint. Binocular dressing after tenotomy and advancement of the horizontal extrinsic muscles is unnecessary.

Peter C. Kronfeld.

Boles, W. McD. **Combined sodium "pentothal" and local anesthesia for selected cases of eye surgery, with a note on the additional use of curare.** South. M.J. 42:13-18, Jan., 1949.

The use of sodium pentothal is recommended because it does not explode, its use is simple and does not interfere with the operative field. Nausea and vomiting seldom occur postoperatively. There is also a lowering of intraocular tension which is favorable in cases of glaucoma.

Oxygen is advised for the cyanosis which may result from respiratory depression. The use of atropine intravenously prevents the sneezing and coughing that result from the stimulating effect of the sodium pentothal on the parasympathetic nervous system.

Local anesthesia is used to block pain stimuli and curare is added for further muscular relaxation. (1 figure.)

Herman C. Weinberg

Cripps, Mary. **The treatment of traumatic and inflammatory lesions by X rays and ultra-short wave diathermy combined.** Tr. Ophth. Soc. U. Kingdom 66: 333-345, 1946.

Ultra-short wave diathermy was extremely useful in the relief of pain due to mechanical factors such as the increased tension of glaucoma. Irradiation by X rays

alone was invaluable for the relief of nerve pain and prevention of irritation and sympathetic ophthalmia. The combined use of X rays and ultra-short wave in 195 patients caused improvement in various types of inflammatory and traumatic lesions. In 88 cases of acute trauma there was no occurrence of sympathetic ophthalmia. One patient in whom sympathetic ophthalmia had been diagnosed came for treatment 14 days after a penetrating wound with an increase of mononuclear leucocytes, and the attack was aborted. Ultra-short wave diathermy was usually used first to reduce the ocular tension, X rays relieved the pain and deep ciliary injection. A summary of the data is given. Beulah Cushman.

Davis, F. A. What the general practitioner should know about ophthalmoscopic examinations. Post grad. Med. 4:473-500, Dec., 1948.

The author advises a thorough understanding of the structure of the tissues which make up the fundus, some knowledge of the underlying disease processes which manifest themselves in these parts, and painstaking daily use of the ophthalmoscope. He describes the anatomy of the structures of the eye and pathologic changes found in diseases, with many illustrations of different parts of the eye. With accompanied illustrations, he discusses various diseases.

Theodore M. Shapira.

Endt, P. M., and ten Doesschate, J. A theoretical plan of a method for removing non-ferro-magnetic metallic intra-ocular foreign bodies by means of electro-magnetic forces. Brit. J. Ophth. 33:97-100, Feb., 1949.

The author presents the theory on which a method for removing non-ferro-magnetic metallic intraocular foreign bodies by building up high frequency-electro-magnetic fields is based. Copper,

for example, is pushed out of a magnetic field; with its generator behind the head a fragment of copper could theoretically be removed from the eye. A considerable amount of heat is generated in the particle. It is questionable whether a field of sufficient intensity can be produced and the difficulties of heat generation overcome. Orwyn H. Ellis.

Freusberg, O., and Weigelin, E. Some sources of error in measuring the diastolic pressure in retinal arteries after Bailliart. Klin. Monatsbl. f. Augenh. 113:209-220, 1948.

The speed with which the dynamometer is pressed down on the eyeball influences the diastolic pressure only little. The rapid production of pressure tends to give slightly higher values. The very first small pulsations are indicative of the diastolic pressure and to observe them a clear and sharply focused image of the optic disc is imperative. If they escape observation the readings will be too high. Repeated dynamometry tends to lower the intraocular pressure. The proper application of the instrument to the eyeball is important and the authors recommend that one assistant hold the instrument, a second read the scale, while the observer devotes himself fully to the observation of the fundus. Nervousness tends to raise the diastolic retinal pressure by about 4 mm. Hg in health and disease. A second reading after a 15-minute period of rest is suggested. The following routine is recommended: mydriatic, determination of brachial blood pressure, corneal anesthesia, ocular tension, dynamometry, repeated in 15 minutes, brachial pressure, and tension. Max Hirschfelder.

Giudice, Mario del. Retrobulbar saline injections in ocular therapy. Rev. brasil. de oftal. 7:69-73, Dec., 1948.

Beginning with ulcerative keratitis, the author tried the effect first of subcon-

junctival and then of retrobulbar injections of physiologic salt solution, which he later modified to one-percent solution of sodium chloride. He added one-percent novocain solution because of the pain produced. He gives briefly the details of several cases of inflammatory lesion in which such injections were beneficial. Pain and other inflammatory symptoms were diminished. W. H. Crisp.

Halbron, P., Lepage, F., Leconte, C., and Mawas, H. **Penicillin ophthalmic prophylaxis of the new-born.** Ann. d'ocul. 181:676-680, Nov., 1948.

In a series of 2000 births, no cases of gonorrheal conjunctivitis lasting more than 48 hours were observed after penicillin treatment. Two drops of a solution containing 5000 units per cc. were instilled immediately after birth and an ointment with 1000 units per gram was employed later. There were no corneal complications. In 22 infants conjunctivitis due to staphylococcus, streptococcus, pneumococcus, diplobacillus or Kochs-Weeks bacillus was promptly cured by this treatment. Chas. A. Bahn.

Halldén, U. **An instrument for the examination of the central field with binocular fixation.** Klin. Monatsbl. f. Augenh. 113:266-267, 1948.

The patient observes a spot of polarized light through polaroid lenses. A screen covered with aluminum paint reflects the spot of polarized light which can only be seen by one eye. The screen itself is diffusely illuminated by unpolarized light and its central fixation point can be observed binocularly. (1 figure.)
Max Hirschfelder.

Huber, A. **The effect of calcium therapy upon the eye.** Ophthalmologica 116:235-244, Oct.-Nov., 1948.

The effect of systemic calcium therapy upon the permeability of the blood-aque-

ous barrier was determined by observing the entrance into the aqueous of intravenously injected fluorescein. The rate of entrance of fluorescein into a normal eye is not altered by calcium therapy. In anterior uveitis, congestive glaucomas and ocular injuries the fluorescein method reveals a definite permeability-lowering, "anti-exudative" effect of systemic calcium therapy. Peter C. Kronfeld.

Jacobs, M. L. **Radiation therapy of eye diseases.** Ann. West. Med. and Surg. 3:68-69, Feb., 1949.

Inflammatory and non-neoplastic lesions are usually treated with beta radiation and neoplastic lesions with X or Gamma rays. The beta applicator emits rays which do not penetrate more than 2 mm. and are similar to the low voltage or Grenz rays. These have a healing effect on corneal ulcers and are also used for tuberculosis of the anterior segment, corneal scarring, granulation tissue and pterygium. Neoplastic diseases usually respond to X-ray or radium therapy.
Orwyn H. Ellis

Jacot, P. **The treatment of ocular tuberculosis with P501.** Ophthalmologica 116:290-292, Oct.-Nov., 1948.

P501, identical with promin, is perhaps the first step in the search for a satisfactory chemotherapeutic drug with specification on the tubercle bacillus. It may prove an adjuvant to streptomycin in ocular tuberculosis.
Peter C. Kronfeld.

Larsson, Harry. **An apparatus for the determination of the axial length of the eyeball.** Acta Radiol. 30:237-242, 1948.

The technique and instrument used by the author for the determination of the axial length of the eyeball, essential to the localization of intraorbital foreign bodies, is a modification of the Rushton procedure reported in 1938. The impor-

tance of knowing the exact axial length of the eyeball is apparent when it is realized that this measurement is not the same in all eyes.

Francis M. Crage.

Lauber, H. **The permanent magnet.** Klin. Monastbl. f. Augenh. 110:577-587, 1945.

Adequate electric current for electromagnets was often not available during the war. Permanent hand magnets of an iron-nickel-aluminum mixture proved very successful.

Gertrude S. Hausmann.

Lopez, Enriques M. **Improvement of the "Oculus" ophthalmoscope.** Arch. Soc. oftal. hispano-am. 8:1145-1148, Nov., 1948.

The author describes several modifications for improving the electric ophthalmoscope in use in Spain. They consist of an illuminating handle, which utilizes a nitra lamp of 8 volts and 3.8 amperes, a condensor, and a Rekoss disk provided with diaphragms of two sizes, two slits, and red and red-free filters. (1 figure.)

Ray K. Daily.

Loewenstein, A., and Foster, J. **Fatty embolism of the retinal artery found in eyes after enucleation and orbital exenteration.** Brit. J. Ophth. 32:819-823, Nov., 1948.

Four eyes removed by enucleation and by exenteration were examined internally with the slit lamp after equatorial section of the globe. In each case the central retinal artery was white for some distance from the disc. Serial sections revealed fatty embolism which was more or less fluid and consisted of a fine fatty emulsion which stained a shining red with scarlet red. No red blood cells were found within the milky areas, but distal to the embolism there was the regular column of blood. The presence of the fat is ex-plained by accidental cutting by the scissors of orbital fat with subsequent sucking of the fat into the artery and its emulsification by the orbital blood. This observation shows the ease with which fatty droplets can enter opened vessels and also a potential danger in foreign body extraction by the posterior route.

Morris Kaplan.

Moron-Salas, Jose. **On gonioscopy.** Arch. Soc. oftal. hispano-am. 8:1108-1113, Nov., 1948.

After a detailed discussion of the optical obstacles to be overcome before seeing the anterior chamber angle, Moron-Salas points out that his contact lens with a deep liquid chamber succeeds in eliminating the astigmatism of oblique rays, which is not achieved by the Goldman or Allen lenses. He admits that Troncoso's valid criticism that a reflected image of the angle loses something of its precision, applies to his lens. However, this is a defect of minor importance, far outweighed by the advantage of being able to do a gonioscopy through the corneal microscope. Ray K. Daily.

Neuenschwander, M. **Placenta therapy of retinitis pigmentosa.** Ophthalmologica 116:262-272, Oct.-Nov., 1948.

In about one-half of 27 patients with far-advanced retinitis pigmentosa who were subjected to tissue therapy after Filatof, results were positive, and at times amazing. In the discussion Bietti sums up his own experiences by saying that therapy with biogenic stimulants must not be considered a complete failure.

Peter C. Kronfeld.

Post, L. T. **Diagnostic significance of failing vision.** J.A.M.A. 139:303-305, Jan. 29, 1949.

This is a brief survey of some of the commoner causes of visual failure, with the note that mutual effort between the

ophthalmologist and practioners of other branches of medicine is very often necessary and of great benefit. The causes of visual failure are listed under the headings cornea, iris, ciliary body and choroid, retina, optic nerve, lens, vitreous, and disuse. Bennett W. Muir.

Richardson, A. W., Duane, T. D., and Hines, H. M. **Experimental lenticular opacities produced by microwave irradiations.** Arch. Phys. Med. 29:765-768, Dec., 1948.

The authors state that a direct single exposure of rabbit eyes to 12.24 cm.-microwaves at 5 cm. distance for 15 minutes with 100 watts power output resulted in the development of lenticular opacities after 3 to 9 days. After a single exposure the average temperature of the vitreous at the posterior pole of the lens was 55.1°C. and that of the cornea 49.4°C. A series of repeated exposures of a smaller magnitude resulted in lenticular opacities after 2 to 42 days. Four rabbits irradiated for 17 to 20 minutes at 5 cm. distance revealed cataract formations immediately. The practical applications of these microwaves are discussed.
Theodore M. Shapira.

Rintelen, F. **The treatment of blepharospasm with parpanit.** Ophthalmologica 116:217-220, Oct.-Nov., 1948.

Parpanit has proved beneficial in postencephalitic and arteriosclerotic forms of Parkinson's disease. The author advocates the use of the new drug in cases of idiopathic blepharospasm of older people in whom there is a possibility of an organic, extrapyramidal spastic mechanism.
Peter C. Kronfeld.

Trotter, R. R. and Grant, W. M. **Electronic flash (gas discharge) tube in photography of the anterior segment of the eye.** Arch. Ophth. 40:493-496, Nov., 1948.

For photography of the anterior seg-ment of the eye, an electronic flash tube of 9,500 lumen seconds' output provides more satisfactory illumination than the illuminants in common use for this purpose. Life-size color pictures can be taken with a desirably small lens aperture, yet with relatively little discomfort to the subject. Ralph W. Danielson.

6

OCULAR MOTILITY

Bischler, V. **Binocular triplopia.** Ann. d'ocul. 181:724-732, Nov., 1948.

This phenomena is not infrequently observed after operations for nonparalytic strabismus. Diplopia, in this condition, is avoided by suppressing the image of one eye, or by associating an eccentric image of one eye with a centric image of the fixing eye. After a review of several cases reported by Javal, Claasen, Bielschowsky, Tschermak, and Cass, the author explains the basic principles involved. Binocular triplopia may be observed from several months to years after strabismus operations. Chas. A. Bahn.

Boldrey, E., and Miller, E. R. **Unilateral paralysis of eye muscles associated with intracranial saccular aneurysms.** California Med. 70:96-98, Feb., 1949.

Congenital saccular aneurysms arise from weak areas in the walls of intracranial arteries where there has been incomplete involution of the embryonal vessels, or from defects at the point of bifurcation of larger intracranial vessels. They arise most frequently from the carotid artery or its principal branches. Three cases are reported in which the diagnosis was made early and treatment by intracranial ligation was successful. Unilateral ocular muscle palsy is an early diagnostic sign. Orwyn H. Ellis.

Lees, V. T. **A new method of applying the screen test for inter-ocular**

muscle balance. Brit. J. Ophth. 33:54-59, Jan., 1949.

The new test employs two Hess screen pointers, perpendicular to each other and similar, which are, however, not red and green and no colored goggles are necessary. Instead, a small plane mirror with a reflecting surface on each side bisects the right angle between the screens. The mirror blocks out the eye not being tested, yet the reflected image of the screen on that side is superimposed on the image of the other screen so that binocular fixation is obtained with monocular vision for the test object. Details of construction of the instrument are described.

Morris Kaplan.

Scheyhing, H. **Tenotomy in convergent squint.** Klin. Monatsbl. f. Augenh. 110: 313-321, May-June, 1944.

Of 134 patients who had been operated on for convergent strabimus in the years 1933 to 1942, 39 had developed divergence. In more than half of them the muscle was completely paralyzed, in the others considerably weakened. In 45 patients without secondary divergence the function of the internal rectus was impaired. The recorded data on all the patients are most thoroughly analyzed and it is obvious that tenotomy with or without a safety suture is an unreliable operation that frequently gives very poor cosmetic results. It should be abandoned in favor of the physiologically more appropriate strengthening of the lateral rectus by shortening and advancement. It is evident from the paper that the fundamental rule to measure the excursions of the eyes before and after the operation was completely neglected.   George Brown.

Tóth, Zoltan. **A new suture in resection of the muscle.** Klin. Monatsbl. f. Augenh., 110:321-324, May-June, 1944.

The muscle is exposed and isolated, cut at its insertion, pulled forward and two double-armed U-shaped sutures are inserted. One suture enters the distal edge of the conjunctiva, is passed through the muscle as far back as possible, eventually through the insertion and the conjunctiva. The second runs in the opposite direction, through the conjunctiva close to the cornea and muscle insertion, then again through the muscle as far back as possible, and the overlying conjunctiva. One of the sutures should be white, the other black. Finally the muscle is resected and the upper and lower black sutures simultaneously tied to the upper and lower white sutures respectively.

George Brown.

Urrets Zavalia, A. **Abduction in elevation.** Arch. de oft. de Buenos Aires 23: 124-134, April-June, 1948.

Because of the action of the inferior oblique muscles the visual axes tend to diverge when the gaze is directed upward, and conversely they tend to converge when directed downward. This must be recognized in the interpretation of examinations of muscle function. (6 figures, 12 references.)   A. G. Wilde.

7

CONJUNCTIVA, CORNEA, SCLERA

Appelmans, M. **The keratoconjunctivitis sicca of Gougerot-Sjögren.** Arch. d'opht. 8:577-589, 1948.

Appelmans discusses in detail the historical, clinical, and pathologic features of this syndrome and its relation to the syndrome of Mikulicz. He points out that Gougerot, a prominent French dermatologist, first described the essential features of the syndrome in 1926, before Sjögren's description of it appeared in 1933. Appelmans considers that Mikulicz's disease is a separate entity in spite of the fact that the two syndromes have much in common. He stresses the role of lacrimal dys-

function in the production of filamentous keratitis, which may be a facultative and episodic complication of keratoconjunctivitis sicca. He points out, however, that filamentous keratitis may follow other unrelated conditions such as relapsing keratitis, dendritic keratitis, chronic glaucoma, or herpes zoster.

In discussing the etiology the author considers in turn the avitaminosis theory, the sympathetic dysfunction theory, the neurotoxin theory, and the endocrine dysfunction theory. He suggests the possibility of a chemical mediator, which he calls secretin, which might be concerned in initiating the function of the serous glands. He considers that vasomotor action supplements the chemical action and concludes that the sexual hormones may be concerned with the vasomotor action. He notes that the majority of medications are poorly tolerated in keratoconjunctivitis sicca. Hormonotherapy has been successful early in the disease and closure of the canaliculi has been valuable.

P. Thygeson.

Boulanger, Jacques. **Vitamin D-2 and old tuberculin in tuberculous keratitis.** L'Union med. du Canada 77:1439-1441, Dec., 1948.

An alcoholic solution of vitamin D-2 containing 300,000 international units per cc. is recommended as a valuable adjunct to old tuberculin in the treatment of tuberculous interstitial keratitis. Three cases are reported. The dosage recommended is 100 drops three time a week for the first week, 100 drops twice a week for the next three weeks, and 100 drops per week for the following six months. Daily milk and additional calcium are indicated.

Irwin E. Gaynon.

Cometta, F. **The preservation of corneas in liquid paraffin.** Ophthalmologica 116:307-310, Oct.-Nov., 1948.

In four of ten keratoplasties done with donor corneas that were preserved and stored in paraffin oil after the method of Buerki, the grafts remained clear. In one case the donor cornea had remained in paraffin for 42 hours.

Peter C. Kronfeld.

Friede, R. **Keratoplasty for total leucoma. (A case of total sclerosis of the cornea.)** Klin. Monatsbl. f. Augenh. 113: 147-152, 1948.

Penetrating keratoplasty has been disappointing in eyes with total and adherent leucoma. Central transplants become opaque and, when too large, develop into a staphyloma. Total replacement of the cornea also is not promising. Friede used a modification of the usual method in eight eyes of which 83 percent healed with opacification, 17 percent were partially opaque, and none remained entirely clear. He tried this procedure in a patient who had a severe sclerosing keratitis with highly inflamed and vascularized corneas. Vision was reduced to recognition of hand movements. A crescentic mass of corneal tissue of one eye was removed down to Descemet's membrane. The defect was filled with a similar shaped donor implant which was held in place by sutures. Six months later a small penetrating keratoplasty was performed in the center of the cornea on the inner curvature of the implanted crescent. This implant stayed clear for several weeks, but got slightly hazy later. In the other eye a large part of the cornea was removed down to Descemet's membrane. The central parts of Descemet's membrane were then removed, leaving a peripheral margin as support for the relatively large donor transplant. The implant became moderately hazy in the following months. The author feels that a large partially penetrating keratoplasty with preservation of Descemet's membrane preparatory to a subsequent smaller total keratoplasty may improve the

outlook for these unfavorable cases of total leucoma.   Max Hirschfelder.

Frischer, M., Jablonski, W., and Loebel, M., The treatment of allergic external diseases in Palestine. Ophthalmologica 116:335-349, Dec., 1948.

Gutmann thinks that vernal conjunctivitis in Palestine is due to an allergy to fungi superimposed on a chronic infection. Specific desensitization and removal of the focus of infection are effective treatment which, however, is too complicated and costly to be used on a large scale. Privine and antistine topically, plus antistine systemically, have given favorable results.   Peter C. Kronfeld.

Gorman, J. E. The Stevens-Johnson syndrome; report of two cases. U. S. Nav. M. Bull. 49:50-54, Jan., 1949.

The author reviews the literature and reports two cases.   Orwyn H. Ellis.

Gray, J. D. A. Meningococcal conjunctivitis. Brit. M. J. pp. 17-18, Jan. 1, 1949.

Purulent conjunctivitis in a 3½-year-old boy healed within eight days under local therapy with 30-percent sodium sulphacetamide, penicillin solution (2,000 units per ml.), and atropine. Meningococcal conjunctivitis is more frequent than is commonly thought; it is erroneously diagnosed as gonococcal. (References.)
          Bennett W. Muir.

Healy, J. J. Two cases of exogenous tuberculous conjunctivitis displaying Parinaud's conjunctivo-adenitis syndrome. Tr. Ophth. Soc. U. Kingdom, 66: 455-466, 1946.

Two patients had granulomatous swelling of the upper tarsal conjunctiva which seemed to be a primary exogenous infection by tubercle bacilli, and swelling of the parotid gland on the same side as in typical Parinaud's conjunctivitis. Tuber-

cle bacilli, in one of the human type and in the other bovine, were found in the tissue and in the discharge. Both patients recovered with minimum scarring on general hygienic and local care. No tuberculin was used.   Beulah Cushman.

Howell, S. C. and Benton, Curtis, Jr. Keratitis nummularis (Dimmler); report of five cases. South. Med. J. 42:94-97, Feb., 1949.

In four of five cases both eyes were involved. The disease is usually unilateral. Slitlamp examination showed lesions immediately behind Bowman's membrane, which had dense circular centers and sharply defined edges, surrounded by a less dense halo. These lesions were facets with shallow edges. None of the patients had positive tests for brucellosis. (3 figures).   Bennett W. Muir.

Klainguti, R. Chestnut bur injuries of the eye. Ophthalmologica 116:247, Oct.-Nov., 1948.

Eye injuries due to chestnut burs are apparently quite common in Switzerland. During harvesting a chestnut may strike the eye and one or several burs may become implanted in the cornea. The protruding portion of the bur usually breaks off, but removal is accomplished quite easily in most cases. Penetration of the tip of a bur into the anterior chamber is rare.   Peter C. Kronfeld

Marín Amat, Manuel. Two cases of fatty degeneration of the cornea, consecutive to corneal herpes. Arch. Soc. Oftal. hispano-am. 8:891-896, Sept., 1948.

One case followed an insignificant corneal injury. Fifteen days after the removal of a corneal foreign body the cornea presented a typical picture of herpetic keratitis, and in spite of therapeutic procedures total fatty degeneration of the cornea, with loss of vision ensued. In the second case there was no

trauma, and three weeks after the onset of corneal herpes the cornea had undergone a complete fatty degeneration. The pathogenesis of fatty corneal degeneration is discussed in detail. The invisible lipoids of the cornea become transformed into visible lipoids through lack of oxidation. The condensation of the fine invisible fatty emulsion in the cellular protoplasm is followed by reaction similar to that of a foreign body in the cells of the reticuloendothelial system; at first the reaction is defensive, but then it proceeds to proliferation of fibroblasts and cicatrization. Inadequate local oxidation is the basic pathologic process, but excessive cholesterol in the diet, disturbances in the lipoid metabolism, hereditary predisposition, and vascular disturbances may be important factors. It is suggested that procedures stimulating local oxidation, such as subconjunctival injections of oxygen should be tried in the therapy of these refractory diseases.

Ray K. Daily.

Mitter, S. N. Scleral degenerations: a case of scleromalacia perforans. Brit. J. Ophth. 32:899-904, Dec., 1948.

The author reviews the literature on scleral degenerations briefly and points out their differences. He reports a cystic swelling of the sclera of a young man which extended into the cornea and progressed until the eye became atrophic.

Orwyn H. Ellis.

Motolese, F. Pseudotrachomatous acute follicular conjunctivitis, due to nonhemolytic streptococcus. Boll. d'ocul. 27:456-463, July, 1948.

Discussing three cases, Motolese revives the famous autoinnoculation experiment performed by Theodor Axenfeld decades ago in order to show the difficult differential diagnosis between conjunctival diseases with follicular formation other than trachoma. Therapeutically he

favors gentle massage of the everted lids with a cotton applicator soaked in mercury bichloride solution. K. W. Ascher.

Orzalesi, F. One more case of probably herpetic involvement of the corneal endothelium. Boll. d'ocul. 27:424-438, July, 1948.

Orzalesi describes an acute unilateral eye disease in an otherwise normal patient, 50 years of age. It started as an iritis with severe neuralgia of the first branch of the fifth nerve, and later affected the central area of the posterior corneal strata, where intense haziness and pseudoprecipitates were observed. Folding of Descemet's membrane and marked edema of the corneal stroma and epithelium followed. The author classified the disease as Favaloro's keratoendothelio-Descemetitis and assumed that herpes was the cause. He wonders whether the herpes virus can become localized in the endothelium and on Descemet's membrane as it does in the corneal epithelium and Bowman's membrane and whether a deep herpetic keratitis can originate from a primary invasion by way of the aqueous humor. (3 figures.) K. W. Ascher.

Orzalesi, F. An unusual type of fatty degeneration of the cornea in a trachomatous eye. Boll. d'ocul. 27:561-584, Sept., 1948.

A 70-year-old man had trachoma with entropion and trichiasis in his only eye and severe scarring of the cornea which was gray with partially protruding yellowish dots. Tension was normal. A corneal transplantation was preformed and the excised disc was examined histologically. The excised disc showed irregularity and increase in layers of the epithelium, the basal cells of which were elongated and rested upon the corneal fibers where the membrane of Bowman had been destroyed; up to 15 rows of

polygonal cells could be counted in some places. There, however, places where the epithelium was very thin and only one layer of keratinized cells covered the parenchyma. The latter showed severe destruction; many spongy cells like those in-xanthomatosis were seen between the ruptured, barely recognizable fibers. Only Descemet's membrane had persisted; its endothelial lining was deficient in many regions. Fat staining revealed the presence of numerous fatty deposits of granular or droplet shape. The pathogenesis of these changes is discussed. (Stereophotograph, 5 photomicrographs, 45 references.) K. W. Ascher.

Radnót, M. Posterior progressive scleritis. Ophthalmologica 116:167-171, Sept., 1948.

Radnót reports a case of chronic rheumatoid arthritis and chronic bilateral uveitis of more than ten years' duration. Because of intractable pain, glaucoma, poor light projection and exophthalmos one eye was removed. The histologic examination revealed a noncharacteristic diffuse uveitis and a chronic proliferative scleritis of the posterior half of the sclera which had been greatly thickened and transformed into granulation tissue.
Peter C. Kronfeld.

Sie-Boen-Lian. Epidemic keratoconjunctivitis in Batavia during 1946 and 1947. Ophthalmologica 116:86-100, Aug., 1948.

An epidemic of epidemic keratoconjunctivitis broke out in Batavia in May, 1946, reached a first peak in November, 1946, and a second one in July, 1947. During the Japanese occupation the author did not see a single case of the disease. He believes it was brought in by the Indian and English army. Indonesians, Chinese and Caucasians appeared to be equally susceptible. The clinical course did not differ significantly from the European or American form of the disease. The author found systemic sulfathiazole therapy beneficial in that the conjunctival condition usually improved rapidly within five days from the inception of the sulfonamide treatment. The literature is reviewed. Peter C. Kronfeld.

Sorsby, A., and Ungar, J. Preliminary note on the treatment of hypopyon ulcer by crystalline penicillin in adrenalin in doses in excess of 50,000 units injected by subconjunctival or retrobulbar routes. Brit. J. Ophth. 32:878-881, Dec., 1948.

The authors found that amounts of penicillin injected subconjunctivally up to 500,000 units at 24 hour intervals were well tolerated, and most hypopyon ulcers responded rapidly and satisfactorily. This is a preliminary report with most promising results thus far. Retrobulbar injections of similar doses appear to be somewhat less efficient, but show clinical response. Orwyn H. Ellis.

Wolff, J. E. Ocular complications in erythema exudativum multiforme with mucous membrane lesions. Brit. J. Ophth. 33:110-119, Feb., 1949.

The author reviews the literature of erythema exudativum multiforme, also known as Stevens-Johnson disease and presents two case reports. The etiology is unknown but four causes have been suggested: hematogenous tuberculosis, virus, vitamin deficiency and allergy.
Orwyn H. Ellis.

Zibikowski Margarida, E. Some details of pterygium surgery. Arch. Soc. oftal. hispano-am. 8:1017-1023, Oct., 1948.

All pterygium operations can be divided into two groups: those in which the raw surface of the sclera is covered completely, and those in which several millimeters of sclera adjacent to the limbus are left exposed. The operation practiced by the author belongs to the latter

group. The cornea is cleared meticulously of every vestige of the pterygium with a knife made of a portion of a razor blade; a flap is then cut away from the lower portion of the pterygium and the remainder is buried under the conjunctiva of the lower fornix. Healthy conjunctiva is thus pulled down from above to cover the space occupied by the pterygium, and an elliptical area of sclera adjacent to the cornea is left exposed. (4 figures.)

Ray K. Daily.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Caballero del Castillo. **Iridodiastasis.** Arch. Soc. oftal. hispano-am. 8:897-900, Sept., 1948.

A case of this rare congenital anomaly in a woman, 20 years old, is reported. In the inferior external portion of the iris a hole occupied the outer half and was bridged by some thin iris tissue strands. The pupil was slightly oval, and displaced up and in. This anomaly is the result of imperfect closure of the embryonal cleft. The differential diagnosis between a congenital and an acquired traumatic lesion is discussed in detail, and it is pointed out that Dupuy-Dutemps' statement that in congenital anomalies the pupil is round is not always true. A large congenital deformity may give rise to some distortion of the pupil. (1 figure.)

Ray K. Daily.

Dufour, R. **Ocular manifestations of early pulmonary tuberculosis.** Ophthalmologica 116:298-303, Oct.-Nov., 1948.

In young adults shortly after their first pulmonary infection with tuberculosis, that is during the stage of the primary complex, serous iridocyclitis and retinal periphlebitis took a torpid course, probably because of a low degree of local (ocular) allergy to tuberculin.

Peter C. Kronfeld.

Fleming, Norman. **A case of pigmented leiomyoma of the iris.** Brit. J. Ophth. 32:885-892, Dec., 1948.

The author presents an interesting report of a case of pigmented leiomyoma of the iris, which was completely removed by iridectomy. Section showed spindle cells, palisading of nuclei, and a regular pattern of cell bundles. Myoglial fibers were demonstrated, pigment was present throughout the tumor, and the diagnosis of melanotic neuroectodermal leiomyoma was justified. A review of the other three published cases is given. These tumors are believed to arise from the neural epithelium just as does the dilator muscle. All four published cases have occurred in the lower half of the eye.

Orwyn H. Ellis.

Gómez da Silva, Avelino. **A case of cilium in the anterior chamber.** Arq. brasil. de oftal. 11:153-159, 1948.

In a man of 35 years, examined because of hypertensive retinitis, a cilium lay across the anterior chamber, adhering by its bulbous root to the posterior surface of the iris. There were slight corresponding spots of clouding of the lens capsule and cornea. Removal was not undertaken. (References.)

W. H. Crisp.

Greeves, R. A. **A contribution to the microscopic anatomy of the sympathizing eye.** Brit. J. Ophth. 32:545-550, Sept., 1948.

The history and histologic description of sections of 13 cases of the sympathizing eye in sympathetic ophthalmia are presented briefly. The diagnosis was quite obvious from the history. All patients had had surgery on the other eye. The time of onset after the surgery varied from 5 weeks to 9 years. In seven cases the inflammatory cells were purely lymphocytes and plasma cells, in six cases epithelioid cells wer present and in three of these, giant cells were seen. The

only constant factor common to all was the presence of an iridocyclitis which varied considerably in character and intensity. In five eyes the choroid was normal and in 6 there were areas of infiltration with lymphocytes and plasma cells only. The author concludes that no special characteristic of the sympathetic inflammatory process is invariably found in the sympathizing eye.

— Morris Kaplan.

Halberg, J. P., and Doret, J. P. Tuberculosis of the choroid in a case of miliary tuberculosis treated by streptomycine. Ann. d'ocul. 181:485-492, Aug., 1948.

A 16-year-old boy with acute familial pulmonary tuberculosis developed cervical adenopathies with the other classical signs of miliary tuberculosis. During five months he received approximately 250 grams of streptomycine beginning with a dosage of three grams daily which was gradually decreased with the clinical arrest of the disease. During the attack a central choroidal focal lesion was observed in the right eye, and several nodules in the periphery of the fundus of the other. These regressed without anterior uveal involvement and without appreciable loss of sight. The treatment is believed to have favorably influenced healing. — Chas. A. Bahn.

Iñigo, L. Ophthalmia produced by caterpillar hair. Arch. Soc. oftal. hispano-am. 8:988-1001, Oct., 1948.

Iñigo reports a case of ophthalmia nodosa, in a man, 21 years old, who was struck in the left eye with a caterpillar. A violent inflammatory reaction was set up, and five days later his eye presented a picture of an acute keratoconjunctivitis, with numerous corneal infiltrations. A number of vascularized nodules were also found in the bulbar conjunctiva. With the slitlamp, the lower half of the cornea was found studded with a multitude of fine needles, some of which were in irregular clumps or bundles. They were lying in the parenchyma either parallel to the epithelium or obliquely, reaching to Descemet's membrane and deeper. An attempt at removal soon demonstrated the futility of the task, because of the deep situation of some of these needles. Under symptomatic treatment the case ran its usual clinical course. It begins with a phase of violent inflammatory signs and symptoms which lasts from five to eight days; this is followed by a second period, in which the inflammatory symptoms subside, vision is recovered, and the cornea acquires a tolerance to the encapsulated foreign bodies; this period lasts about three months. There is, however, always a danger of recurrence of the inflammatory phenomena, with loss of the eye from glaucoma, cyclitis, or retinitis. A detailed description is given of the caterpillar hair and it is demonstrated that the fine needles penetrating the cornea or skin are the contents of a pouch on the dorsal protuberances of the caterpillar, which forms a part of a complicated defense mechanism. The tiny needles are barbed in their posterior portion, which makes their removal difficult after they become imbedded in the tissue. They are propelled deeper into the tissue by ocular movements, by blinking, and by rubbing the eyes. The acute inflammatory phenomena are caused by poison carried by these invading needles. Because of late complications the prognosis should be guarded. Treatment should consist of removal of the invaders, whenever possible; when they are too numerous, mydriatics and lubricating ointments should be used to hasten encapsulation of the foreign bodies at their point of entry. (5 illustrations.) Ray K. Daily.

Klainguti, R. Circumscribed iris atrophy in Behcet's disease. Ophthalmologica 116:211, Oct.-Nov., 1948.

In a typical case of Behcet's disease (recurrent iritis with hypopyon, associated with recurrent oral aphthae and genital ulcerations) small areas of circumscribed stroma atrophy of the iris developed and increased in size and number as the disease continued to recur.

Peter C. Kronfeld.

McPherson, S. D., Jr. **Sympathetic ophthalmia: a review of 61 cases.** South. M. J. 42:120-124, Feb., 1949.

This is a review of 61 cases of sympathetic ophthalmia observed in the Wilmer Institute in the 10 years that preceded 1948. The shortest interval between injury and onset of the disease was seven days and the longest 23 years; in all but five the disease began after three weeks to one year. Many types of therapy were used but the value of any particular type of treatment is very difficult to assess. In 10 percent the final vision was 20/20 in the sympathizing eye, in 33 percent 20/100 or better, in 46 percent 10/200 or less, and in 5 cases total blindness resulted. It seems wise to reserve enucleation for patients in whom sympathetic ophthalmia has been known to exist in the second eye for one week or less. (5 tables, references.) Bennett W. Muir.

Oxilia, Efisio. **Ocular pathology in Grassi's hereditary elastodystrophy (Cannata's systemic type of dyselastic mesodermosis).** Ann. di ottal e clin. ocul. 73: 385-427, July, 1947.

Three cases of angioid streaks, two of which were associated with pseudoxanthoma elasticum, are presented and discussed at great length, with particular reference to pathogenesis. The evidence points to a generalized dysembryoplastic mesenchymopathy, that is, a congenital anomaly of development affecting particularly the elastic tissue but also all the connective tissue of the body in general. A choroidal angiopathy may explain the association of angioid streaks with macular degeneration of the Junius-Kuhnt variety and with peripheral pigmentary disturbances in the retina. Only 13 cases of angioid streaks have been previously reported in Italy, whereas their frequent occurrence has been noted in Anglo-Saxon countries. (2 figures, bibliography 1936-1946.) Harry K. Messenger.

Redi, F. **Senile changes in the choroid, studied histologically.** Boll. d'ocul. 27: 531-547, Aug., 1948.

The eyes from 41 cadavers were studied histologically for senescence of the choroidal tissue. The results are meticulously evaluated and shown in five photomicrographs and in two tables. Thickness and blood vessel content of the choroid decrease with increasing age; the connective tissue of the choroid becomes sclerotic with advancing age and diminishes in extent. Elastic fibers become more numerous throughout life. The decrease in thickness of the choroid is least marked in the vicinity of the ciliary body; the average thickness in the equatorial region and in the posterior polar region is greatest in the 25 to 50-year age group. It was 132 and 170 µ respectively, whereas in persons younger than 25 years these figures were 119 and 134 µ, and after the age of 50 years, 97 and 114 µ. (References.) K. W. Ascher.

Samuels, B. **Participation of the ocular appendages in sympathetic ophthalmia and its bearing on enucleation.** Brit. J. Ophth. 32:569-575, Sept., 1948.

Samuels is convinced that, although sympathetic ophthalmia is primarily a disease of the inner eye, the appendages of the eye may also be involved simultaneously, and after enucleation of the exciting eye these infected appendages are often left in the orbit to spread the disease. He agrees with Parsons that the immediate etiology of sympa-

thetic ophthalmia is a filtrable virus and that this virus enters the eye at the time of the penetrating injury. The virus leaves the inner eye by the same routes as those chosen by the cells of a malignant melanoma of the choroid. It passes through the sclera by way of the numerous emissary veins into Tenon's space. The infection spreads to become a leptomeningitis of the intervaginal space and actually may appear as a collar around the optic nerve. It is certain, however, that the infection is not transferred to the other eye through the optic nerve and chiasm because the opposite nerve never shows signs of descending inflammation. In removing the exciting eye as a preventive measure before any signs of infection have appeared, the ordinary technique may be employed with safety. If, however, the signs of sympathetic ophthalmia are present, enucleation should include resection of the optic nerve and of the inferior oblique muscle as far back as possible and the wound should be left open to drain. If some degree of vision remains in the exciting eye enucleation should be postponed. The benefits of the operation are problematic and sacrificing even the faintest vision is not justified. (5 figures.)   Morris Kaplan.

Snell, A. C. Postoperative iridocyclitis. New York State J. Med. 48:2710-2714, Dec., 15, 1948.

Inflammation is produced by the irritants which are liberated from the injured cells. Bacterial toxins and allergic conditions influence the reaction of the tissues. Traumatic iridocyclitis is discussed. Postoperative iridocyclitis is reviewed from the standpoint of the tissue damage caused by the cutting, tearing and crushing which occurs during surgery. Exposed lens cortex is a source of toxic degenerating tissue, and makes possible irritating bacterial products and allergic reactions. Intraocular hemorrhage can cause iritis after surgery by the liberation of toxic degenerative products and also by the ability of the blood to organize a fibrous tissue. The methods in which a loss of vitreous can cause iridocyclitis are reviewed. (8 figures.)

H. C. Weinberg.

Verhoeff, F. H. Histological findings in a case of angioid streaks. Brit. J. Ophth. 32:531-544, Sept., 1948.

The histologic sections of the eye of a 50-year-old patient who died of cardiovascular failure and who had previously been observed to have angioid streaks were studied. Only two deviations from the normal were found. Bruch's membrane was definitely basophilic and there were breaks in it with gaping edges. The change in the staining of the membrane is ascribed to calcification but this calcification must differ from that which is common in senile eyes because in the latter the elasticity of the choroid is absent and there is no gaping of the edges in rupture of the membrane. The ophthalmoscopic appearance of the streak is a result of the visibility of the chorio-capillaris through the break. Three disturbances associated with angioid streaks too often to be merely coincidental are cardiovascular disease, Paget's disease and pseudoxanthoma elasticum. No satisfactory explanation for this association has been suggested.   Morris Kaplan.

Verrey, F. Environmental effects upon intraocular inflammations. Ophthalmologica 116:204-210, Oct.-Nov., 1948.

A general discussion of some of the factors that influence the course of uveitis by altering the susceptibility of the affected person is presented.

Peter C. Kronfeld.

Weekers, L., and Weekers, R. Technique of iridencleisis. Brit. J. Ophth. 32: 904-910, Dec., 1948.

The authors describe a modified iridencleisis. They make a small Graefe incision under a conjunctival flap. The prolapsed iris is torn radially and both pillars are left under the flap. The wound is closed with interrupted sutures. The gonioscopic findings are clearly illustrated.

Orwyn H. Ellis.

Witmer, R. **Cavernous hemangioma of the choroid.** Ophthalmologica 116:285-288, Oct.-Nov., 1948.

A bluish-gray, choroidal tumor in a 33-year-old man caused gradual atrophy and later detachment of the overlying retina. Since the tumor slowly increased in size and opaqueness (upon translumination) the eye was enucleated and found to harbor a typical cavernous hemangioma of the choroid. Peter C. Kronfeld.

9

GLAUCOMA AND OCULAR TENSION

Arruda, J. D. **Iridencleisis.** Arq. brasil. de oftal. 11:145-151, 1948.

For the Portuguese reader, a brief summary of the history, the classical steps, and some authors' modifications of the operation is given. (References.)

W. H. Crisp.

Barkan, O. **Goniotomy for the relief of congenital glaucoma.** Brit. J. Ophth. 32:701-728, Sept., 1948.

In the past this disease has resulted in a high percentage of blindness. Barkan urges earlier and more accurate diagnosis of congenital glaucoma and prompt treatment by goniotomy. He has operated on 76 eyes with satisfactory result in 66. The symptoms of increased intraocular pressure in congenital glaucoma may be present at birth, or their onset may be sudden during the first few months of infancy and consist of cloudy cornea, photophobia and signs of irrita-

tion and congestion. Rarely there is a gradual onset without signs of congestion. Pressure should be measured with a tonometer under ether anesthesia which must be sufficient to assure complete relaxation.

The initial cloudiness of the cornea is associated with roughening of the corneal epithelium and is the chief cause of the irritative symptoms and photophobia. If allowed to persist, it is superseded by permanent scarring with associated irregular astigmatism and amblyopia. Glaucomatous atrophy of the optic nerve is the exception and occurs late. If increased tension is made normal by goniotomy soon after its inception transparency of the cornea is almost completely restored and maintained and vision develops normally. The technique, mode of action, advantages, disadvantages, indications and contraindications of goniotomy are described in detail. (12 figures.)

Morris Kaplan.

Blodi, F. **Nevus flammeus of the face and glaucoma.** Ophthalmologica 117:82-89, Feb., 1949.

The clinical findings in two cases of nevus flammeus of the face with unilateral glaucoma but without enlargement of the globe are reported. The second patient had epilepsy and his ailment may, therefore, be a case of Sturge-Weber syndrome. Peter C. Kronfeld.

Brückner, R. **The effect of drugs upon the ocular hypertension produced by Trendelenburg's position.** Ophthalmologica 116:200-203, Oct.-Nov., 1948.

A short stay in Trendelenburg's position raises the ocular tension in man and rabbits. The effect upon this ocular tension of various drugs was studied under conditions of topical as well as systemic administration. The author concludes that enhancement of the aqueous drain-

age by way of Schlemm's canal is only *one* of the factors through which drugs can lower the ocular tension.

Peter C. Kronfeld.

Busacca, A. **Gonioscopic examination of a case of hydropthalmia.** Ann. d'ocul. 181:627-628, Oct., 1948.

In a 13-year-old girl with corneas measuring 14 mm., the peripheral areas of the iris were atrophied and the insertion of the iris was displaced by the trabeculum. These changes resulted in a circular goniosynechia, and Schlemm's canal contained blood. The author believes that a vascular communication must have existed between this canal and the conjunctival veins, or the former would have been bloodless from pressure of the contact glass. Chas. A. Bahn.

Dellaporta, A. **Late infection after filtering operations.** Ophthalmologica 116:322-334, Dec., 1948.

Eleven cases of late infection after filtering operations are reported. Nine occurred after trephinings, two after sclerectomies after Lagrange. The value of sulfonamides is uncertain since milk injections alone control the infection. Antibiotics were apparently not available. Two eyes became phthisic.

Peter C. Kronfeld.

Desvignes, P., and Naudin. **Nonperforating cyclodiathermy in the treatment of certain glaucomas.** Arch. d'opht. 8:589-592, 1948.

The authors have employed nonperforating cyclodiathermy according to the technique of Weekers in the treatment of glaucoma when intraocular surgery was contraindicated. They have used it successfully in cases of secondary glaucoma, in infantile glaucoma, and in chronic simple glaucoma after failure of fistulizing operations. They mention satisfying results in two cases of traumatic subluxation of the lens with secondary glaucoma. In hemorrhagic glaucoma the results obtained were variable and in absolute glaucoma poor.

The technique consisted of retrobulbar anesthesia followed by applications of the flat electrodes of Coppez to the sclera 5 to 7 mm. from the limbus on the meridians of 12, 3, 6, and 9, eight applications in all. The apparatus is regulated so that a temperature of 90°C. is maintained for 10 seconds. No complications have been observed. The drop in tension is not immediate but gradually develops after a slight and transient rise in pressure. The full effect is not attained until the tenth to fifteenth day. If there is a recurrence of elevated tension, the operation can be repeated. This procedure does not replace the ordinary fistulizing operations but is a valuable supplement to them.

P. Thygeson.

François, J. **Cysts of the ciliary processes observed gonioscopically.** Ophthalmologica 116:313-317, Dec., 1948.

For the relief of acute congestive glaucoma an iridencleisis was performed on the only seeing eye of a male patient, 32 years of age. The postoperative course was uncomplicated and a filtering scar developed. The ocular tension has remained below 25 mm. Hg Schiøtz for four years. Gonioscopic examination of the area of the operation reveals the inner aperture of the operative wound to be tightly healed. In the pseudocoloboma created by the meridional iridotomy a number of ciliary processes are plainly visible. Two small cysts are situated between the processes. The contents, as well as the major portion of the wall of the cysts, are colorless.

In the author's experience the inner aperture of the iridencleisis wound is always completely closed, without the

slightest dehiscence between the wound lips. The incarcerated iris functions as a drain. The existence of a filtering scar is not necessary for a tension-lowering effect of the iridencleisis. The latter is chiefly due to a modification of the fluid exchange and of the metabolism in the iris and in the ciliary body.

<div align="right">Peter C. Kronfeld.</div>

Goldmann, H. **Outflow pressure and glass-rod phenomenon.** Ophthalmologica 116:195-198, Oct.-Nov., 1948.

Pressure exerted on the eyeball by means of an instrument like the Souter tonometer placed against the center of the cornea, increases the intraocular pressure and modifies the circulatory conditions in the aqueous veins. The smallest amount of pressure thus exerted which causes a noticeable widening of an aqueous vein is called outflow pressure. This pressure is related to the resistance which the aqueous encounters during its passage from the anterior chamber to the anterior ciliary veins, and to the amount of aqueous passing through these channels. The fact that in wide-angle glaucoma Ascher's glass-rod phenomenon is nearly always negative indicates that in this disease the pressure in the canal of Schlemm is relatively low. The outflow pressure, however, is definitely increased. Goldmann concludes that the resistance between anterior chamber and canal of Schlemm is abnormally great in chronic simple (wide-angle) glaucoma.

<div align="right">Peter C. Kronfeld.</div>

Grant, W. M. **Miotic and antiglaucomatous activity of tetraethyl pyrophosphate in human eyes.** Arch. Ophth. 39:579-586, May, 1948.

Tetraethyl pyrophosphate is comparable to physostigmine and di-isopropyl fluorophosphate in miotic activity and may be used when there is local sensitivity to other miotics. In several instances,

0.05 to 0.1-percent solution of the drug in peanut oil used twice a day was more effective than 4 percent pilocarpine nitrate used more often. An excessive dose may cause aching about the eye, and in certain eyes an increase in tension occurred. The drug acts as an inhibitor of cholinesterases. Ralph W. Danielson.

Kapuscinski, W. J. **Contribution to the clinical study of glaucoma.** Ann. d'ocul. 181:542-555, Sept., 1948.

In approximately 40 patients the usual provocative tests for glaucoma were of little practical value. Diminished light adaptation is of greater value diagnostically. Several case histories of juvenile glaucoma are presented to illustrate that miotics such as pilocarpine may increase ocular tension and that atropine may lower tension. The characteristic disk excavation as well as central and peripheral visual changes of glaucoma are not infrequently associated with normal tension as is illustrated by several case reports. No single theory yet presented explains all the objective symptoms of the juvenile type, nor the acute and chronic primary types of glaucomas in adults.

<div align="right">Chas. A. Bahn.</div>

Di Luca, G. **Biomicroscopic examination of the cicatrices of antiglaucomatous operations.** Rassegna ital. d'ottal. 17:304-317, Sept.-Oct., 1948.

Di Luca bases an explanation of the mechanism of action in successful surgery in glaucoma on the postoperative biomicroscopic examination of 23 eyes and a study of the literature. Anastomosed collateral circulation develops across the area of operation for the normalization of tension. These subconjunctival vessels unite with the uveal vessels to supplement the outflow of fluid from the globe. (7 figures.)

<div align="right">Eugene M. Blake.</div>

Majoros, J. **Postmortem ocular pressure.** Arch. Ophth. 39:665-668, May, 1948.

The ocular pressure falls at the moment of death, but some pressure remains. In numerous ophthalmic and general diseases the pressure is sometimes as low as it is in death. The glaucomatous eye retains its pressure after death and after enucleation. .Ralph W. Danielson.

Monfette, Claude. **Treatment of chronic glaucoma with nicotinic acid.** L'Union med. du Canada 77:1433-1435, Dec., 1948.

The author states that glaucoma is a diencephalic affection, a dysfunction of the thalamus and hypothalamus with vasomotor predominance involving the capillary circulation in which there is localized edema and an increase of blood and interstitial fluids in the eyeball.

Nicotinic acid is used in a concentration that will not impair the choroidal circulation. A test dose of 2 mgm. is given intravenously. The vision and tension are taken every 15 minutes for one hour. If the reaction is favorable, the recommended dose is I mgm. in distilled water twice a day by mouth. It is not indicated in acute glaucoma, secondary glaucoma with anterior segment lesions, hemorrhagic glaucoma, old chronic glaucoma, and when the tension is above 50.
Irwin E. Gaynon.

Much, V. **Contributions to the surgical treatment of glaucoma.** Ophthalmologica 117:36-42, Jan., 1949.

The author reports in considerable detail a case of bilateral chronic noncongestive glaucoma for the relief of which a sclerectomy after Lagrange was performed on the right eye and a cyclodialysis on the left eye. Although neither operation accomplished normalization of the tension the operations may be considered as successful. The tensions of the cyclodialyzed eye were, in general, higher than those of the other; and a better visual field was preserved. The lowering of tension is not the only beneficial result of surgery. Peter C. Kronfeld.

Posner, A., and Schlossman, A. **Treatment of glaucoma associated with iridocyclitis.** J.A.M.A. 139:82-86, Jan. 8, 1949.

The use of mild miotics in combination with phenylephrine hydrochloride ("neosynephrine hydrochloride") is advocated for the syndrome of glaucomatocyclitic crises and for other conditions in which posterior synechiae are not formed. It seems more effective than for secondary glaucoma. Theodore M. Shapira.

Posner, A., and Schlossman, A. **Development of changes in visual fields with glaucoma.** Arch. Ophth. 39:623-639, May, 1948.

Approximately 2,000 visual fields in 350 cases of primary glaucoma were studied and classified. The development of the characteristic field changes was analyzed by breaking down these defects into their component units, namely, the arcuate scotoma, the nasal field defect and the juxtacecal step. A relationship exists between the circulatory and the neural elements of the glaucomatous field and most defects result from a mixture of these two components. The authors feel that damage to nerve fibers at the margins of the cup and by traction from the receding lamina cribrosa is not of greatest importance. Ralph W. Danielson.

Radnót, M. and Németh, B. **The eye first affected in glaucoma.** Ophthalmologica 117:60-62, Jan., 1949.

The records of 902 patients with glaucoma show that either eye may be affected first, whereas Holst found the left eye involved more often.
Peter C. Kronfeld.

Schmelzer, Hans. **Investigations of glaucoma in the present war.** Klin. Monatsbl. f. Augenh. 110:289-296, May-June, 1944.

Before the war the author had found a hypercholesteremia, a positive xanthoprotein reaction, frequently an increased bilirubin index in the blood-serum and a disturbance of the liver function in the majority of his patients with glaucoma. During the war the blood cholesterol was decreased because of restriction in fat, alcohol and coffee. Thus the war imposed a "liver-saving diet" on patients with glaucoma. Twenty-one patients with glaucoma who had had an average blood cholesterol of 273 mg. percent before the war were re-examined. The average blood cholesterol was 202 mg. percent and there was no progress of the glaucoma, except in three patients. In two of the latter, well nourished farmers, the tension was high, visual fields and central vision had become worse and the blood findings were the same as before the war.

George Brown.

Silva, M. A. da. **Iridencleisis.** Arq. brasil de oftal., 11:122-132, 1948.

The technique of the Holth operation is described for the reader of Portuguese with a tabular statement of the results obtained in series of cases of trephining, cyclodialysis, and iridencleisis respectively. Iridencleisis is as yet very little used in Brazil. (6 figures.)

W. H. Crisp.

Stocker, F. W. **New ways of influencing intraocular pressure.** New York State J. Med. 49:58-63, Jan. 1, 1949.

The principles upon which glaucoma is treated by miosis or surgery are reviewed. Of 32 negroes who had been treated by cyclodiathermy puncture twenty had normal pressures almost three years later, seven were improved and five were not improved. The place of Etamon and Pris-

col and their paralyzing effects on the autonomic nervous system in causing lowered ocular tension is discussed. The use of the rice diet met with some success in reducing ocular tension under certain circumstances. Rutin was used to prevent the increase in permeability of the blood-aqueous barrier which occurs after the use of miotics. The increased outflow of aqueous produced by miosis is often nullified by this increased permeability of the blood-aqueous barrier. Twenty-six patients were given 20 mg. of rutin three times a day; there was improvement in 17, no improvement in 5 and questionable improvement in 4. The author recommends dosage up to 50 mg. of rutin three times a day. (4 figures, 3 tables.)

H. C. Weinberg.

Vidal, F., Brodsky M., and Travi, O. C. **Dynamic ocular tone and metabolic disturbances.** Arch. de oft. de Buenos Aires 23:92-93, April-June, 1948.

The elevation of tension is but a stage in the evolution of glaucoma, and is primarily dependent on changes in the metabolism of the various ocular tissues. The abnormal alterations are made manifest by asthenopia, headaches, diminution in the sensitivity to light, and visual clouding and result from increased cholestrinase in the retina, emotional upsets, infections, and abrupt alterations of temperature.

A. G. Wilde.

Villaseca, Alfredo. **Nonperforating cyclodiathermy in the treatment of glaucoma.** Arch. chilenos de oft. 4:425-456, 1947.

The author begins this 32-page paper by urging emphatically that recent studies have deposed the idea that the fundamental change in glaucoma occurs at the angle of the anterior chamber. He uses an electric needle whose head is perfectly flat and 1.75 mm. in diameter. After dis-

section of conjunctival and subconjunctival tissue, the exposed sclera must be rendered perfectly dry and free from blood. Each application is made for five seconds only, using firm pressure (Albaugh and Dunphey recommend 8 to 10 seconds). The intensity of current considered adequate is such as to cause first retraction and then a "parchment-like" effect in the sclera for 0.5 to 1 mm. around the electrode. The applications are made over a quadrant or more and as far back as 5 to 6 mm. from the limbus when the previous tension was below 35 to 40 mm., and up to one half of the circumference if the tension was above 40 to 50 mm. There should be a frank rise of ocular tension at the end of the operation. If there is no appreciable rise of tension at that time, some of the applications should be intensified or additional applications made. The eyeball is painful for 24 hours, more or less.

In 17 of the author's 30 cases the tension was reduced to normal by diathermy. Further deterioration of vision or visual field was not produced. However, there was a definite corneal anesthesia in the sector operated upon. Usually this did not have major consequences, but in two patients serious trophic changes occurred. Once or twice the tendency of the eye to atrophy was accelerated. The author regards this as the operation of choice in hemorrhagic glaucoma, in painful ab-absolute glaucoma, and in rubeosis of the iris; and it was also serviceable in the chronically glaucomatous aphakic eye, in advanced simple chronic glaucoma with greatly restricted visual field, in posterior luxation of the lens, in glaucoma of aniridia, and in buphthalmos. (Tabular summary; references.)   W. H. Crisp.

Weekers, L. and Weekers, R. Nonperforating thermometric cyclodiathermy in treatment of hypertensive uveitis. Arch. Ophth. 40:509-517, Nov., 1948.

The diathermy apparatus, thermometer circuit and technique of operation are described; 12 to 16 coagulations 8 mm. from the limbus are made through the conjunctiva. The operation is similar to that of Albaugh and Dunphy, but differs in that the Weekers do not regard dissection of the conjunctiva as necessary, they do not limit themselves to one-half the circumference of the ciliary body because previous experimental researches have demonstrated that when the operation is performed in a small territory it becomes necessary to use a more intense diathermy current to obtain a sufficient effect on the ocular pressure, and use a thermometer electrode, which enables them to regulate their intervention and to repeat it under identical conditions. The authors used to practice iridencleisis ab externo in the treatment of ocular hypertension with uveitis, but now prefer nonperforating cyclodiathermy. The main indications for thermometric nonperforating cyclodiathermy are uveitis complicated by intraocular hypertension, hypertension persisting after a filtering operation, painful absolute glaucoma, and intraocular hypertension after corneal transplantation.   Ralph W. Danielson.

Weekers, L., Weekers, R., and Roussel, F. The mode of action of the nonperforating cyclodiathermy. Ophthalmologica 117:65-73, Feb., 1949.

A flat round electrode, 0.75 mm. in diameter, at 90°C. is applied to the sclera 7 mm. from the limbus for 15 seconds in 20 areas. On patients with chronic primary or iridocyclitic glaucoma operated by this method the author studied the pupillary responses to the topical application of drugs. Since the cyclodiathermy injures the ciliary nerves, parasympathetic and sympathetic denervation is expected. The irides of these patients proved highly sensitive to mecholyl and epinephrine and insensitive to cocaine.

The response to eserine was equivocal. The authors conclude that their operation causes extensive denervation of the anterior uvea. The resulting permanent loss of the vasoconstrictor control causes alterations in the fluid exchange of the eye.   Peter C. Kronfeld.

10

CRYSTALLINE LENS

Andradee, Lopes de. **The intracapsular cataract extraction.** Ophth. Soc. U. Kingdom 66:241-245, 1946.

The author has tried to simplify the operative procedure by opening the eyelids with stitches and fixing the eyeball by means of sutures passed through the superior, inferior and internal rectus muscles.   Beulah Cushman.

Comberg, W. **Surgery of unilateral cataract.** Klin. Monatsbl. f. Augenh. 110: 340-343, May-June, 1944.

The peripheral vision of an aphakic eye without correcting lens is about one-third normal 25 degrees eccentrically, and about two-thirds at 55 degrees. The extraction of a unilateral cataract seems indicated because of the considerable gain in visual field even though optical correction is not tolerated. The total disability is not more than 10 to 15 percent.
                      George Brown.

Crámer, F. E. K., and Foglia, V. G. **Experimental diabetic cataracts in rats.** Arch. de oft. de Buenos Aires 23:101-117, April-June, 1948.

Extirpation of 95 percent of the pancreas will regularly produce cataract in the rat in a minimum of seventy days. The major changes are in the cortex.
                      A. G. Wilde.

Csillag, F. **Loop extraction of subluxated cataracts.** Ophthalmologica 116:172-176, Sept., 1948.

Attempts to grasp the lens capsule with a smooth capsule forceps may fail because of defectiveness of the zonule, hypertension within the lens and its capsule, and fluidity of the lens cortex. When the zonule is defective the author recommends extraction with a modified loop which is introduced into the anterior chamber in front of the lens and applied like a lasso to the portion of the equator opposite the incision. When the defect is in the lower part but the upper is intact the incision is made above, as usual, and after a total iridectomy the loop is carefully slipped into the anterior chamber and around the lower part of the equator of the lens. Once this has been accomplished the extraction of the lens is easy.
When there is hypertension in the lens, or the cortex is fluid the author recommends needle puncture of the lens near the equator above.
                      Peter C. Kronfeld.

Fanta, H. **Rupture of the wound following cataract operation.** Ophthalmological 116:149-161, Sept., 1948.

This report from Lindner's clinic in Vienna stresses the value of corneoscleral sutures which "proved a sure protection against ruptures of the cataract incision, even during the bombing of the city." In the routine technique of intracapsular cataract extraction at Lindner's clinic a small limbus-based flap is prepared and one de Mendoza (McLean) suture is placed in the corneosclera at 12 o'clock. After an incision with the Graefe knife a sliding forceps extraction is performed by means of an Arruga forceps applied just anteriorly to the upper equator. The suture is tied and two peripheral iridectomies are made, one on each side of the suture. Hilding's experimental work (American Journal of Ophthalmology 28:871, 1945) is quoted in detail and corroborated by clinical observations.   Peter C. Kronfeld.

Franceschetti, A. **Cataract operation on an eye with sympathetic ophthalmia.** Ann. d'ocul. 181:530-534, Sept., 1948.

A successful cataract extraction was performed on a woman, aged 25 years, who, 12 years previously, had sympathetic ophthalmia. The injured eye was removed nine weeks after an injury from a dart. The sympathizing eye which had long been inactive had good light projection. A keratome incision was followed by iridectomy, detachment of synechia, and lens extraction with a spoon. The ultimate corrected vision was 0.3. A brief survey of the literature follows.

Chas. A. Bahn.

Franceschetti, A. **Successful cataract extraction from an eye with sympathetic ophthalmia.** Ophthalmologica 116:213, Oct.-Nov., 1948.

The author reports the case of a young woman who at the age of three years sustained a perforating injury to her right eye. Nine weeks later the left eye developed sympathetic ophthalmia which took a prolonged and severe course, in spite of the enucleation of the injured eye (time of enucleation not stated). When the patient was 13 years old, two iridectomies were attempted but accomplished only partial removal of iris stroma. The posterior layers of the iris could not be lifted up with forceps. Several years later the uveitis appeared inactive, the cornea had undergone band-shaped degeneration, there was seclusion of the pupil and a complicated cataract. The patient was operated on again. The author succeeded in making an iridectomy. Through the coloboma he introduced a spatula and broke most of the posterior synechiae. The lens was delivered with a loop. Three years later the patient's corrected vision was 0.3 and the eye was quiet.

Peter C. Kronfeld.

Giri, D. V. **Technique of intracapsular extraction of cataract with retention of** conjunctival bridge. Tr. Ophth. Soc. U. Kingdom 66:247-260, 1946.

The author advised the use of nembutal and of liberal local anesthetics, and atropine and adrenalin for dilatation of the pupil, but no retrobulbar injection. A conjunctival bridge is made at the time of the corneal section, with or without an iridectomy. The lens can usually be removed in its capsule. (5 figures.)

Beulah Cushman.

Holland, H., and Holland, R. W. B. **Notes on 221 intracapsular cataract extractions performed in three weeks at Khairpur in 1947.** Brit J. Ophth. 33:101-106, Feb., 1949.

The author performed these intracapsular extractions by the Smith method which is recommended only for experienced surgeons. Only two cases of retinal detachment have been observed in over 30,000 intracapsular extractions at this center. If the upper pole of the lens does not present immediately after the beginning of the delivery, the lens is extracted extracapsularly. Orwyn H. Ellis.

Hruby, K. **Simplified corneoscleral suture in cataract extraction.** Wien. klin. Wchnschr. 60:748-749, Nov. 19, 1948.

Hruby describes his modification of the Mendoza suture as practiced by Lindner and claims for it the advantages of the firm wound closure that Lindner's technique gives and much less technical difficulty. After preparation of the conjunctival flap he makes two short superficial incisions, instead of one, in the outer sclera to receive the suture, one at the limbus, the other 1 to 2 mm. behind it. There is ample room for the cataract knife between them and it rarely cuts the suture, an accident which is relatively frequent with Lindner's operation. In 252 cataract operations this accident occurred only twice, whereas with Lindner's technique in 95 operations the su-

ture was cut 11 times. A detailed description of the operative procedure is given. (1 figure.)   B. T. Haessler.

Kirby, D. B. The rupture of the zonule in intra-capsular cataract extraction—a new method. Brit. J. Ophth. 33:3-21, Jan., 1949.

The rupture of the zonula fibers is essential in the intracapsular extraction of the lens and the finding of many resistant zonules is accounted for by the number of immature cataracts extracted. The point of rupture of the fiber is just at its junction with the capsule which accounts for the absence of retinal separation. A common error of judgement is to attempt to rupture all zonules by the same method instead of adapting a suitable method to each eye. For rupturing the fibers indirectly, Kirby prefers a combination of the three methods, pressure from without, traction on the capsule, and rotation of the lens in the capsule. After making the section, he uses enough pressure on a point within the corneal limbus at the 6, 8 and 4-o'clock positions to indent the cornea 2 to 3 mm. and to make the wound gape. Pressure outside the limbus is unnecessary, ineffectual and dangerous. Almost simultaneously with the point pressure and while the wound is gaping, the capsule forceps is applied to the anterior capsule just below the equator. He much prefers the forceps to the loop, the pointed hook, the electro-coagulation electrode and the various types of erisiphakes. Kirby describes his new forceps which is a combination of the Kalt, Arruga and Verhoeff forceps and has a cylindrical handle. His traction is actually a rotation from side to side and he often uses two forceps rather than one. Direct rupture of the zonule is indicated when the zonule is unduly resilient, when patient and surgeon are both relaxed, and when the zonule can be made tense by elevating the lens at least 3 mm. He has

used direct rupture for 10 years with excellent results. (7 figures.)

            Morris Kaplan.

Knapp, Arnold. (Bowman Lecture.) The present state of the intracapsular cataract operation. Tr. Ophth. Soc. U. Kingdom 66:133-178, 1946.

The history of intracapsular cataract surgery is reviewed from 1903 when Henry Smith developed the intracapsular technique in India to the present time.

Three features of the anatomy of the zonule are important in the understanding of the technique of the intracapsular extraction; they are the origin of the fibers, the independence of the zonular membrane from the hyaloid part of the vitreous, and the insertion of the zonular fibers in the lense capsule. The knowledge of the slight variation in the thickness of different parts of the lens capsule and of the consistency of the lens makes it possible to decide where the capsule should be grasped. The lens can usually be more easily dislodged tangentially, but the thickness, tenseness and elasticity of the lens capsule are important. The older the patient (usually over 60 years of age) the easier the subluxation, and intracapsular extraction is not suitable in persons under 45 years of age.

Smith brings about subluxation of the lens by pressure straight back on the lower half of the cornea, which causes the head to present, and pressure downward on the lowest peripheral point causes the lens to somersault. A slight turning of the lens around in the transverse axis aids in breaking the zonular fibers. The suction cup devised by Halen and popularised by Barraquer also turns the lens on the transverse axis. Verhoeff subluxates by torsion and traction. Kalt introduced the use of capsular forceps and now the use of different types of forceps with some counter pressure is almost universal. The capsule forceps

must be small and firm, the speculum light in weight and easily removable with one hand. Akinesia and retrobulbar injection which temporarily weakens the extraocular muscles, especially the inferior rectus, simplify the operation. The use of corneoscleral sutures ensures a quick restoration of the anterior chamber. There should be no traction of the flap and no constriction of the tissues. The injection of air into the anterior chamber counteracts any tendency to anterior adhesion of the hyaloid membrane or of the iris.

The complications of intracapsular operation depend on the proper selection of the cataract. The intumescent cataract with swollen cortex is tense and most difficult to hold with blunt forceps; in its removal the suction procedure is helpful. Many nuclear cataracts, posterior cortical cataracts and sclerosed lenses are the most favorable for the intracapsular procedure. The loss of vitreous is the most important complication and may occur directly after the incision, during subluxation or after delivery of the lens. The loss of vitreous or injury to it is often followed by a pupil which is drawn up because of cicatrical contraction of the vitreous and adhesions of the iris. Rupture of the capsule during extraction of the cataract may be serious if the hyaloid membrane is also ruptured. Iridocyclitis occurs after intracapsular extractions but is usually very mild. In the more severe types it may be followed by deep vascularization of the cornea and glaucoma. Glaucoma is usually secondary to anterior adhesions of the capsule to the incision or it may follow an anterior adhesion of the hyaloid membrane to the posterior surface of the cornea or to the incision. Trauma to the corneal endothelium may cause the hyaloid membrane or iris to become adherent before the anterior chamber is established. The injection of air or salt solution into the anterior chamber at the close of the operation will help

prevent an anterior adhesion of the vitreous body. Detachment of the retina usually seems to be associated with low grade cyclitis. Complications of the intracapsular operation are difficult to treat satisfactorily. The future of the operation lies in the reduction of the difficulties by improvement in the methods of operating.

Beulah Cushman.

Knüsel, O. **Two cases of electric cataract.** Ophthalmologica 116:212, Oct.-Nov., 1948.

In the two cases reported the electric shock consisted of very brief exposures to electric current (8,000 to 11,000 volts). The lens opacities which had remained almost stationary for several years, apparently were the only permanent residue of the electric shock. The latent period of electric cataract is stressed.

Peter C. Kronfeld.

Loutfallah, M. **Bilateral detachment of the retina in aphakia.** Eye, Ear, Nose and Throat Monthly 28:73-75, Feb., 1949.

The author reports an interesting detailed case report of bilateral detachment of the retina successfully operated upon with scleral diathermy. The lenses had been removed six and nine years previously, extracapsularly and without discission. The literature is reviewed.

Orwyn H. Ellis.

Samuels, Bernard. **Proliferation of the epithelium of the lens.** Tr. Ophth. Soc. U. Kingdom 66:467-491, 1946.

The author summarizes the proliferation of the epithelial cells of the lens in 185 cases of nontraumatic cataract. The greatest proliferation was found in corneal scars, spontaneous iritis and detachment of the retina and when a low grade chronic alteration in the metabolism had existed over the longest period. The least proliferation occurred with in-

traocular tumors and glaucoma. (28 figures.)   Beulah Cushman.

Sobhy Bey, M. **My method of cataract extraction.** Ophthalmologica 116:38-42, July, 1948.

The professor emeritus at the hospital Kasr-el-Aini in Cairo (Egypt) describes the technique of cataract extraction at which he arrived after 40 years of extensive practical experience. Until 1926 his method of choice was the extracapsular extraction of mature cataracts. A trip to Barcelona in 1926 revolutionized his technique and he became an ardent follower of Barraquer. Sobhy Bey describes his procedure as follows. A patient with bilateral advanced cataract is operated upon when the vision of the better eye becomes too bad to follow his profession. The eye with the advanced cataract (which is usually mature) is operated on by the extracapsular method. A V-shaped incision is made in the anterior lens capsule by means of the cystotome and the piece of capsule thus outlined is removed with a toothed forceps. After expression of the nucleus the anterior chamber is thoroughly irrigated. As soon as this eye has become quiescent, the second eye is operated upon by the intracapsular method. If the patient has only one eye and the indications are against total extraction (as in high myopia), the extracapsular extraction method is used, and that after repeated discission in order to be certain of the complete ripeness of the lens.

       Peter C. Kronfeld.

Venco, Luigi. **A "two-stage" capsulolenticular cataract extraction.** Ann. di ottal. e clin. ocul. 73:428-438, July, 1947.

Venco describes and discusses his modification of the intracapsular method of extraction with forceps. The cataract is removed in two stages at a single oper-ation. First a large peripheral capsulotomy is done above along the margin of the widely dilated pupil, and the lens substance is removed by pressure and irrigation; then the capsule is grasped with a special forceps and extracted. In the majority of cases the entire capsule can be removed, but the operative result is satisfactory if only enough of the capsule is removed to leave clear the pupillary area. This operation is especially recommended when the unruptured capsule is hard to grasp. If the capsule ruptures when it is grasped in the course of the usual method of intracapsular extraction, the operation may be satisfactorily concluded by this two-stage method. (2 figures.)

       Harry K. Messenger.

Wynne Parry, T. G. **Post-operative security in cataract operation.** Brit. J. Ophth. 33:128-129, Feb., 1949.

The author uses a catgut, purse-string suture for closure of a complete conjunctival flap in cataract operations.

       Orwyn H. Ellis.

11

RETINA AND VITREOUS

Alvares Pires, Ari. **Inferoversion of the retina.** Rev. brasil. de oftal. 7:75-86, Dec., 1948.

Two cases are reported. The first patient was a man of 32 years, who at the age of 16 years had developed cataract in the right eye as the result of an explosion, but had obtained a fair visual field after extracapsular extraction. Two weeks ago this eye had lost its vision without apparent cause. The detached retina lay almost entirely below the horizontal line, depending from a promontory which corresponded to the optic disc. No vessels could be seen. There was a line of tear in the upper inner quadrant. The sec-

ond patient had received a kick in the right eye during a football match, and the retinal condition was apparently somewhat similar to that of the first patient. W. H. Crisp.

Alvares Pires, Ari. **Cyst of the vitreous.** Arq. brasil de oftal. 11:133-134, 1948.

Routine ophthalmoscopic examination in a man of 23 years disclosed a black spot in the lower part of the pupillary area. With the slitlamp the spot was found to be pigmented, about 1 mm. in diameter, and attached to the lowest third of the posterior lens capsule. The vitreous adjacent to the lower pole of the cyst contained numerous scattered pigment points resembling those of the cyst. There were no remains of the hyaloid artery. The author accepts Uribe Troncoso's opinion that the pigment deposits in the vitreous originate in the uvea.

W. H. Crisp.

Arruga, H. **How can we improve the operative results of surgical detachment?** Arch. Soc. oftal hispano-am. 8:1085-1089, Nov., 1948.

The percentage of successful surgical results can be raised by attention to certain details. In vitreous hemorrhage, not part of recurrent retinal hemorrhages in the young, retinal detachment should be suspected, and the patient put to bed. Once a diagnosis is made a binocular bandage is of undoubted value in arresting the extension of the detachment. Direct and indirect ophthalmoscopy should be used to find the hole and study it in detail. Arruga implies that the value of indirect ophthalmoscopy is not appreciated in the United States, and that failure to make use of it accounts for some of our surgical failures. In early cases, with slight detachment at the level of the hole and good pupillary dilatation operation should be done promptly. An inflam-

matory reaction and pupillary rigidity are indicative of a mild uveitis, and operation should be postponed until these symptoms subside. In general, operation should be performed at the time when the detachment is minimal. Marked detachment at the level of the retinal hole is an indication for delay until the detachment flattens and the retina becomes reapplied. Eyes with large holes and disinsertions do not improve on rest in bed, and immediate surgery is indicated. When there is failure of the retina with a small hole to become reapplied after rest in bed the prognosis is poor, since it is evident that the choroid's capacity for absorbing the subretinal exudate is impaired. If after 18 or 20 days of bed rest the retina has not reapplied, further delay is useless, although surgical success is improbable. An extension of the detachment in spite of rest in bed is an indication for delaying operation lest the choroid may not absorb the subretinal exudate, or perhaps respond with an inflammatory reaction. Absolute postoperative rest in bed is essential, and its duration is determined by the structural changes in the coagulated area. The development of an adhesive retinochoroiditis is indicated by the appearance of pigment in the gray coagulated zone. When being transported patients should be seated so that the jars of the vehicle are not transmitted to their head.

Ray K. Daily.

Babel, J. **Senile macular pseudotumors.** Ann. d'ocul. 181:613-620, Oct., 1948.

In senile disciform and allied retinopathies the following stages occur. An edema begins at the posterior pole and involves the choriocapillaris and lamina vitrea. Irregularities in Bruch's membrane, hyaline band-like deposits in the choroidal capillaries, and local elevations in the pigment epithelium appear. The

hyalin may penetrate the subadjacent exudate with resulting vascular perforations. It may also provoke new exudates with resulting proliferation of fibroblasts and scar tissue. The consequent vascular sclerosis may also be associated with degenerative changes of the circinate type. The frequent hereditary tendency shows that constitution is an important factor. Several illustrative cases are presented.

Chas. A. Bahn.

Babel, J. The histologic development of the senile pseudotumor of the macula. Ophthalmologica 116:277-278, Oct.-Nov., 1948.

The primary changes are in the lamina vitrea and in the choriocapillary layer. The lamina undergoes irregular thickening and hyaline spurs extend into the choriocapillary layer. On the other side of the lamina an exudate forms which lifts the pigment epithelium off the lamina. The latter becomes permeable to cells and capillaries. The whole disease may be due to a selective sclerosis of the choroidal vessels. Peter C. Kronfeld.

Ballantyne, A. J. The state of the retina in diabetes mellitus. Tr. Ophth. Soc. U. Kingdom 66:503-543, 1946.

The progressive changes in diabetic retinopathy are described and the finding in 178 patients out of 561 diabetics are exhibited.

The duration of the diabetes is of the greatest consequence, whereas the treatment with insulin is not. The typical retinopathy may occur in patients in whom the blood sugar had been controlled without insulin. Of 170 patients with diabetic retinopathy 120 had diastolic pressure of less than 100 mm. Hg and only 50 above that level. Probably a chronic stasis on the venous side of the retinal circulation produces anoxia and nutritional changes in the walls of the capillaries and veins. About one-third of the diabetic patients develop pathologic changes in the retina.

Beulah Cushman.

Bedell, A. J. Ophthalmoscopy and operations for reduction of high blood pressure. Arch. Ophth. 40:483-492, Nov., 1948.

"At the beginning of any consideration of hyperpiesia it must be understood that the vast majority of patients with hypertension present no lesion of the fundus. This statement cannot be repeated too often." The ophthalmologist should be able to state with reasonable certainty whether a given fundus pattern indicates a favorable postoperative outcome, one of doubtful value, or a disappointing result. He must know the life history of the retinal variations and estimate the life expectancy of the individual patient. If the patient has no serious involvement of the heart, kidneys or cerebral vessels and no retinopathy, the ophthalmologist can sanction operation. If a retinopathy is present, with cotton wool patches, hemorrhages and exudates, approval may be given only when the results of physical and laboratory tests seem to warrant an operation, with the expectation that life will be lengthened. If the patient has definite arteriosclerosis, as indicated by white-walled vessels; if he has round, deep, red, granular retinal hemorrhages; if there is considerable retinal edema, as evidenced by a decrease in the visibility of the retina, or if there are intense, widespread edema of the retina and obscuration of the margins of the discs, with or without newly formed vessels on or about the disc; if there has been recent closure of a retinal artery or vein, operation is contraindicated. If there is marked papilledema with narrowing of the arteries or fulness of the veins, operations should be opposed.

Ralph W. Danielson.

Blum, J. D., and Babel, J. The histologic differences between true and pseudo-retinitis pigmentosa. Ophthalmologica 116:261, Oct.-Nov., 1948.

In the true degenerative forms of retinitis pigmentosa the primary site of the process is in the cells of the visual neuroepithelium. All other changes are secondary developments. Pseudo-retinitis pigmentosa comprises the chorioretinal diseases due to lues, scarlet fever, measles, vaccination or German measles of the mother. In the latter condition the primary retinal change is in the pigment epithelium. In the other postinflammatory retinal diseases the retinal vessels are primarily involved. Peter C. Kronfeld.

Blum, J. D., and Babel, J. Differential histologic diagnosis of retinal and pseudo-retinal pigmentary degeneration. Ann. d'ocul. 181:468-474, Aug., 1948.

In primary retinal pigmentary degenerations the neuro-epithelium is primarily involved; in the secondary group it may or may not be involved histologically. The successive stages are usually neuroepithelial degeneration, pigment proliferation with migration toward the inner retina, vascular changes with shrinkage, disorganization of the inner retinal layers, gliosis, and atrophy of the retina and disk. In secondary pigmentary involvements, the neuroepithelium is frequently only slightly involved. After fetal rubeola the clinical appearance of the retina may resemble primary pigmentary retinosis, but histologically, the condition is usually nonprogressive and the neuroepithelium is less damaged. A clinically similar picture is the salt and pepper fundus that is usually associated with congenital lues, in which the neuroepithelium is secondarily involved. (6 figures.) Chas. A. Bahn.

Boyden, R. C., and Kettering, H. A. Occlusion of the center retinal vein; report of a case treated with heparin. U.S. Nav. Med. Bull. 48:912-913, Nov.-Dec., 1948.

Heparin therapy was begun 24 days after the onset of thrombosis of a central retinal vein and was given for nine days. Clotting time was kept as close to twenty minutes as possible. Vision on admission to the hospital ten days after the onset was 20/300; 28 days later it was 20/200 in the periphery and 20/300 centrally. The authors suggest further studies using 100 mg. every four hours for the entire day and night. H. C. Weinberg.

Busacca, A. Retinal lesions caused by lightning. Ophthalmologica 116:141-143 Sept., 1948.

Busacca describes and depicts the ophthalmoscopic findings in a case of central retinopathy caused by lightning. The lesion consisted of edema of the macula with stellate opacities and a small detachment. The author wonders whether the lesion is to be ascribed to the electrical discharge or to the dazzling of the dark-adapted eye.

Peter C. Kronfeld.

NEWS ITEMS

DEATHS

Dr. Julian Baker Blue, Memphis, Tennessee, died January 25, 1949, aged 64 years.

Dr. Louis Bothman, Chicago, died January 19, 1949, aged 55 years.

Dr. Robert James Curdy, Kansas City, Missouri, died December 15, 1948, aged 80 years.

Dr. Jule T. Elz, Saint Louis, Missouri, died April 22, 1949, aged 53 years.

ANNOUNCEMENTS

ORTHOPTIC INSTRUCTION COURSE

For details concerning the second annual course of instruction for orthoptic technicians, the first part of which will be given at Nasson College, Maine, June 25 to August 27, 1949, write to the American Orthoptic Council, 1605 22nd Street, N.W., Washington 8, D.C.

MISCELLANEOUS

TO BE ACADEMY GUEST

Sir Stewart Duke-Elder has accepted an invitation to be the guest of honor of the American Academy of Ophthalmology and Otolaryngology and will attend the October meeting.

WANTED SERIES I AND II OF THE JOURNAL

The JOURNAL would like to purchase volumes 1 and 2 of Series I of the American Journal of Ophthalmology and volumes 1 to 7 of Series II. Address communications to the Ophthalmic Publishing Company, 664 North Michigan Avenue, Chicago 11, Illinois.

NEUROMUSCULAR CONFERENCE

The 21st semiannual conference in neuromuscular anomalies of the eyes was held at the Children's Memorial Hospital, Chicago, on May 1st to 6th by Dr. George P. Guibor and Dr. Charles Bahn.

SOCIETIES

ORTHOPTIC GROUPS MEET

The meeting of the midwestern group of the American Association of Orthoptic Technicians was held in Chicago on April 30th and May 1st, at the Eye Clinic Northwestern University Medical School.

The eastern group met in Rochester, New York, on May 2nd and 3rd. The program meeting was held at Strong Memorial Hospital, and a tour was conducted through the Bausch & Lomb factory.

On May 2nd and 3rd, the southern group met at the Henry Grady Hotel in Atlanta, Georgia.

NEW YORK ALUMNI MEET

The New York University College of Medicine-Bellevue Hospital Ophthalmological Alumni Association held its alumni meeting at the New York University College of Medicine on April 18th, 19th, and 20th.

LOS ANGELES OFFICERS

The Los Angeles Society of Ophthalmology and Otolaryngology has elected the following officers for 1949: President, Dr. Warren A. Wilson; secretary-treasurer, Dr. Victor Goodhill; chairman of section on ophthalmology, Dr. George Landegger; secretary of section on ophthalmology, Dr. Harold B. Alexander; chairman of section on otolaryngology, Dr. Alden H. Miller; secretary of section on otolaryngology, Dr. Leland R. House.

The meetings are held at 6 P.M. on the fourth Monday of each month from September to May at the Los Angeles County Medical Building, 1925 Wilshire Boulevard.

MILWAUKEE PROGRAM

The March meeting of the Milwaukee Oto-Ophthalmic Society was held at the Milwaukee County Hospital. The department of otolaryngology presented two papers, "Bilateral facial paralysis," and "Aberrant lingual thyroid gland." Members of the department of ophthalmology spoke on: "Symposium on angiograms: Aneurysm of the circle of Willis," and "Bilateral homonymous hemianopia." The discussion was in charge of the department of neurosurgery.

RENAME PALESTINE SOCIETY

The Palestine Ophthalmological Society (chairman, Dr. Aryeh Feigenbaum, 15 Abyssinian Street, Jerusalem; secretary, Dr. E. Sinai, 9 Bialik Street, Tel-Aviv) has been renamed the Israel Ophthalmological Society.

HOLD JOINT MEETING

The 91st meeting of the Reading Eye, Ear, Nose, and Throat Society was held jointly with the Wilkes-Barre Ophthalmological Society. Clinics were held at the Jefferson Hospital Medical School, Philadelphia, under the direction of Dr. William T. Hunt, Jr., assistant professor of ophthalmology, Jefferson Medical College.

Papers presented at this meeting were: "Physiology of the extraocular muscles," Dr. Arno E. Town; "Detachment of the retina," Dr. James S. Shipman; "Field defects and intracranial pathology," Dr. William T. Hunt, Jr.; "Central field changes as shown by angioscotometry," Dr. N. A. Karakashian; "The treatment of gliomas by radium applicator," Dr. Joseph Waldman; "Dacryocystitis," Dr. Alvin W. Howland; "Ocular therapeutics," Dr. Irving H. Leopold; "Secondary glaucoma," Dr. Carroll R. Mullen.

CÓRDOBA SOCIETY OFFICERS

The Sociedad de Oftalmologia de Córdoba (Argentina) has elected the following officers to serve for the next two years: Chairman, Dr. Roberto Obregón Oliva; secretary, Dr. Alberto Urrets Zavalía (hijo); treasurer, Dr. Roque A. Maffrand; directors, Dr. Rodolfo Laje Weskamp and Dr. Marcos H. de Anquín.

All correspondence should be directed to the secretary at 27 de Abril 255, Córdoba, Argentina.

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LAWRENCE T. POST, M.D.
Saint Louis, Missouri

It was with great pleasure that I accepted the invitation of your society to deliver one of the annual Sanford R. Gifford lectures. "Sandy," as he was affectionately called, was a man whom I was proud to consider an intimate friend ever since we had struggled together at one of the early American Board of Ophthalmology examinations.

This opportunity to pay my small tribute to Dr. Gifford is one that I could not refuse and my sole regret is that this appreciation cannot be a more impressive one. Distinguished son of a distinguished father, Dr. Gifford made an enviable place for himself in the history of ophthalmology in America. It is hard to select his greatest contribution, but probably his textbook would be so considered as it was ideal in its field, broadly informative, accurate, and, above all, readable—a quality characteristic of all of his writing, one so eminently desirable and so seldom achieved.

He was an outstanding ophthalmologist, a charming, cultured gentleman, and a loyal friend.

When asked to present this talk, I recalled that the first Gifford lecture was by Dr. Francis Heed Adler on the etiology of strabismus. It occurred to me that a consideration of the practical side of the subject of strabismus might serve as a humble complement toward completion of the idea, although I must at once admit that this essay can cover only a few general suggestions on a big subject.

I. THE HISTORY

The most important etiologic factor is heredity. It occurs so frequently as to be the rule rather than the exception.

Another important historical factor is age of onset. In those patients in whom strabismus occurs early, roughly before the age of two years, there is almost always an anatomic basis and, in my experience, they are less prone to develop fusion postoperatively than those who develop strabismus later in life. This, I believe, is due to the fact that the children who develop strabismus later probably had already acquired some fusion before the deviation set in and the newly found fusion is merely a reëducation.

On the other hand, my associate, Dr. R. G. Scobee, has noted the acquisition of fusion in 8 of 10 infants with congenital strabismus who were operated on at the age of one year. He argues that given a mechanism permitting alignment of the eyes, fusion will usually develop and aid in holding the eyes straight.

He also believes that 90 percent of all strabismus appearing before the age of six years has an underlying anatomic basis, his point being that check ligaments, muscle slips, and abnormal insertions are found in 90 percent of the cases of strabismus (whereas they are never found in anatomic dissections of normal eyes) and that anatomic anomalies

act as important underlying primary causes when associated with other etiologic factors.

II. The Examination and Procedure

1. A careful study is made of the fundi after full dilatation of the pupils. Abnormalities are noted and a gross estimate of the error of refraction is made. This dilatation is not for refraction but merely for the fundus examination. Atropine is used 3 times a day for 4 days before refraction.

2. Complete occlusion of the fixating eye is used to establish alternation. Elastoplast is a convenient material for this.

3. Glasses that contain full correction as measured under atropine are prescribed for constant wear. Too often ophthalmologists reduce this strength and thereby lose the advantage of full relaxation of accommodation and consequently the greatest relief of overconvergence.

4. As soon as coöperation permits, vision is taken with and without correction.

5. Near point of convergence is measured.

6. Angle Kappa is determined for each eye separately. The patient rests the chin in the cups on each side of the central standard, alternately, and fixates the central target on the perimeter with the fixing eye exactly over the finder. The reflection on the cornea of a flashlight moved along the arm of the perimeter is watched until it is exactly centered over the pupil, and the number of degrees of arc measured from the reflection of this flashlight to the center of the target equals the angle Kappa. If to the right for the right eye, it is plus, and if to the left, it is minus. Just the opposite pertains for the left eye.

7. Heterotropia is estimated by Hirschberg's method in infants. This method depends on the amount of displacement of the corneal image of a light, such as from a small bulb, on the cornea of a deviating eye while the patient fixates the light with the other eye. About 15 degrees of deviation may be estimated if the reflex lies at the pupillary margin of a 4-mm. pupil; if about

half way between the pupillary margin and the limbus, the strabismus is about 30 degrees; if at the limbus, it is about 45 degrees.

8. Heterotropia is actually measured on the perimeter in children old enough to coöperate. The nose is placed in the midline of the perimeter and when the light from a flashlight moved along the perimeter arm is reflected on the exact center of the cornea of the deviating eye, the arc degrees are measured. Each eye is tested in turn; first, without glasses—with each eye fixing; then with glasses—with each eye fixing.

9. Heterotropia is also measured by screen and parallax.

10. Primary and secondary deviations are measured with prisms at this time. The patient is directed to fixate the light at 20 feet, first without correction and then with correction, with one eye and then with the other. Such prisms as are necessary to eliminate the movement when they are held before each eye in turn measure the primary and secondary deviations. In a similar manner tests are made at 13 inches. Ductions and versions are estimated and recorded on charts, but not measured in degrees, primarily to determine the vertical elements. Measurements in degrees in extreme positions of gaze have been found to be so variable that they have been discarded as more misleading than helpful.

III. Treatment

As early as possible, usually at about the age of 4½ years, orthoptics are instituted. An attempt is made to determine the nature of the correspondence and, if abnormal, to break it up and restore normal correspondence. Frequently orthoptics are impossible because of the remoteness of the patient's home, in which case, if the wearing of glasses, plus occlusion, does not accomplish straightening of the eyes, surgery is routinely recommended.

Although fusion is undoubtedly desirable because of some advantage of stereopsis in life, its greatest value is in preventing later

deviations which are much more prone to occur if fusion is absent.

It is fortunate that the majority of obvious muscle anomalies are in the horizontal field and since one general rule is to attempt to correct the principal defect first, the surgery of the horizontally acting muscles is usually the first to be done. This is the saving factor for many who do not analyze their cases carefully but correct only the horizontal deviation. They often get a good cosmetic effect. It is true also that vertical anomalies are less noticeable than horizontal.

It has been observed that the greater defect should receive first attention. It is important to remember that correction of the lateral deviation in cases in which there is also a vertical deviation may either increase or decrease the latter, depending on the muscles involved. For example, if a vertical rectus is involved, the deviation will be greater after correction of esotropia because returning the eyes to the primary position will bring them nearer the field of the maximum action of the vertical recti; whereas, if the difficulty is with an oblique, the effect of the correction of esotropic abnormality will be an apparent lessening of the strabismus caused by the abnormalities of an oblique muscle. Correction of an exotropia will act similarly but in a reverse manner.

If a cosmetic result is the surgeon's primary goal, a careful study of the angle Kappa is most important. The ratio of positive angle Kappa to negative angle Kappa is about 50 to 1. The average for each eye is about 5 degrees. Obviously a plus angle makes a convergent strabismus appear less than it actually is. Some people have such high plus angle Kappas that they actually appear to have an exotropia.

A surgical undercorrection in such a case will be compensated for cosmetically to whatever extent a plus angle Kappa may have been present before operation and, similarly, overcorrection is desirable for appearance sake, not for function, in cases of exotropia with a positive angle Kappa because

the positive angle will make the exotropia appear greater than it actually is. However, it must be emphasized that this has no bearing on the development of fusion.

In choosing whether one eye or two are to be operated on in cases of lateral tropias, the following should be noted. Both eyes should be operated on if there is alternation, and a bilateral recession of the medial recti may be done if necessary if the near point of convergence is small; if larger than normal, more than 4 cm. from the bridge of the nose, and a secondary convergence palsy is present, not more than one medial rectus should be recessed. It is also true that other tests may indicate a contracture of a medial rectus as by abnormal check ligaments, muscle slips, or abnormal tendon insertions. These must be severed, as simply working on the medial recti tendons alone will be insufficient.

If the deviation is greater for near than for far in esotropia and esophoria, there is usually considered to be a convergence excess; but if greater for far than for near, a divergence weakness is presumed to exist. The near point of convergence is, however, a better gauge of the desirable surgery. In the former case, bilateral recession of the interni is usually indicated and, in the latter, a bilateral advancement or tuck of the lateral recti may theoretically be best, but it is seldom performed and the aforementioned considerations should weigh heavily in the decision as to the type of surgery. Any defective muscle must be investigated for possible abnormal check ligaments or other restricting abnormalities.

To be borne in mind is the help furnished by hypermetropia in combatting an overcorrection of esotropia. For example, presuming a high hypermetropia and a surgical overcorrection of a convergent strabismus, it is often possible to get a good result, including fusion, by prescribing an undercorrection of the hypermetropia, thus stimulating convergence.

Similarly, full correction, or even a little

overcorrection, will often compensate for surgical undercorrection.

In like manner, in cases of exotropia or exophoria, if the deviation is greater for near than for far, the condition is supposed to be a convergence weakness and, if greater for far than for near, it is supposed to be divergence excess. In the former case, resection of one medial rectus and recession of the lateral rectus in the same eye or a bilateral resection of the medial recti may be done and, in the case of divergence excess, bilateral recession of the lateral recti is to be done.

All of the factors mentioned and others also must be evaluated to determine the best remedial surgery in the given case. To reiterate, of the above considerations the near point of convergence is probably the most important.

Several consoling facts in the surgery of strabismus may be mentioned. Parents do not often demand a perfect result, being satisfied with a good postoperative appearance. Fusion and its value, unless stressed by the surgeon, mean little to them or to the child. Lastly, third-degree fusion is often obtainable without an exact correction of the deviation, since the innate fusion desire, plus fusion training, may bring this about.

The technique of the surgery is not considered of as great importance by me as is the diagnosis that indicates what should be done surgically, provided that: (1) the muscles are so sutured that they will be well spread out in their new positions and will not slip, (2) anatomic anomalies and check ligaments, when found, are cut, and (3) muscle sheaths are not unnecessarily removed.

It must be understood that I do not think that it is always possible to determine just what surgical procedure will be best until the patient is under anesthesia and the muscles inspected. Observation under anesthetic should then include (1) noting the difference in the amount of the deviation at that time from that before operation, (2) the action of the eye when pressure is made in the canthus opposite that of the deviation,

(3) the condition as regards check ligaments and intermuscular septa and insertions, and (4) the elasticity of the severed muscles in order to determine the extent of the surgery to be done on each.

IV. SURGICAL TECHNIQUE

My technique for both recessions and resections is as follows: The tendon of the muscle to be recessed is exposed by a 10-mm. curved incision over the tendon insertion. Tenon's capsule is lifted at the upper or lower border of the muscle and snipped. A muscle hook is introduced under the tendon and brought out at the opposite border after another snip is made in the capsule at the point of exit of the hook.

The muscle is secured by one arm of a double-armed, 3-0, plain catgut suture introduced at the junction of the upper and middle thirds of the tendon and carried through the middle thickness of the tendon to the border and then looped behind the muscle to its center, the needle being brought out proximal to the suture and passed through the loop of the suture and drawn taut.

The other half of the double-armed suture is introduced similarly through the lower third of the tendon. The tendon is cut very close to its insertion. It is then held away from the globe, and the conjunctiva and all check ligaments and abnormal bands between the recti are cut with sharp scissors until the muscle retracts freely into the orbit, care being taken not to strip the muscle sheath away from the muscle. It is then secured by suturing the two free ends of the tendon to the globe at the desired points at least 5 mm. apart. A surgical knot is used so that there will be no slipping as the knot is tightened.

Closure of the conjunctiva is with the remnants of the catgut. Three sutures are used. These are later absorbed or fall out. This is much simpler than the removal of nonabsorbable sutures in intractable children.

Resection is performed in a similar

manner. The suture is placed in the tendon at the desired distance from the insertion, and the free end of the tendon between the suture and the insertion is excised. It is wise not to cut the lateral and other attachments.

One point is of utmost importance and, although often mentioned, is not sufficiently observed. It is the cutting of check ligaments. These bands extending to the orbital wall, especially large and prominent from the medial recti, if not carefully severed will usually nullify the effect of surgery on these muscles. The usual illustrations suggest that they are single sheets, but actually they almost never occur singly but more often radiate from the muscle sheath in fan-shaped planes.

Abnormal muscle slips, especially between the recti, must also be looked for and, if found, must be severed for a like reason. The surgeon should be sure that the muscle will retract freely into the orbit after it has been cut from its insertion and that no check ligaments remain. For a comprehensive discussion of the importance and handling of these ligaments, I would refer you to a recent paper by Dr. R. G. Scobee,[1] who has also pointed out the value of making pressure in each canthus to determine the binding effect of each rectus. If firm adhesions or constrictions exist, the eye will be pushed back and will not turn freely. This may be an important guide to surgery.

Another point, previously mentioned, is whether or not under anesthesia the contracted muscles relax and the eyes appear straighter than before anesthesia. If they do, there are less apt to be strong contractures. In those cases in which the eye rotates readily upon pressure of the strabismus hook or the convergence is much less under anesthesia, the strabismus is probably on an innervational basis and surgery, especially advancement, must be most conservative or an overcorrection may result.

In cases of alternating convergent squint, if the patient uses his right eye when looking left and his left eye when looking right, there is usually no overactivity of the medial recti and the convergence near point may even be remote. The general rule that only one medial rectus should be recessed in such cases must be followed or a divergence may result. On the other hand, if a convergent alternator uses the right eye when looking right and the left eye on looking left, abduction is usually good and the medial recti are habitually overacting and bilateral recessions of these muscles can be done safely.

I concur in Payne's[2] recommendation that a patient with what appears to be paralysis of a lateral rectus should have a full resection of the apparently paralysed muscle and a recession of the antagonist rather than a Hümmelsheim operation as the first procedure because often such surgery will show that the muscle was not truly paralyzed, and the more elaborate operation of splitting the superior and inferior recti and utilizing their halves to aid the nonacting muscle may prove unnecessary.

Surgery of the obliques is occasionally indicated. The question then arises whether the weak oblique should be advanced, as has been done very successfully by McLean and others, or the yoke muscle weakened. This latter has been the method I have used, but such good results are claimed for working on the weaker muscle that I am not convinced that my method is the better procedure.

A point to be made is that the section of the inferior oblique should be made near its insertion and not, as often recommended, at its origin. The reason for this is that there is much variation in the insertion and that the suspensory ligament of Lockwood acts as a secondary origin and, since this is distal to the part sectioned in tenotomy near the origin, there is often very little accomplished by the operation.

Fink[3] has brilliantly pointed out numerous variations in the insertions of the inferior oblique. The insertion can be exposed without sectioning the lateral rectus, which is pulled upward by an assistant who reaches outward below the tendon of the lateral rectus and hooks the tendon of the inferior

oblique upward and medially before it is severed.

The superior oblique may be reached either by sectioning the superior rectus and hooking the superior oblique downward, opening its sheath horizontally and cutting the tendon in its sheath, or, as Berke[4] has advocated, without cutting the superior rectus tendon. If more effect is desired, a few millimeters of the tendon can be resected. I have found that sectioning of the superior rectus makes the operation much simpler.

The problem of exophoria-exotropia is a constantly recurring one. Exercises sometimes develop good fusion and comfort when discomfort has been noted. The tendency, however, as time goes by, is toward increasing divergence and finally results in failure of fusion from disuse. Surgical correction is simple and usually effective. Principles already outlined should govern the type of surgery. I have had consistent success with this procedure.

Conclusion

There should be a thoughtful and complete study of each case of strabismus before surgery and the role of the vertical recti in producing the defect should be carefully analyzed and a two-stage operation performed in cases in which both lateral and vertical deviations occur.

640 South Kingshighway (10).

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Ophthalmic Miniature

Like cloudy vapours,
these the Eyes o're cast,
Yet vanished as the dew,
by sunne at last:

Long practice, careful skill,
with observation,
Will teach the mystery
of the operation,
To end this worke,
that perfect it may stand,
God guide with carefull skill
our Eye, our Heart and hand.

Richard Banister, Mr. In Chyrurgery,
Oculist and Practitioner in Physicke.

BETA IRRADIATION OF THE EYE*

WILLIAM F. HUGHES, JR., M.D.
Chicago, Illinois
AND
CHARLES E. ILIFF, M.D.
Baltimore, Maryland

Recent reports and discussion of the value and dangers of irradiation of the eye with the beta rays of radon have been both enthusiastic and pessimistic.[1-4] The present uncertainty can be attributed to many factors, among which may be mentioned: (1) Variability in dosage and technique of application, with too little attention being paid to the characteristics of the irradiation used, the distance of the applicator from the eye, localization of the area to be treated, and possible cumulative effects; (2) ignorance of the differential sensitivity of the normal tissues of the eye and those tissues which are to be destroyed by irradiation; and (3) difficulty in comparing the results of beta treatment with untreated controls. Often the beta irradiation clinic becomes a convenient spot to which hopeless cases can be referred regardless of theoretical or practical justification.

In this paper, the various techniques and effects of beta irradiation will be discussed in an effort to arrive at a selection of suitable cases for treatment, and to utilize a dose sufficiently large to destroy undesirable tissue without undue damage to the normal structures of the eye. In addition, we will report some preliminary experiments on the use of beta irradiation following chemical burns of the eye, especially in regard to vascularization of the cornea.

TECHNIQUES FOR THE USE OF BETA IRRADIATION

The Burnam applicator, which contains a concentrated source of radon in a single glass bulb, has been described previously.[1, 5] The alpha particles or helium nuclei are completely absorbed by the soda glass bulb containing the radon. The beta particles or electrons are directed through a 4-mm. opening at the end of a brass tube of walls 2 mm. in thickness. The gamma rays, comparable to hard X rays, are emitted simultaneously with the beta particles but only in comparatively low concentration. According to Failla and others,[6] radon emits 96.5-percent beta and 3.5-percent gamma in terms of electrostatic units of ionization.

From a bulb such as the Burnam applicator, the center of which is 2.5 mm. from the tissue, 75.2 percent of the irradiation is absorbed within the first millimeter of tissue, 93.7 percent within the first 2 mm., 96.1 percent within the first 3 mm., and 98.9 percent within the first 5 mm.

The ratio of beta to gamma varies at different tissue depths as follows: at 1 mm. = 88-percent beta; at 2 mm. = 78.5-percent beta; at 3 mm. = 67.6-percent beta; at 4 mm. = 55.5-percent beta; and at 5 mm. = 43-percent beta. Therefore, it is possible to give therapeutically useful doses of beta without significant gamma irradiation which might damage the lens or deeper structures of the eye.

Because of the unavailability of radon in many localities, a radium applicator for ocular use has recently been described.[7] Although the applicator contains 50 mg. of radium, the effective output of beta particles is only about 30 mc. Such a relatively low output necessitates prolonged treatment times, and because of this a mechanical holder is desirable.

This applicator is apparently satisfactory for most conditions, but the source is not

sufficiently localized and concentrated for use in the obliteration of corneal vascularization. Also, the safety ratio between the output of beta and gamma is reduced by almost half. This type of criticism can be applied to many sources of beta radiation in which the mass itself filters out a significant number of the beta particles.

DOSAGE

One gram of radium is equivalent to one curie or 1,000 mc. of radon, a gaseous emanation of radium which emits radiations identical to those of radium. The dose of beta particles is dependent on the amount of radon and the duration of treatment, and can be calculated as follows:

$$\text{No. secs. exposure} = \frac{\text{No. gram secs. desired} \times 1,000}{\text{No. millicuries of radon}}$$

(or)

$$\text{No. mins. exposure} = \frac{\text{No. millicurie minutes desired}}{\text{No. millicuries of radon}}$$

For conversion:

No. gm. secs. $\times$ 16.66 = No. millicurie mins.
No. gm. secs. $\times$ 0.278 = No. millicurie hrs.

The intensity of irradiation varies inversely with the square of the distance of the applicator from the target. Therefore, a slight variation in distance results in a large difference of effective dose. In addition, with the so-called "spray technique" in which the applicator is held from 1 to 3 mm. above the tissue and is moved slightly back and forth, there is an uneven and uncertain distribution of the total dose over a poorly defined area.

For these reasons during the past two years treatments have been given by placing the applicator in contact with the lesion. The dosage for such contact therapy varies between 3 and 5 gram seconds per treatment. Ordinarily, treatments are not administered more frequently than every two weeks to the same area in order to avoid cumulative effects. In all initial treatments, and especially in children, even smaller doses should be given to avoid undue reactions in

hypersensitive individuals. The rabbit eye is more resistant to the effects of beta particles than the human eye, tolerating approximately three times the dose for human beings.[8, 9]

THE ACTION OF IRRADIATION ON TISSUES

Irradiation has no effect on tissues unless it is absorbed. In addition, the intensity of the effect is directly related to the amount of effective quantum energy, an inverse function of the wave length, at the site of absorption. It is generally agreed[9-12] that the biologic actions of various types of irradiation on the individual cell and supporting structure are similar. When the beta particles or high speed electrons strike a cell, changes are produced in both the cytoplasm and nucleus associated with ionization of the tissue. Large doses cause immediate death of the cell, perhaps by mechanical rupture of the structural portions of the cell and chromosomes. This is particularly true of beta irradiation in which 75 percent of the dose is absorbed within the first millimeter of tissue, producing a more concentrated number of "hits" and ionization than with X ray or gamma rays, which are absorbed more diffusely and deeply in the tissues.

Following smaller doses of irradiation, histologic changes are well demonstrated in the corneal epithelium.[8, 13] A few hours following a small dose of ultraviolet or beta irradiation, normal mitotic figures disappear from the basal layers of the epithelium. With somewhat larger doses, a small proportion of cells develop nuclear fragmentation, the chromatin material sometimes assuming the configuration of abnormal mitoses.

In agreement with experiments using other types of irradiation, the resting cell seems to be relatively resistant to damage. However, the cells which later develop abnormal mitoses and nuclear fragmentation are probably in a specially sensitive state at the time of exposure; namely, a premitotic or very early stage of prophase.[11] This may explain why rapidly proliferating tissues are

especially sensitive to irradiation—embryonic tissue, the tissues of young growing children, germinal epithelium, and certain neoplasms.

As will be pointed out later, rapidly proliferating endothelium of capillaries growing into the cornea can be inhibited by a smaller dose of beta than that required to obliterate an already formed vessel. In order to catch as many cells as possible in the sensitive premitotic stage, most radiotherapists use repeated small doses to destroy undesirable proliferating tissue, thereby reducing the amount of damage to less sensitive normal tissue.

Clinically, nuclear fragmentation in the corneal epithelium produces a superficial punctate erosion stainable with fluorescein. Larger doses of beta irradiation readily cause necrosis and disappearance of corneal stromal cells, thus emphasizing the need for caution in radiation treatment of any condition directly over the cornea, especially if there has been some loss of stromal cells previously from the disease process (recent chemical burn, corneal ulcer, and so forth).

Irradiation also causes a swelling of collagen,[10] one of the important structural components of the corneal stroma. Since a significant proportion of beta does not penetrate deeper than the cornea or sclera, doses sufficiently large to cause the perforation of a rabbit's cornea can be given without the development of cataract. A few rabbit eyes received 12 gram seconds of radon every 2 weeks for 8 months without the development of cataracts.[8] Clinically, we have not seen any radiation cataracts from radon treatment over the course of 10 years, and this experience is corroborated by Ruedemann.[2]

In agreement with almost all radiologists, we have found no evidence of stimulating action following irradiation. In fact, all regenerative processes seem to be retarded following the use of beta; namely, regeneration of the corneal epithelium, proliferation of new stromal cells, and vascularization of the cornea.[8]

The well-known cumulative effects of radiation apply to beta radiation of the eye. The interval during which a second application of beta is additive to a previous dose varies directly with the size of the dose. In general, however, cumulative effects are obtained if two therapeutic doses are given within a period of two weeks.

RADIOSENSITIVITY

Since the principle underlying all radiotherapy consists of a differential sensitivity of the diseased tissue to be destroyed and the normal surrounding structure, the relative radiosensitivity of various cells becomes important.

Desjardins[14] listed these in order of diminishing sensitivity as follows: lymphoid cells, polymorphonuclear and eosinophilic leukocytes, epithelium, endothelium, connective tissue, muscle, bone, and nerve.

Other factors which increase radiosensitivity are as follows:[9] undifferentiation and immaturity of the cell, state of activity (premitotic), active metabolism (related both to oxygen consumption and growth), and increased blood supply (in inflammatory conditions).

EFFECTS OF BETA IRRADIATION TREATMENT OF CONDITIONS INVOLVING THE GLOBE

The dramatic responses of certain bulbar conditions to the application of beta irradiation have been described elsewhere[1, 2] and will not be repeated here except to point out *the reasons for the outstanding successes* and possible explanations for the failures.

VERNAL CONJUNCTIVITIS

The excellent therapeutic response following the use of beta irradiation in both palpebral and limbal forms of vernal conjunctivitis has been amply demonstrated by many clinicians. In early cases, the papillae consist of lymphoid cells, young fibroblasts, and blood vessels, and these elements are very radiosensitive. However, old "pavement-stone" vegetations which contain areas of hyaline degeneration and old fibrous tissue are more resistant. Successful radiotherapy

of vernal conjunctivitis also reduces the number of recurrences.

Papillomas

Papillomas of the lids, conjunctiva, and limbus usually respond dramatically to beta irradiation. Since an intraepithelial epithelioma of the limbus spreads superficially over the cornea, this neoplasm can be destroyed by beta irradiation without damage to the underlying normal corneal stroma. Of course, beta cannot be used for any tumor which extends into the eye or orbit because of its lack of penetration.

Angiomas

Except for the nevus flammeus or port-wine stain, angiomas of the lids, conjunctiva, and caruncle are very radiosensitive.

Vascularization of the cornea

The possible importance of the ingrowth of blood vessels into the cornea to relieve anoxemia or remove toxic inflammatory products cannot be evaluated at present. However, several undesirable features of corneal vascularization may be listed.

1. Reduction in the transparency of the cornea. "Shadow vessels" ordinarily cause little reduction in vision. However, Spicer has described a late secondary opacification around such vessels giving the appearance of "lines of clearing" and resulting in a significant decrease of visual acuity.

2. Following extensive injuries of the corneal stroma including the limbus, there is a pronounced tendency toward the ingrowth of blood vessels, accompanied by a pterygiumlike tissue over the surface of the cornea. A nodule of granulation tissue may form on the cornea, persisting as a thick scarred cornea of uneven surface.

3. Many heavily scarred and vascularized corneas remain chronically irritated, edematous, and show evidence of retarded healing.[15]

4. A heavily vascularized cornea makes a poor candidate for later keratoplasty.

Beta irradiation has been used clinically to prevent or more often to obliterate corneal vascularization. To determine the most effective technique for this purpose, we have applied beta to the vascularization of rabbit corneas which followed intracorneal injection of sodium hydroxide.

Technique of experiments

Corneal vascularization was induced by the intracorneal injection of 0.05 cc. or 0.1 cc. of N/20 sodium hydroxide. The most marked and consistent vascularization was produced when the opaque area of injection touched the limbus. When the injected area was located centrally and was surrounded by a zone of clear cornea, vascularization was minimal.

On the other hand, extravasation of the sodium hydroxide into the region of the limbal vessels resulted in ischemic necrosis of this region, and subsequent vascularization of the cornea usually arose from the intact limbal vessels at the edge of the lesion. The severity of the important corneal symptoms was graded numerically according to the following scale of maximal values:

Corneal Opacity: intensity plus 4 × area in millimeters = total grade.
Corneal Vascularization: millimeters of limbal circumference from which vessels enter cornea × millimeters of distance the vessels enter the cornea.

Comparison of treated and untreated areas was made either between two separated areas in the same cornea (0.05 cc. of N/20 sodium hydroxide injected in each area), or more often between two eyes of the same animal (0.1 cc. of N/20 sodium hydroxide injected in each eye).

Since it was technically impossible in most instances to produce two exactly similar lesions for comparison, some allowance was made in Table 1 for the fact that the most severe opacity was usually treated. This was done as follows: (a) the initial reading of the corneal opacity to be treated was given a plus value and the control area a negative value; (b) the final reading of the treated

cornea was given a negative value and the control area a positive value; and (c) a final value to determine any possible effect of treatment was obtained by taking the algebraic sum of the original difference and final difference between the treated and control areas. A plus value would therefore suggest a beneficial effect of treatment and a minus value a detrimental effect.

vessels, as illustrated in Figure 1. However, because the area covered by the applicator was only 4 mm. in many of the eyes treated in this manner, large trunk vessels would pass between the sites of treatment and enter the cornea, thence fanning out and thoroughly vascularizing the entire burned area.

Efforts were made to obliterate already

TABLE 1

TREATMENT OF ALKALI BURNS WITH BETA DIRECTLY OVER LESION

Experiment Number	Beta Rx No. Gram Secs. (Day of Rx)	Total Dose of Beta (Gram Secs.)	Difference in Treated and Untreated Areas						No. Days Followed
			Original Reading		Final Reading		Total Difference or Improvement		
			Corneal Opacity	Pannus	Corneal Opacity	Pannus	Corneal Opacity	Pannus	
1	24(0)+24(7)+12(35)+12(49)	72	+6	− 9	− 3	−30	+ 3	−39	189
2	24(0)+18(35)+18(49)	60	+5	−14	−10	−10	− 5	−24	189
3	24(0)+12(35)+12(49)	48	+4	−11	− 4	−10	0	−21	189
4	24(0)+18(35)	42	+9	− 6	−19	−10	−10	−16	74
5	12(0)+12(7)+12(35)+12(49)	48	0	−16	+ 5	− 8	+ 5	−24	189
6	12(0)+18(35)+18(49)	48	+7	+ 7	+ 2	−30	+ 9	−23	189
7	12(0)+18(35)+18(49)	48	−3	−13	− 3	−15	0	−28	189
8	24(7)	24	−8	0	+10	+36	+ 2	+36	16
9	24(7)	24	+7	+ 2	−10	− 3	− 3	− 1	16
10	24(7)+18(35)+18(49)	60	0	+ 2	− 4	0	− 4	+ 2	74
11	24(7)+12(35)+12(49)	48	+2	+ 4	0	−40	+ 2	−40	74
12	R.E. 12(0)+12(7)+12(35)+12(49)	48							
	L.E. 18(35)+18(49) (Eyes looked the same on 35th day)	36	0	− 4	+ 3	0	+ 3	− 4	74

Eyes Nos. 1, 2, 3, 4, 8, 9, 10, 11 received two areas of injection in each cornea of 0.05 cc. of N/20 NaOH each. Two areas compared in a single eye.
Rabbits Nos. 5, 6, 7, 12 received a single injection of 0.1 cc. of N/20 NaOH in each cornea. Two eyes compared.
Burnam applicator and Lucite contact glass used (8), the glass bulb containing radon being 6 mm. above the area treated.

Results

1. Treatment over lesion (table 1). Application of varying doses of beta at varying intervals directly over the area of corneal involvement had little effect on the ultimate corneal opacity, but, if anything, made the pannus more intense.

2. Contact therapy without lucite holder. In 21 eyes, the Burnam applicator without lucite holder was placed in direct contact with the limbus adjacent to the area injected 24 hours previously. An average number of 4 applications at one sitting was performed, the dose for each site ranging from 6 gram seconds to 24 gram seconds. This single treatment with beta had little effect on the corneal opacity. A dose of 12 gram seconds was sufficient to inhibit the ingrowth of

formed vessels by direct application of the Burnam applicator at the source of the vessels at the limbus. A dose of 6 gram seconds was insufficient to obliterate even superficial loops of vessels, 12 gram seconds effectively obliterated superficial vessels of moderate size, and 18 gram seconds occluded deeper vessels. Doses of 18 to 24 gram seconds also seemed to cause some additional necrosis of the already injured corneoscleral tissue, a few eyes developing perforations at the site of heavy treatment and chemical necrosis. Mulberrylike elevations of granulation tissue on the surface of the cornea could be reduced by 12 gram seconds applied directly over the area. However, the obliteration of large trunk vessels by beta could only be accomplished at the expense of excessive
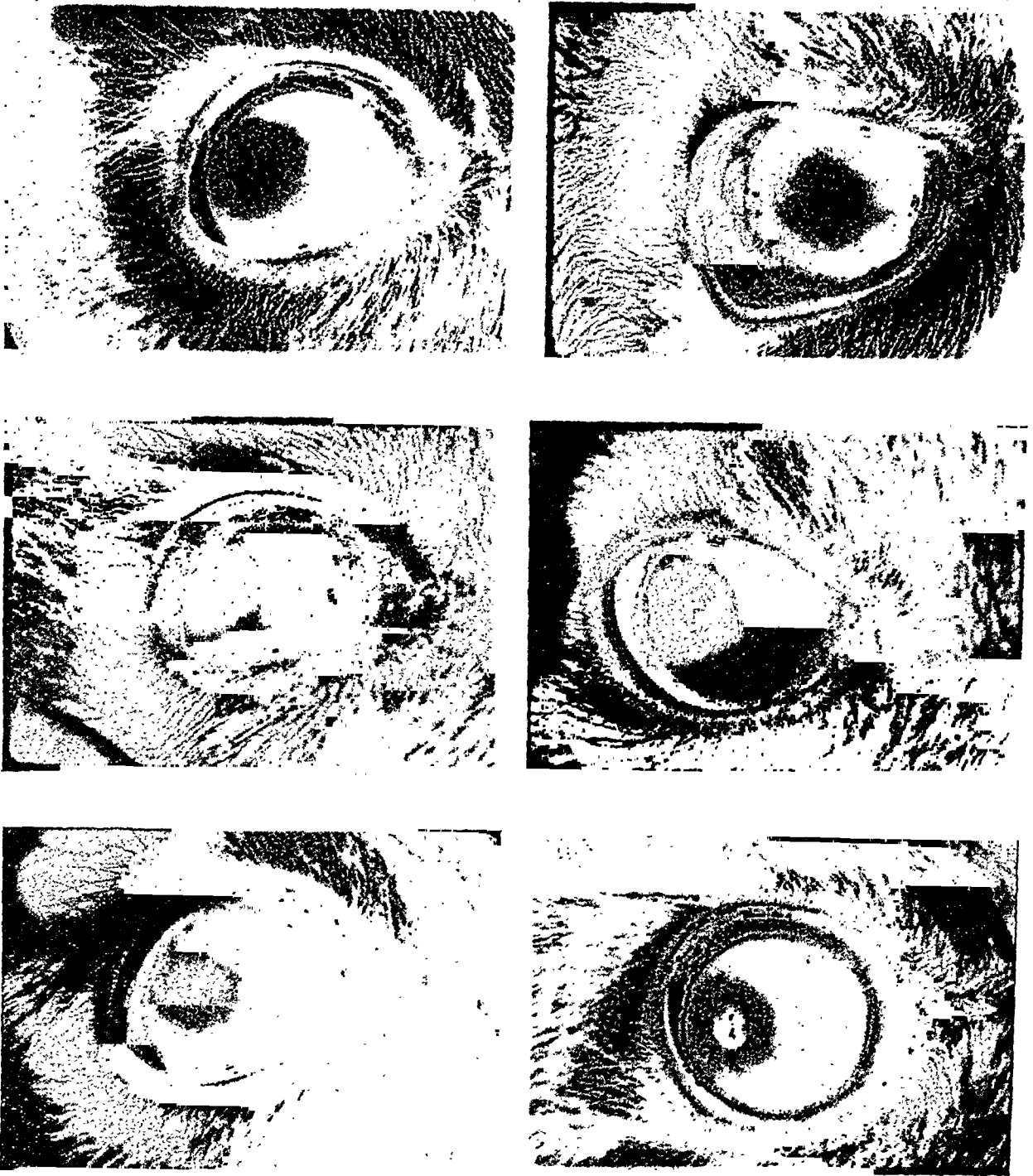
Fig. 1 (Hughes and Iliff). *Right eye* (pictures on left). Intracorneal injection of 0.1 cc. of N/20 sodium hydroxide treated one day later with 12 gram seconds of beta irradiation at each of three sites on the limbus adjacent to the involved area. Photographs (top to bottom) at 15 days, 21 days, and 29 days after injection. *Left eye* (pictures on right). Untreated control. Photographs (top to bottom) at 15 days, 21 days, and 29 days after injection.

scleral necrosis, and could have been more easily accomplished by means of electrolysis or cautery.

3. Spray therapy at limbus with lucite holder (table 2). Because of the great tendency for vessels to slip between and around the sites of beta application, a lucite holder was used in the following series of experiments in order to provide a wider area of exposure (11 mm.) and some overlapping.

The radon bulb was held 6 mm. above the tissue with this holder. In this small series

of experiments, little significant effect of beta on the residual corneal opacity and pannus could be detected after "spray therapy" over the limbus. However, the maximal intensity of pannus was significantly lower in 7 eyes which received an application of 75 gram seconds over two limbal areas 24 hours after the injection of sodium hydroxide.

Several striking results were seen repeatedly following the use of beta in these experiments: (a) A dose of 6 gram seconds held 6 mm. over the limbus prevented the ingrowth of superficial but not of deep

a control for the beta experiments previously described, dry ice was applied for 15 seconds to the sclera adjacent to the area of corneal opacification produced by the injection of 0.1 cc. of N/20 sodium hydroxide two days previously. In 5 rabbits followed for 52 days, the treated eyes showed an average maximum pannus of 36 compared with a grade of 26 for the untreated eyes, and the average residual vascularization after 52 days was 9 points worse in the treated eyes. No effect was noted on the intensity of the corneal opacification. The effect of beta, therefore, either has a more

TABLE 2
TREATMENT OF ALKALI BURNS WITH BETA APPLIED OVER LIMBUS

Dose for Each Area (Gram Secs.)	No. Areas Treated	Day of Treatment	No. Rabbits	Difference in Treated and Untreated Eyes				No. Days
				Original Reading Corneal Opacity	Max. Pannus	Final Reading Corneal Opacity	Pannus	
6	4–5	1	4	+4	−72	−19	−31 Deep Vessels	48
12	3–6	1	5	+3	− 6	−10	−16	59
12	6	4	1	0	0	+11	−15	106
12	3, 5	8	2	+1	+ 4	− 4	−15	114
25	3	1	2	+1	−60	−12	−42	79
25	2	8	1	+2	+ 6	0	− 7	44
75	2	1	7	+2	+27*	+ 2	+ 8	52

* Standard error of differences = 6.4.

vessels, and 12 gram seconds largely prevented deep vascularization of the cornea. (b) Normal limbal vessels were unaffected by doses of 12 gram seconds, although 24 gram seconds produced ischemia and edema. (c) With single small doses insufficient to prevent corneal vascularization indefinitely, a delay of from 2 to 3 weeks in vascularization was noted. (d) Budding loops of vessels growing into the cornea could be stopped at any point by beta, the ends of the vessels becoming bulbous, tortuous, and associated with small blood lakes.

4. *Effect of dry ice on corneal vascularization.* The application of dry ice to tissue is a good method of producing cellular destruction without much structural alteration. As

specific effect on the proliferation of capillary endothelium, or a more prolonged action.

Summary

With rabbit corneas previously exposed to sodium hydroxide, the use of beta irradiation was most effective in the reduction of granulation tissue masses on the surface of the cornea and in the obliteration of small superficial blood vessels crossing the limbus.

Vascularization of the cornea could be prevented by the alert and judicious use of beta, the best results being obtained by covering a relatively wide area of the limbal sclera adjacent to and slightly beyond the limits of the cornea involved by the chemical

burn. The inhibitory effects of the irradiation lasted from 2 to 3 weeks. The relatively small doses of beta required to prevent the ingrowth of vessels must inhibit the proliferation of capillary endothelium, because clinical and histologic examination revealed no thrombosis of the vessels.

Once the vessels had become established in the cornea, larger doses of beta were required over the limbus to obliterate the vessels. Large trunk vessels were difficult to obliterate by beta treatment, and direct cauterization, electrolysis, or the use of diathermy current as advocated by Gundersen[15] would have been preferable.

As mentioned previously, not more than one third of the dose necessary for rabbits need be used for human eyes in whom a dose of 5 gram seconds contact therapy with the Burnam applicator over the sclera is sufficient to obliterate vessels.

The following clinical conditions associated with corneal vascularization have been treated with irradiation, the results of which have been reported favorable: (1) In conjunction with superficial keratectomy to prevent the revascularization of the cornea; (2) before and after keratoplasty in cases with heavily vascularized corneas; (3) chemical burns such as sulfur dioxide; (4) acne rosacea keratitis and other vascularizing keratitis of unknown etiology.

PTERYGIUM

Beta irradiation has been employed as a primary treatment for pterygium.[2] It is particularly useful in those cases of "malignant" pterygia which recur after surgical transplantation and are associated with marked vascularization.

INFECTIONS

The effects of roentgen irradiation in the treatment of inflammations have been reviewed well by Pendergrass and Hodes.[16] It is generally agreed that doses tolerated by the tissues are not bactericidal. Large doses apparently depress the defense mechanisms of the body, especially the reticuloendothelial system, and the most effective results are obtained by using no more than one fourth to one third of a skin erythema dose.

The reasons for the beneficial effects of small doses of X ray on acute inflammations are uncertain, but have been attributed to a destruction of leukocytes with liberation of proteolytic enzymes and antibodies,[17, 18, 19] liberation of antibodies from other sources, and the production of an active hyperemia.[16]

Chronic infectious granulomas, such as tuberculosis, respond favorably to somewhat higher doses of X ray, probably because of the radiosensitivity of epithelioid and giant cells which are replaced by fibrous tissue,[9] and perhaps because of the liberation of antibodies.

The relatively few attempts to treat pyogenic corneal ulcers with beta irradiation have been unsuccessful,[1] in some instances leading to perforation of the cornea. It may be that the concentrated character of this type of irradiation is unsuitable for acute infectious processes, that the dosage employed was too large, or that a beneficial hyperemia is impossible in the avascular cornea.

On the other hand, Woods[20] and Iliff[1] have reported that of 72 eyes with anterior ocular tuberculosis treated with beta irradiation, 52.8 percent were healed for at least one year, 38.9 percent were improved, and 8.3 percent were unimproved. Improvement in visual acuity of at least two lines occurred in 42 percent, vision was maintained at the same level in 46 percent, and decreased in 12 percent. No effect on recurrences of the attacks was noted. Because of the wide variation in the characteristics and ultimate prognosis of anterior ocular tuberculosis, statistical certainty that beta irradiation has been of value in this condition is impossible.

A few cases of ocular sarcoid have not responded favorably to beta treatment. Iliff[1] reported one case of blastomycosis of the outer canthus treated successfully with beta. Cases of pemphigus and lupus erythematosis have not responded.

CORNEAL SCARS

The ultimate clarity of the cornea following a condition which involves the stroma cannot be estimated accurately because of normal recovery powers including absorption of inflammatory exudate, subsidence of edema, disappearance of blood vessels, and regeneration of the corneal corpuscles. Such reduction in the size and intensity of the opacification is especially prominent in children, and the cornea may continue to become clearer for several years. For this reason, any results obtained in the treatment of corneal scars with irradiation should be interpreted cautiously. Although fibroblasts

Clinically also, beta irradiation was found to have no effect on old corneal scars of various types.[1] Doses sufficiently large to destroy old fibrous tissue destroy normal stromal cells and in fact retard normal regenerative processes. It is difficult to see how the use of beta on scarred corneas could have anything but a detrimental effect since there is no known stimulating effect of any type of irradiation on the proliferation or growth of cells. It is possible that irradiation during the stage of active proliferation of fibroblasts may diminish the ultimate amount of scarring, but it may be undesirable to inhibit such repair of a recently damaged cornea because of the danger of perforation.

TABLE 3

TREATMENT OF CORNEAL SCARS FOLLOWING SODIUM HYDROXIDE
BURNS WITH BETA IRRADIATION

Dosage*	No. Rabbits	Average Difference between Treated and Untreated Eyes†		Days Followed
		Corneal Opacity	Pannus	
6 gram seconds on 7th day after NaOH injection and every 2 weeks for 18 weeks.	9	+1	−2	198
6 gram seconds every 2 weeks for 12 weeks beginning 71 days after NaOH injection.	5	−8	+4	170

* Using Burnam applicator and Lucite holder, radon 6 mm. above cornea.
† Plus value = treated eye improved over untreated eye.

are sensitive to irradiation, fibrocytes in old scar tissue are not.

Relative to this problem, the corneal lesion in one eye of each of 9 rabbits which had received an intracorneal injection of 0.1 cc. of N/20 sodium hydroxide was treated with 6 gram seconds every two weeks for 18 weeks, beginning 7 days after the injection. This dose was previously found to be the maximally tolerated dose for a normal rabbit cornea. After 198 days, there was no significant difference between treated and untreated eyes (table 3).

A second experiment consisted of 5 rabbits with old sodium hydroxide scars, and the use of beta was without beneficial effect on these eyes (table 3).

CONCLUSION

Beta particles of radon represent a concentrated source of irradiation which is largely absorbed within the first 2 mm. of tissue and is therefore useful in the treatment of superficial conditions of the lid, the conjunctiva, cornea, and sclera. The effective use of beta irradiation in ophthalmology depends upon an exact knowledge of the differential between the sensitivity of normal tissues and the pathologic tissues to be destroyed.

In general, lymphoid tissues (the follicles in vernal conjunctivitis), epithelial growths (papillomas), and vascular endothelium (in corneal vascularization) form the most sensitive tissues which can be destroyed by

beta irradiation without undue injury to the normal ocular structures.

Because of the great sensitivity of the corneal epithelium and stroma cells, direct irradiation over the cornea should be used with caution.

Corneal vascularization is best obliterated by irradiation over the scleral portion of the limbus.

An ocular condition associated with great cellular destruction or pyogenic infection may respond poorly to beta irradiation.

1853 West Polk Street (12).

The Johns Hopkins Hospital (5).

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FIG. 1
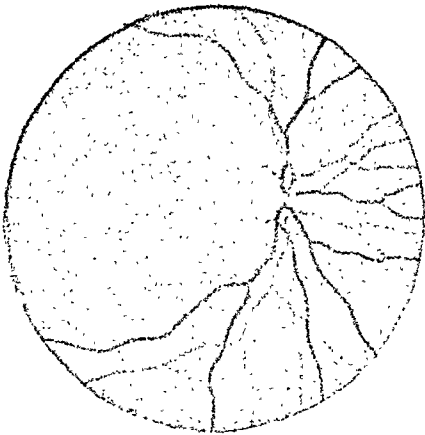
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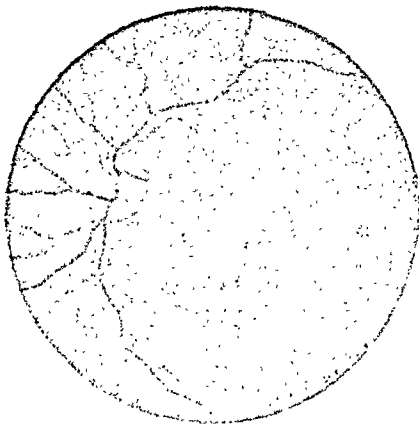
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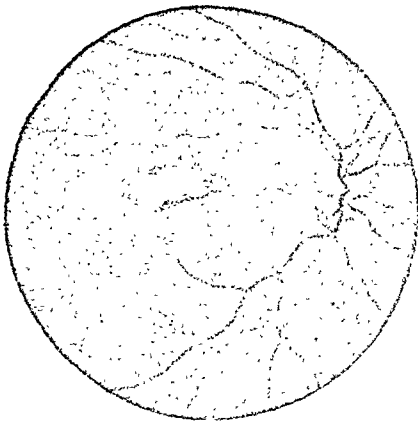
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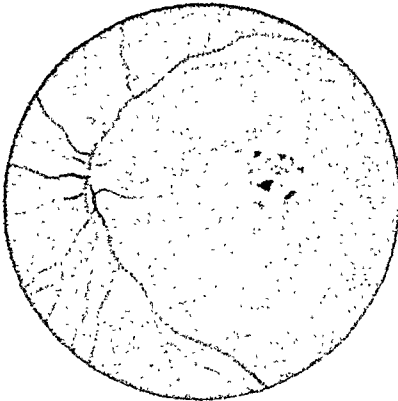
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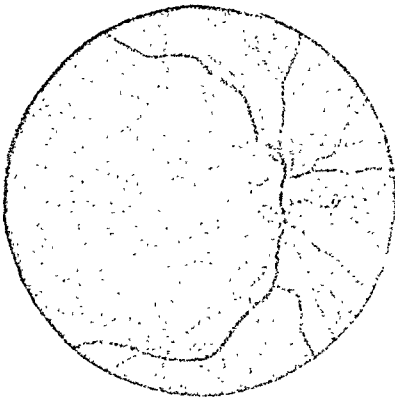
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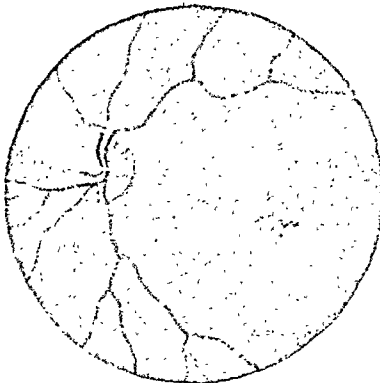
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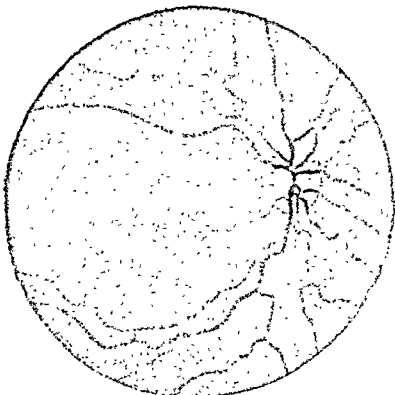
FIG. 8
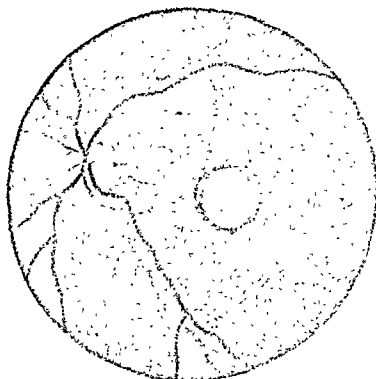
HEREDODEGENERATION OF THE MACULA

WILLIAM L. BERKLEY, CAPT., (MC) U.S.N.
Bayshore, L. I., New York

AND

FRANK R. BUSSEY, M.D.
New York

Degenerations of the macula appear in the literature under a host of disease entities. Closer observation reveals many of these so-called entities are closely allied, if not actually identical. The confusion, which is apparent after reviewing the literature, is partially justified because of the absence of a pathologic study in the great majority of these central lesions. Thus, classifications have been based on history, funduscopic findings, and personal interpretations.

Behr,[1] in 1920, made a noteworthy attempt to clarify the situation by suggesting that a number of macular degenerations of familial and hereditary incidence be placed in one great group which he elected to call heredodegeneration of the macula. Since then there have been numerous additions to the literature of such cases. Lloyd[2] further suggested the need of "streamlining" the nomenclature of these macular lesions. The more recent texts, as Elwyn's,[3] are agreed that a condensation of the classification is preferable to the individual listing of a plethora of closely allied conditions.

This report does not purport to offer a new classification nor to suggest a modification of an older one. It is hoped simply that the presentation of another family group showing macular degeneration with some interesting associated findings (red hair and

color blindness) will prove of some value toward the final understanding of this disease. Chart 1 shows the family in question. Each case, with pertinent findings, will be discussed separately.

REPORT OF A FAMILY

GENERATION I

Case 1. A white woman, now deceased, about whom no history other than "bad eyes all her life" is known, is listed as suspected of having macular involvement.

GENERATION II

Case 1. A woman, aged 48 years, who had experienced defective vision since early childhood.

Ocular findings. Visual acuity was: O.D., 1/20 corrected to 6/20 with a +2.75D. sph. ⊃ +4.75D. cyl. ax. 15°; O.S., 1/20 corrected to 6/20 with a +3.0D. sph. ⊃ +4.5D. cyl. ax. 170°.

Funduscopic examination showed: O.D. an irregular, yellow-brown degeneration of the macula. A clearly demarcated, circular area similar in nature but of lesser degree enveloped the more central degeneration just described. The entire involved area measured 1½ disc diameters in size (fig. 1); O.S. showed a similar degeneration of lesser size but greater intensity (fig. 2).

FIGS. 1 TO 8 (BERKLEY AND BUSSEY). (FIGS. 1 AND 2) CASE 1 OF GENERATION II. O.D., THE ENTIRE INVOLVED AREA MEASURED 1⅓ DISC DIAMETERS; O.S., THE AREA OF DEGENERATION WAS SMALLER BUT OF GREATER INTENSITY. VISION: O.U., 1/20, CORRECTIBLE TO 6/20. (FIGS. 3 AND 4) CASE 1 OF GENERATION III. O.D., THE IRREGULARLY SHAPED LESION HAD A YELLOW CENTER AND A BROWNISH, PIGMENTED BORDER; VISION, 1/20, CORRECTIBLE TO 2/20. O.S. SHOWED A SIMILAR BUT MUCH OLDER LESION; VISION, 1/20, CORRECTIBLE TO 7/20. (FIGS. 5 AND 6) CASE 3 OF GENERATION III. O.D., A WELL-DEFINED, SLIGHTLY ELEVATED DISCOLORATION WAS PRESENT IN THE MACULAR REGION; VISION, 16/20, CORRECTIBLE TO 20/20. O.S., A YELLOWISH DEGENERATION INVOLVED THE ENTIRE MACULAR AREA; VISION, 1/20, NOT CORRECTIBLE. (FIGS. 7 AND 8) CASE 2 OF GENERATION IV. O.D. A CENTRAL YELLOWISH DEGENERATION HAD A CIRCUMSCRIBED AREA OF APPARENT HYPEREMIA. VISION, 16/20, CORRECTIBLE TO 20/20. O.S., THE CENTRAL LESION WAS SURROUNDED BY A MARKEDLY HYPEREMIC BORDER; VISION, 1/20, NOT CORRECTIBLE.

As a child, this patient showed a convergent squint, but no muscle imbalance was now apparent.

Case 3. A woman, aged 51 years, first noted defective vision at the age of 40 years.

Ocular findings. Visual acuity was: O.D., 1/20 not further corrected with a +1.25D. sph.; O.S., 5/20 corrected to 16/20 with a +2.75D. sph. ⊃ −2.5D. cyl. ax. 95°.

condition common to the macular area of the right eye.

Case 4. A man, aged 45 years, refused to submit to examination, stating, "I've been to eye doctors all of my life and none ever help me." This case is listed as suspected of having pathologic conditions similar to others in the family.

Case 5. A man, not available for examina-
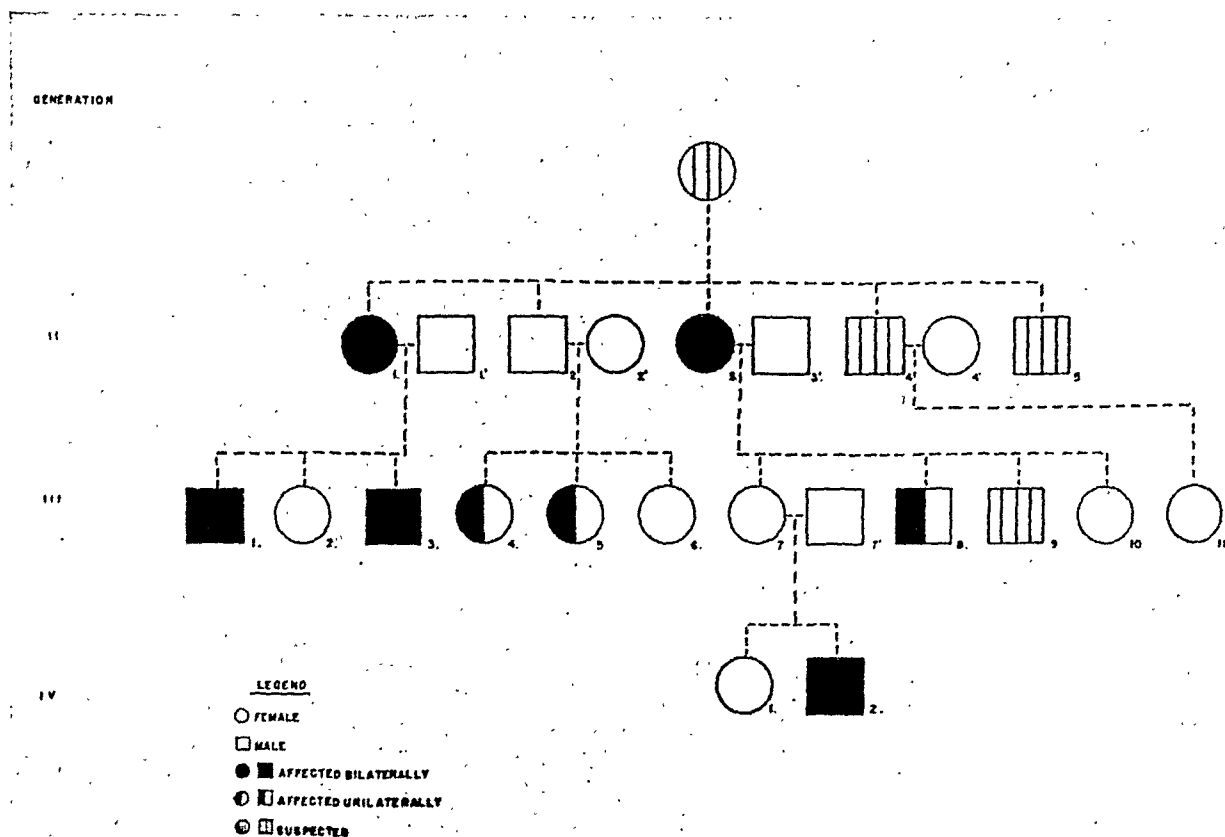
Chart 1 (Berkley and Bussey). Occurrence of macular degeneration in a family group.

Funduscopic examination revealed: O.D., an irregularly shaped, rusty, "salt-and-pepper" appearing area of macular degeneration measuring about 2½ disc diameters in size. The degenerated portion was clearly demarcated from the rest of the macula (pictures not obtainable); O.S., a small, sharply demarcated, homogeneous circular lesion about one third disc diameter in size, located in the region of the macula. A rusty, irregular degeneration was noted at the upper border of the lesion. This portion of involved retina appeared to have an increased vascularity, a

tion, who is listed as suspected on the basis of a history of "bad eyes."

GENERATION III

Case 1. A young man, aged 19 years, was known to have defective vision in the left eye since the age of 12 years. One year ago he began to have defective vision in the right eye.

Ocular findings. Visual acuity was: O.D., 1/20 corrected to 2/20 with a +2.5D. sph.; O.S., 1/20 corrected to 7/20 with a +4.5D. sph.

Funduscopic examination showed: O.D.,

an extensive area of degeneration in the macular region. The lesion was irregularly shaped and was composed of a yellow center with a brownish, pigmented and poorly demarcated border that contained occasional fresh hemorrhage. The involved area measured about 2 disc diameters in size and was encompassed by a circular area of perimacular edema. (Examination recently revealed

16/20 corrected to 20/20 with a +3.0D. sph. ⊃ +1.0D. cyl. ax. 120°; O.S., 1/20 not improved with refractive correction of +4.5D. sph. ⊃ +0.75D. cyl. ax. 90°.

Funduscopic examination showed: O.D., a well-defined, circular, slightly elevated discoloration in the macular region. The lesion measured about 1½ disc diameters in size (fig. 5); O.S., presented an irregular, yel-
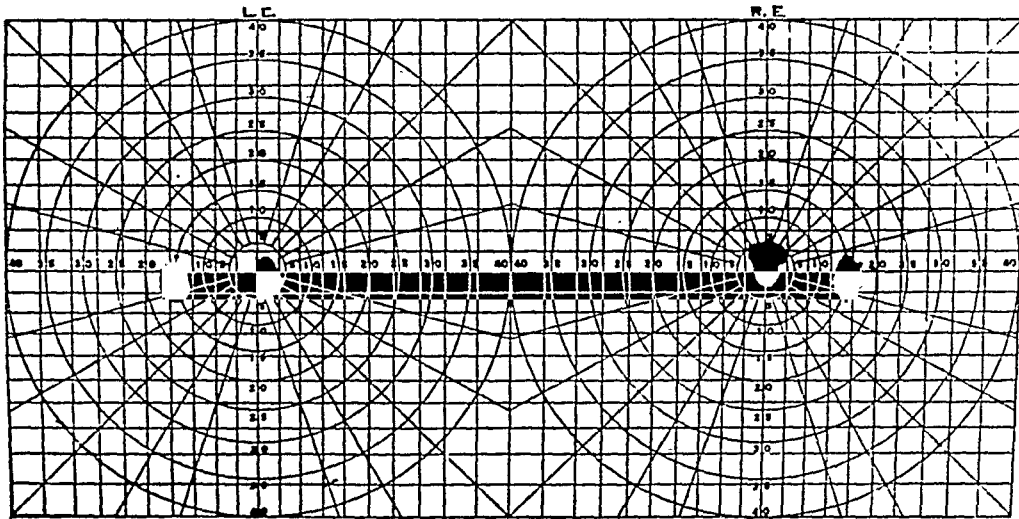
Fig. a (Berkley and Bussey). Visual field studies of Case 1, Generation III, showed a normal peripheral field with the presence of central scotomas.

the lesion to be quiescent with subsidence of the hemorrhage and the perimacular edema. See Figure 3.); O.S. showed a similar but much older lesion as evidenced by pigment deposits, lack of hemorrhage, edema, or other evidence of activity (fig. 4).

Field studies showed the peripheral field to be normal but the presence of central scotomas (fig. a). There was also a moderate degree of left hypertropia.

Case 2. A young woman, aged 18 years, was free of any apparent macular involvement. She is listed merely to note the presence of a marked weakness of the left superior rectus with resultant right hypertropia.

Case 3. A boy, aged 14 years, noted defective vision in the left eye at the age of 12 years. There were no complaints referable to the right eye save the need for the refractive correction.

Ocular findings. Visual acuity was: O.D.,

lowish degeneration of the entire macular area (fig. 6).

Case 4. A young woman, aged 25 years, has had no complaints referable to the eyes.

Ocular findings. Visual acuity was: O.D., 16/20 corrected to 20/20 with a +1.5D. sph.; O.S., 20/20.

Funduscopic examination showed: O.D., the macula had a definite moth-eaten appearance typical of an early stage of degeneration; O.S., normal.

Case 5. A woman, aged 23 years, complained of "weakness of the right eye."

Ocular findings. Visual acuity was: O.D., 16/20, not further correctible; O.S., 20/20.

Funduscopic examination presented: O.D., a rusty appearance of the macula with a small amount of punctate stippling which is considered characteristic of an early stage of macular degeneration; O.S., normal.

Case 8. A man, aged 28 years, had no visual complaints.

Ocular findings. Visual acuity was: O.D., 20/20; O.S., 20/20.

Funduscopic examination showed: O.D., a faint homogeneous and circular area of apparent degeneration was present in the macular region; O.S., normal.

Case 9. A man, aged 26 years, was not available for study. Listed as suspected on basis of history of longstanding "bad eyes."

GENERATION IV

Case 2. A boy, aged 8 years, had a history of poor vision in the left eye since infancy.

Ocular findings. Visual acuity was: O.D., 16/20 corrected to 20/20 with a +2.0D. sph.; O.S., 1/20 not further corrected with a +4.5D. sph., the retinoscopic finding.

Funduscopic examination showed: O.D., the macular area had a central yellowish degeneration with a circumscribed area of apparent hyperemia more than 1 disc diameter in size (fig. 7); O.S., the macula had a distinct circular degenerative area about 1½ disc diameters in size. The central lesion was surrounded by a markedly hyperemic border (fig. 8). Examination six months later showed development of some pigmentation in both eyes.

An esotropia was present in early childhood, but the condition had been slightly improved by his refractive correction.

DISCUSSION

Genetically, this family revealed "a condition of dominant transfer with imperfect penetrance" according to a personal communication from Dr. T. H. Dobzhansky.[4] He further stated that "if Case 2* in Generation II and Case 7* in Generation III had evidence of the disease, the conditions for perfect dominance would have been satisfied." Rechecks were done of these two cases but no evidence could be found of any pathologic condition.

According to the pattern of onset, which in this study showed a wide variation (from

infancy to adulthood), it is still possible that these two cases may develop evidence of the disease. This is especially true of the individual in Case 7 of Generation III who is still relatively young.

PATHOGENESIS

The literature is sparse and nonrevealing as to a definite pathology or etiology of heredodegeneration of the macula. Lues, tuberculosis, and other systemic diseases have been designated as causative factors. Ferrié[5] recently presented four additional cases of degenerative macular disease associated with definite evidence of tuberculosis. However, it would appear that this finding was merely coincidental.

There was no evidence to suggest consanguinity, lues, tuberculosis, or central nervous-system disorder in any of the cases we have presented. The optic nerve in most of the cases showed a definite temporal pallor. This observation has been noted in connection with degenerative macular disease by others (Crawford[6]).

GENERALITIES DRAWN FROM THIS REPORT

The disease is interesting from the standpoint of the ophthalmologist and the geneticist, and should be borne in mind in studies of macular abnormalities. Much assistance to the patient may be offered in the form of correction of refractive error, assurance that blindness will not ensue, and elimination of unnecessary empirical approaches to therapy.

SUMMARY

1. A family group showing positive occurrence of macular degeneration in 8 cases and possible occurrence in 3 additional cases is presented.

2. Color illustrations representative of typical lesions are shown.

3. The cases are reviewed individually and certain associated findings are noted. These include similar funduscopic appearance, hyperopia with and without astigmat-

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* Not reported herein.

tism, muscle imbalances, central scotomas, temporal pallor of the nervehead, red hair, and color blindness.

4. Onset (clinical) seemed relative to periods of physiologic stress and cases are listed as occurring at infancy, puberty, adolescence, early adulthood, and presenile period.

5. The hereditary transfer in this family was "dominant with imperfect penetrance."

St. Albans Naval Hospital.
321 East Tremont Avenue (57).

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CORRELATION OF THE CEREBROVASCULAR RESISTANCE AND THE GRADE OF HYPERTENSIVE RETINAL FINDINGS*

IRVING H. LEOPOLD, M.D., SEYMOUR S. KETY, M.D., WILLIAM A. JEFFERS, M.D., JOSEPH H. HAFKENSCHIEL, M.D., AND HENRY A. SHENKIN, M.D.
Philadelphia, Pennsylvania

Within recent years there has been an increasing interest in the hypertensive patient. Many hypertensive patients are being studied with the hope that they may improve following a thoracolumbar sympathectomy. It is not always a simple matter to determine which patients may be expected to benefit from the operative procedure. Various studies are employed in order to aid in the proper patient selection. Studies such as electrocardiogram, orthodiagram, influence of sodium-amytal narcosis on blood pressure, effect of a differential spinal, cold-pressor test, tests of renal function, and eyeground evaluation are all made. At present hypertensive patients are being studied at the Hospital of the University of Pennsylvania by a group of physicians who hope to correlate their data and, perhaps, eventually to arrive at some firm basis on which to select patients for surgical treatment. During this study the eyegrounds have been examined and classified according to the retinal vascular findings.

The classifications of eyeground findings as suggested by Wagener, Keith, and Kernohan,[2] and others, were deduced primarily on the duration of life of the patient and the severity of the hypertension. It seems desirable, if possible, to correlate these grades of hypertensive retinal changes with other physiologic factors. Such an opportunity presented itself among the hypertensive patients following measurement of their cerebral blood flow. Other data in this same study are reported elsewhere.[1] In this study it has

been shown that the cerebral blood flows are normal in the hypertensive patient.

From the cerebral blood flow the cerebrovascular resistance can be calculated.* The cerebrovascular resistance may be recorded as the pressure reuired to drive 1 cc. of blood through 100 gm. of brain tissue per minute.

similar alteration in the resistance of the cerebral vessels?

Twenty-one hypertensive patients and three nonhypertensive patients were studied. All the eyegrounds were graded according to the method of Wagener, Keith, and Kernohan.[2] It is admitted that it is not always pos-

TABLE 1

CEREBROVASCULAR RESISTANCE AND GRADE OF RETINAL VASCULAR CHANGE IN HYPERTENSIVE PATIENTS

Patient	Age Yrs.	Sex	Color	Mean B.P. mm. Hg	Cerebral Blood Flow cc./100 gm. B.T./min.	Cerebrovascular Resistance mm. Hg cc./100 gm. B.T./min.	Retinopathy Grade
D. M.	30	M	W	85	57	1.5	0
S. H.	26	M	W	93	58	1.6	0
J. B.	23	M	W	90	53	1.7	0
J. F.	46	M	C	120	57	2.1	2
F. H.	54	F	W	124	56	2.2	2
H. H.	31	F	W	146	66	2.2	2
B. P.	37	F	W	159	63	2.5	2
L. T.	46	M	C	137	55	2.5	2
F. L.	26	M	W	142	54	2.6	3
L. S.	48	M	W	171	64	2.7	2
F. B.	43	F	W	173	62	2.8	3
A. S.	26	F	C	160	57	2.9	1
L. M.	26	F	C	144	52	2.9	3
L. R.	47	M	W	157	54	2.9	2
N. B.	50	F	W	126	44	2.9	3
R. A.	34	M	W	158	52	3.0	3
G. J.	48	M	C	161	52	3.1	3
D. K.	38	F	W	190	59	3.2	4
N. M.	47	F	C	155	47	3.3	2
P. M.	62	M	W	133	42	3.3	3
M. Mc.	47	F	W	175	52	3.4	2
M. O.	40	F	W	190	54	3.5	4
J. M.	49	M	C	166	45	3.7	3
L. G.	38	M	C	159	38	4.2	4

The cerebrovascular resistance can be compared with the grade of retinal vascular change. At the same time another important factor can be evaluated. Since controversy exists as to whether retinal vascular changes reflect the state of the cerebral vessels, our observations appear to offer a new approach. Does increased retinal vascular resistance, as judged by narrowed vessels, sclerotic vessels, hemorrhages, and exudates, suggest a

sible to decide which type of sclerosis exists or to differentiate sclerosis and spasm, and that many ophthalmologists disagree in their interpretation of actual retinal findings. This classification, however, has been accepted as a helpful guide by many ophthalmologists. The fundi were graded by this method without any previous knowledge of the cerebrovascular resistance.

The cerebral blood flow was measured by the nitrous-oxide method of Kety and Schmidt.[3,4] This employs the use of a gas mixture consisting of 15-percent N_2O, 64-percent N_2, and 21-percent O_2. Specimens

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* The cerebral blood flow (cc. of blood passing through 100 gm. of brain tissue per minute) divided into the mean blood pressure equals the cerebrovascular resistance.
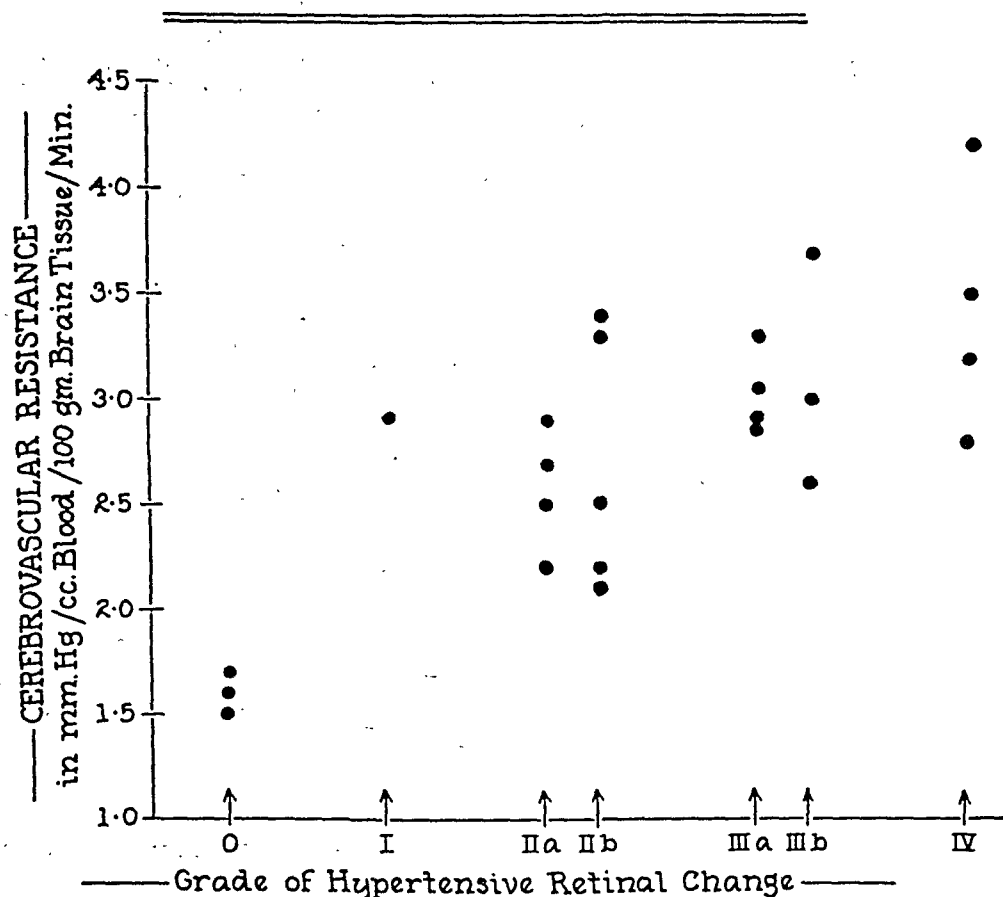
Graph 1 (Leopold, *et al.*). Cerebrovascular resistance in patients with various grades of hypertensive retinal changes.

for analysis were withdrawn simultaneously from the jugular bulb and femoral artery. Mean arterial blood pressure was obtained by means of a damped mercury manometer attached to a needle in the femoral artery. Cerebral metabolic rate in terms of cerebral oxygen consumption and cerebrovascular resistance were calculated as previously described.[3] Blood gas analyses were made in the Van Slyke-Neill manometric apparatus.[5] Potentiometric measurement of blood pH was made anaerobically at 37°C. by means of a glass electrode. Values for blood carbondioxide tension were calculated by means of the nomograms presented by Peters and Van Slyke.[5]

The results of the ophthalmoscopic gradings of the cerebral blood flow and the cerebrovascular resistance for each patient are listed in Table 1. It can be seen from a study of Table 1 and of Graph 1* that there is a tendency for the grade of hypertensive ret-inal change to increase as the cerebrovascular resistance increases. The statistical method†

* In an attempt to spread out the largest groups for graphing purposes, Wagener's Grade II was subdivided into IIa and IIb on the basis of the severity of spastic or sclerotic change. Grade III was also broken arbitrarily into a and b. Less than 10 hemorrhages and exudates in both eyes placed the eye in Grade IIIa.

† Spearman's formula was employed for this calculation

$$rho = 1 - \frac{6\Sigma(D^2)}{N(N^2-1)}$$

Where rho is the measure of correlation
  D is the difference between the two ranks given for each individual
  N equals the number of individuals
The coefficient of correlation (r) can be found by the formula
  r = 2 sin

$$\frac{(\Pi\ rho)}{6}$$

In the case of ties of rank, the bracket method was employed. In this method all ties are assigned the same rank, but the next higher individual is given

of measuring correlation from ranks showed that a significant correlation existed.

From these results it is evident that when the retinal vessels showed signs of hypertension, the cerebrovascular resistance was elevated. Although there is a definite tendency for the grade of retinopathy to increase as the cerebrovascular resistance increases and this has been shown to be statistically significant, it is also true that overlapping occurs. A patient with retinal changes of a Grade I degree may have an increased cerebrovascular resistance that might also occur in a patient with a Grade II or III type of fundus. Although there is a direct relationship between the retinal and cerebral circulation, it is also evident that one cannot accurately predict from an ophthalmoscopic study of the retina and retinal vessels in a single individual the exact extent to which the cerebrovascular resistance has been elevated.

It is conceivable that, if other types of sclerosis, such as localized and diffuse

the rank that would have been assigned if the ties had received successive ranks.

r was found to be 0.67 and p was less than 0.001, indicating a high degree of statistical significance.

atherosclerosis, could be more thoroughly separated from hypertensive retinal vessel changes, a different correlation might exist for, in all probability, these factors also influence cerebral blood flow and cerebrovascular resistance.

SUMMARY

1. The cerebrovascular resistance was calculated from measurements of the mean blood pressure and of the cerebral blood flow, and the eyegrounds were evaluated in 21 hypertensive and 3 nonhypertensive individuals.

2. A statistically significant correlation was found to exist between the grade of retinal hypertensive change and the cerebrovascular resistance. The relationship was a direct one in that as cerebrovascular resistance increased, the grade of retinopathy also tended to increase.

3. It is evident that the retinal findings do reflect with some accuracy the state of the cerebral circulation but the degree of accuracy is not marked in that one cannot predict from the ophthalmoscopic findings the exact extent to which the cerebrovascular resistance has been elevated.

1930 Chestnut Street (3).

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ESSENTIAL PROGRESSIVE ATROPHY OF IRIS*

Louis W. Chang,† M.D.
Nanking, China

AND

Gaylord W. Ojers, M.D.
Philadelphia, Pennsylvania

The purpose of this article is to report three cases of essential atrophy of the iris, two of which showed peripheral anterior synechias in the region of developing iris atrophy. Such a relationship seen in a relatively early development of the disease suggests that the atrophy may be secondary to traction upon the delicate iris tissue. The third case was complicated by a severe secondary glaucoma which suggests that peripheral anterior synechias would have been seen if either a slitlamp or gonioscope had been available for the examination.

Essential iris atrophy is an uncommon disease, occurring predominantly in young women, in which the tissue of the iris disappears slowly and without symptoms. These patients usually consult an ophthalmologist because of an eccentric pupil or symptoms of secondary glaucoma which commonly accompanies the condition. Fortunately, the disease is rarely bilateral.

The atrophy usually begins in such a way that the pupil becomes eccentric and eventually may be pulled to the base of the iris. During this time the pigment epithelium often becomes everted. Opposite the displacement of the pupil, small holes may appear either superficially in the anterior layers or perforating the entire thickness of the stroma. Later these enlarge and may even coalesce. Less frequently the disease begins in another way. Small depigmented areas are noted first. These gradually extend in size and fuse to involve the different layers or entire thickness of the iris.

Although this disease is rare, reports of cases have been appearing in the literature with not too irregular frequency since 1886.[1] Because gonioscopic examination has been done in only five cases (McKeown,[2] Post,[3] Scharf,[4] and Sugar[5]) such an examination of our first patient is of interest.

CASE REPORTS

CASE 1

History. Mrs. A. R., aged 37 years, white, was first seen on April 29, 1947, through the courtesy of Dr. Francis Heed Adler. She had noted that the pupil of the right eye was irregular. Vision was 6/7.5 in each eye uncorrected.

External examination was normal except for the eccentric right pupil which was displaced slightly downward and considerably outward. Both pupils reacted promptly, although the lower outer third of the right pupil seemed quite immobile. Two pigmented areas could be seen at midportion on the iris of the right eye (fig. 1).

Ophthalmoscopy. On the temporal side of the right undilated pupil a space between the iris and the lens exposed the anterior portion of the ciliary processes. The iris appeared to be pulled forward by some cicatricial process in the angle. No mass was seen.

Slitlamp examination revealed that the right iris angle had been obliterated from approximately the 7- to the 8:30-o'clock positions; the iris appeared to be drawn in this direction with resultant pupil displacement. Neovascularization was seen at the point of adherence. No evidence of a perforating injury could be found. The dark areas on the iris previously mentioned represented areas
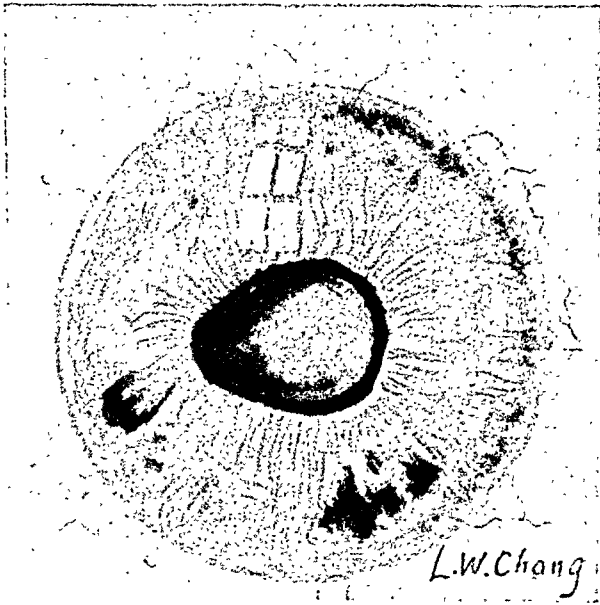
Fig. 1 (Chang and Ojers). External appearance of right eye as seen through a magnifying glass. The deviation of the pupil and holes of iris are clearly shown. (Case 1.)

and the anterior portion of the ciliary body were visible. No mass could be visualized pushing the iris forward (fig. 2).

Tension was 25 mm. Hg (Schiøtz), O.U., on August 25, 1947. No increase of tension was found on successive visits. Peripheral synechias were more extensive on September 27, 1947.

CASE 2

History. The following case of F. W., a 23-year-old white soldier, was contributed by Dr. Harold G. Scheie. The left eye showed a marked iris atrophy with displacement of the pupil temporally.

Gonioscopic examination could not be done but slitlamp examination demonstrated extensive peripheral anterior synechias in the direction of atrophy. The pupil was pulled away from the lens, permitting visibility of the ciliary process between the iris and the lens, much as seen in Case 1. The rest of the ocular examination, including tension, was normal.

CASE 3

History. Miss H. N. C., Chinese, aged 15 years, was admitted to the Central Hospital, Nanking, April 17, 1947, because of progressive visual loss since childhood, greatly accentuated in the last month.

Visual acuity (with and without correction) was: O.D., hand movements at 30 cm.;

of atrophy in the stroma with exposure of the pigment layer. In being displaced, the iris had been pulled so far forward that it was no longer in contact with the lens from the 4- to the 10:30-o'clock positions.

Gonioscopy of the same eye showed extensive peripheral anterior synechias from the 7- to 8:30-o'clock position. Further synechias were found, both at the site of the stromal atrophy (5 o'clock) and at 10 o'clock. The iris at the areas of the larger synechias was pulled forward in such a manner that the underside of its posterior layer

Fig. 2 (Chang and Ojers). Angle chamber of right eye viewed with gonioscope. Note the peripheral anterior synechias pulling the pupillary border toward the periphery and exposing the ciliary processes. (Case 1.)
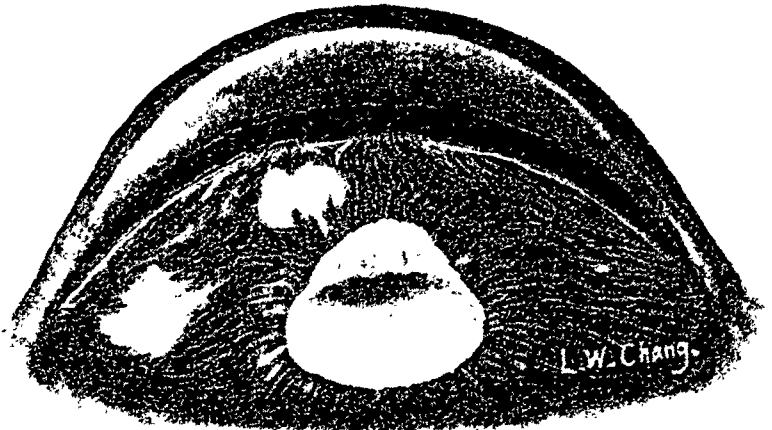
O.S., finger counting at 30 cm. Examination of lids and adnexa of both eyes was negative.

O.D.: The cornea was normal. The anterior chamber was shallow. A large colobomatous iris defect extending to the ciliary body was seen from the 5- to the 9-o'clock positions. Just at the apex of the coloboma was a small elongated hole which contracted sluggishly to light. There were no visible synechias nor ectropion of the pigment margin. Although normal crypts could be seen in the brown iris, there was no distinction between ciliary and pupillary zones (fig. 3, O.D.).

The lens was clear, and its equatorial margin could be seen through the coloboma. Fine white shreds, presumably exfoliating lens capsule, and tiny pigment deposits were present over the anterior surface. The vitreous was clear.

The eye grounds were seen with a −20D. lens. The pale disc was deeply cupped on the temporal side, and an area of choroidal atrophy extended from this side to the normal appearing macular region. Coursing over the tessellated retina were normal retinal vessels.

O.S.: The iris was similar in structure and color; however, the defect was so huge that it occupied about two thirds of the chamber. The defect was kidney-shaped and extended to the temporal limbus from the 1- to 5-o'clock positions. From the 2- to 3:30-o'clock positions a small iris nubbin was seen attached to the ciliary body. There was a small hole at 9 o'clock which extended to the limbal region. As pilocarpine caused this area to constrict, it was assumed to be the remainder of the pupillary aperture. Fine pigment deposits and white shreds were scattered over the surface of the transparent lens. The vitreous was clear (fig. 3, O.S.).

The fundus was seen with a −25D. lens and appeared essentially the same as described for the other eye, except the cupping of the disc was not so pronounced.

Tension was: O.U., 54 mm. Hg (Schiøtz). Visual fields could not be taken because of poor vision. Tension was brought down to 17 mm. Hg, O.U., by the use of pilocarpine nitrate (2 percent) every two hours.

Fig. 3 (Chang and Ojers). External appearance of right and left eyes examined with a loupe. Note the colobomatous defects in both eyes. An attempt has been made to show the white shreds and pigment deposits on the anterior capsules of both eyes. (Case 3.)

The ultimate outcome, however, is unknown, for the patient was observed for only one week before she returned to the interior of China.

DISCUSSION

In a review of the literature of essential iris atrophy, Henderson and Benedict[6] divided the reported cases into three groups. Group I consisted of those cases with no demonstrable cause for the atrophy and uncomplicated by glaucoma. Group II was the same as the above except glaucoma was present when the case was first seen. Group III included all those cases in which the atrophy was suspected to have been secondary to some etiologic agent. Our first and second cases belong to Group I. But our third case is puzzling and may well belong to Group III.

While the appearance of the lens capsule in this last case was that of exfoliation (by loupe examination), the earliest case of glaucoma capsulare previously reported has been in a 41-year-old man (Gradle and Sugar[7]). It is possible, of course, that the process responsible for the atrophy was also detrimental to the capsule. Pigment deposits on the lens capsule may well represent a low-grade inflammatory process. On the other hand, pigment deposits are seen in some cases of primary glaucoma. It is of further interest that this case is bilateral. Only six bilateral cases have been reported (Yao,[8] Fine and Barkan,[9] McKeown,[10] Rosenberg,[11] and Czukrasz[12]) and doubt has been expressed as to the diagnosis in the case reported by Fine and Barkan (Henderson and Benedict[6]).
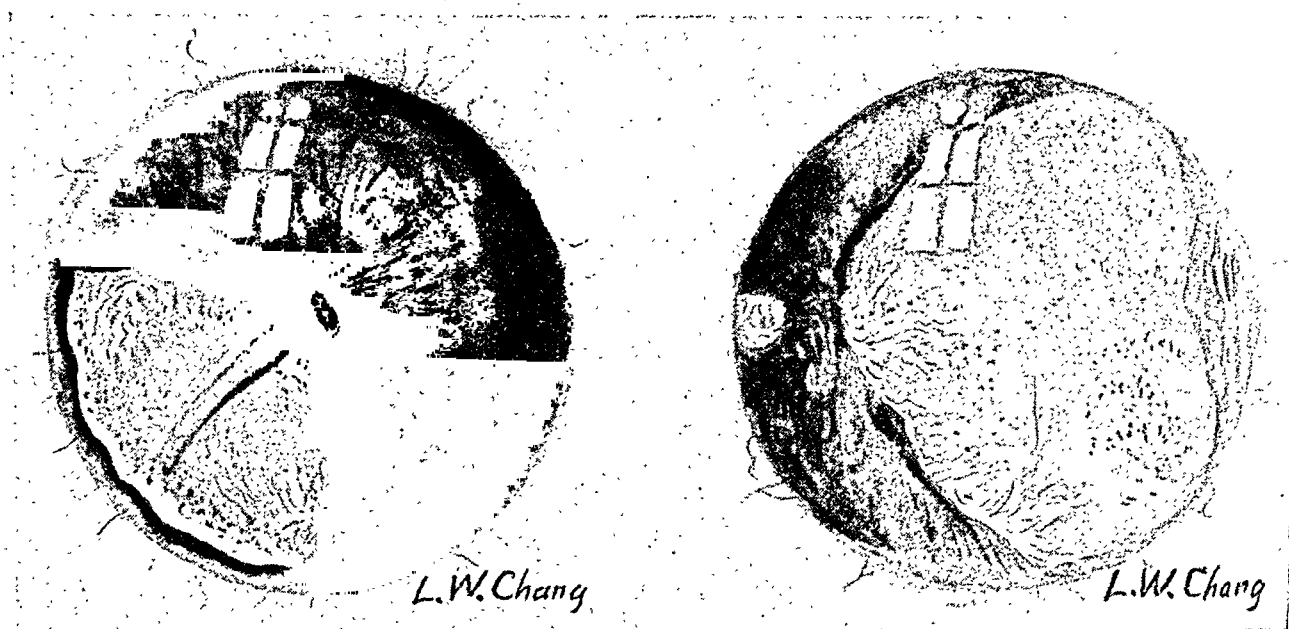
As so often happens when proof is difficult, many theories as to etiology have been presented. Larson[13] feels the condition is a congenital anomaly. Feingold[14] also suggests it is of congenital origin but places the disturbance in the blood vessels of the smaller iris circle. De Schweinitz[15] suggests some autotoxin or possibly abiotrophy.

A cytolytic process representing a perversion of a normal embryonic function has been postulated by Kricker[16] and Jeancon.[17] Von Grosz[18] favors a neurogenic factor. Vascular change is mentioned by Zentmayer[19] and Lane.[20]

Mechanistic theories start with the thought that the atrophy is secondary to the stretching of the iris (Rochat and Mulder[21]). This idea is carried further by Waite[22] who suggests an interference with the blood supply caused by the narrowing or occlusion of the radial vessels as a result of the pull on the iris tissues. The fact that our first two cases were seen to show atrophy in the line of stress caused by the peripheral synechias would support these mechanistic theories.

Evidence as to the causes of glaucoma characteristically complicating the later stages of essential iris atrophy has been well reviewed by Sugar.[5] The constant findings of peripheral anterior synechias, both by gonioscopic examination and microscopic study of enucleated eyes, appear to support Rochat's and Mulder's hypothesis[21] that the cementing together of the iris and cornea results in the slow obliteration of the chamber angle with a consequent rise in tension.

Peripheral anterior synechias were found in our first two cases, but they were not complicated by glaucoma. This need not be surprising. Only as these cases progress to the point where synechias become sufficiently extensive to embarrass the drainage system of the angle will the intraocular pressure rise. It has been estimated that as little as 70 to 90 degrees of an arc of normal angle is sufficient to allow a normal tension in narrow-angle glaucoma with peripheral anterior synechias (Kronfeld[23]). Although no synechias were seen in the case of the Chinese patient, who did have a marked rise in ocular tension, it seems almost certain that peripheral anterior synechias would have been revealed by a slitlamp or gonioscopic examination.

CONCLUSION

1. Three cases of essential iris atrophy are presented.
2. Peripheral anterior synechias were

demonstrated by either slitlamp microscopy or gonioscopy (or both) in Cases 1 and 2. It is felt that anterior synechias were probably present in Case 3 because of the presence of secondary glaucoma.

3. The peripheral anterior synechias in the first two cases were so situated that the atrophy of the iris could well have been due to the mechanical displacement and subsequent stress on the iris.

Hospital of the University of Pennsylvania.

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OPHTHALMIC MINIATURE

The more attentively we observe the phenomena of disease, and consider the effects of remedies, the more we shall be led to adopt simplicity of treatment, and the less confidence shall we place in complicated plans, or great diversity of remedial means.—Sir William Lawrence, *A Treatise on the Diseases of the Eye,* 1833.

INVESTIGATION OF THE BLOOD-AQUEOUS BARRIER IN THE NEWBORN*

I. To Ascorbic Acid

V. Everett Kinsey, Ph.D., and Blanche Jackson, Ph.D.
Boston, Massachusetts

The objective of these studies was to investigate aqueous-humor dynamics in the newborn. Information on this subject may be essential for an understanding of the significance and possible relation of several manifestations of eye pathology observed in retrolental fibroplasia. Specific structural abnormalities which may be related include shallow anterior chamber, thin and elongated ciliary processes, and presence of a vascular system behind the lens. Abnormally low ascorbic acid concentration of the aqueous humor in eyes with retrolental fibroplasia[1] (approximately that found in the blood) indicates that the composition of the aqueous humor differs from that characteristic of the normal, adult human being.

In preliminary studies,[2] the level of ascorbic acid in the aqueous humor of the rabbit at birth was shown to be the same as in the plasma. After the 9th day, a progressive increase occurs until the normal adult level (25 to 30 mg. percent) is reached approximately 27 days after birth. This was thought to indicate that secretion by the ciliary body does not start until the animals are approximately 9 days old.

Further consideration of the implications of these results suggested that the situation is probably more complex, and that additional investigations were necessary for a clearer understanding of the changes undergone in the dynamics of intraocular fluids in the developing eye.

The immediate objects of the present paper were, first, to determine whether the changes in concentration of ascorbic acid in the aqueous humor of other species vary with age in a manner similar to that in the rabbit, and secondly, to consider other mechanisms which might account for the experimental findings.

Methods

Samples of aqueous humor were obtained from rhesus monkeys varying in age from newborn to 4 years.[†] In all instances, the aqueous humor was transferred directly from the microsyringe used for collection of the sample into tubes containing 0.2 ml. of 5-percent metaphosphoric acid. After centrifuging, analysis for ascorbic acid was made by titration with 80 mg. percent 2,6 dichlorophenolindophenol, again utilizing micro techniques.

The specimens of aqueous humor from infants were obtained as soon after death as possible; the time elapsing between death and collection of the sample varied from 45 minutes to 48 hours. Since all of the samples collected 12 hours or more after death fell within the normal adult range, it is assumed that little, if any, destruction of the vitamin occurs *in situ* in the eyes of infants who were placed in cold rooms prior to autopsy. In addition to the samples of aqueous humor obtained after death, several specimens were obtained from eyes enucleated from living individuals.

Results

The ascorbic-acid concentrations of aqueous humor obtained from monkeys of var-

† The monkeys (Macaca mulatta) for this study were made available through the courtesy of Dr. G. van Wagenen of the Department of Obstetrics and Gynecology, Yale University School of Medicine. The colony is maintained through funds donated by the Nutrition Foundation, Inc., New York, New York.

ious ages are given in Figure 1. The concentration from the day of birth until shortly after the first month of life is 2 to 3 mg. percent, or approximately the same level as that in the blood. Following this, the concentration increases until the adult level of 16 to 19 mg. percent is reached about the 6th month.

The ascorbic-acid content of aqueous humor obtained from human beings of different ages is plotted in Figure 2. While the data are few, they seem to indicate that (1)

DISCUSSION

The results of all three species studied—the rabbit, monkey, and man—indicate that the aqueous humor dynamics during the developmental stages of the eye differ markedly from those of the adult with respect to ascorbic acid at least. It seems worthwhile to consider the possible factors which might account for this variation.

As a basis for understanding alterations in the mechanism of aqueous-humor dynamics, particularly as they relate to the transfer of
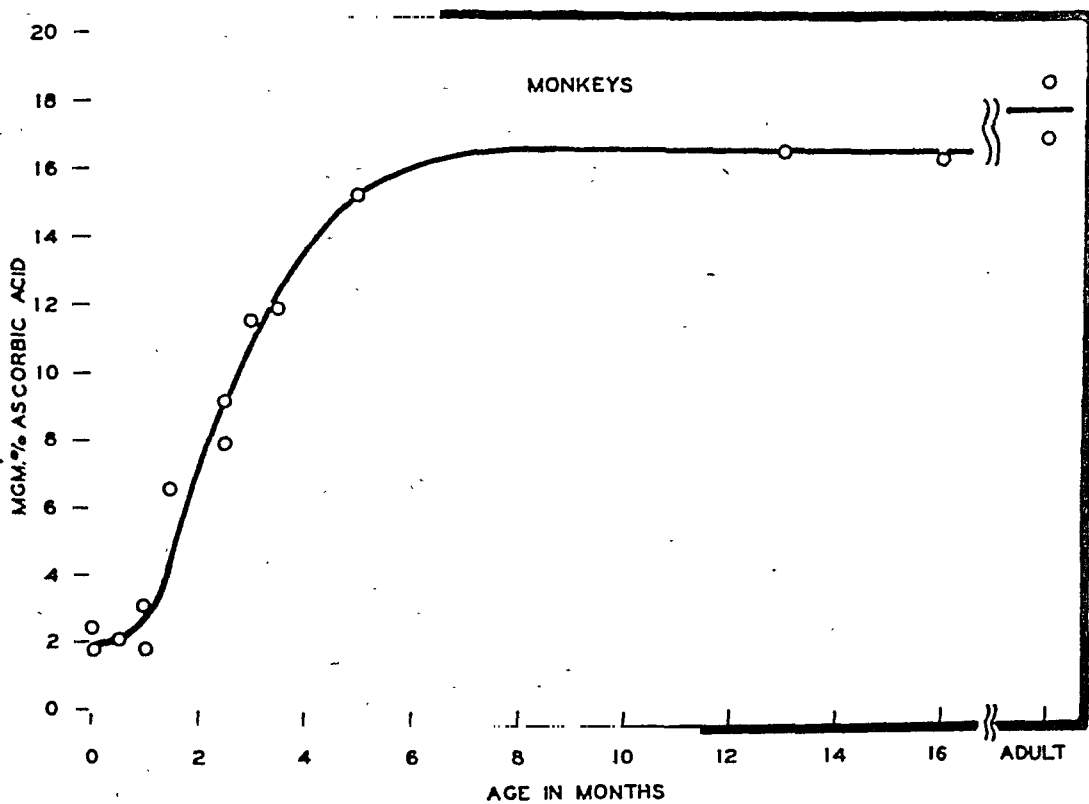
Fig. 1 (Kinsey and Jackson). This graph shows the concentrations of ascorbic acid in the aqueous humor of monkeys at various ages.

the concentration increases during the last 2 months of fetal life, and (2) individual variation of concentration of ascorbic acid in the aqueous humor at birth is less than that encountered later in life. Because of the variation in the ascorbic-acid content of the adult aqueous humor, the normal level cannot be well defined. However, the ascorbic-acid concentration of the aqueous humor of the full-term infant falls within the range of that of the normal adult having an adequate ascorbic-acid intake.

ascorbic acid, some of the factors thought to influence the accumulation of this acid in the adult eye will be described.

Ascorbic acid is believed to act as a mediator in the oxidation-reduction reactions thought to be associated with the transfer of electrolytes from the blood to the posterior chamber.[3] In the chain of energy-yielding reactions, the vitamin apparently is oxidized to the dehydro form, in which state it is presumed to diffuse into the aqueous humor to be reduced by the sulfhydryl

groups in the lens. To account for the relatively high concentration in the aqueous humor compared with that in the blood, it is further assumed that the blood-aqueous barrier is less permeable to the diffusion of ascorbic acid than to dehydroascorbic acid. Steady-state conditions are further depend-

discussed heretofore[2] to account for differences in concentration of ascorbic acid in the newborn and that reached subsequently was alteration of the rate of secretion. Final evaluation of this factor should properly be delayed until evidence is obtained from direct studies of the ciliary body at different
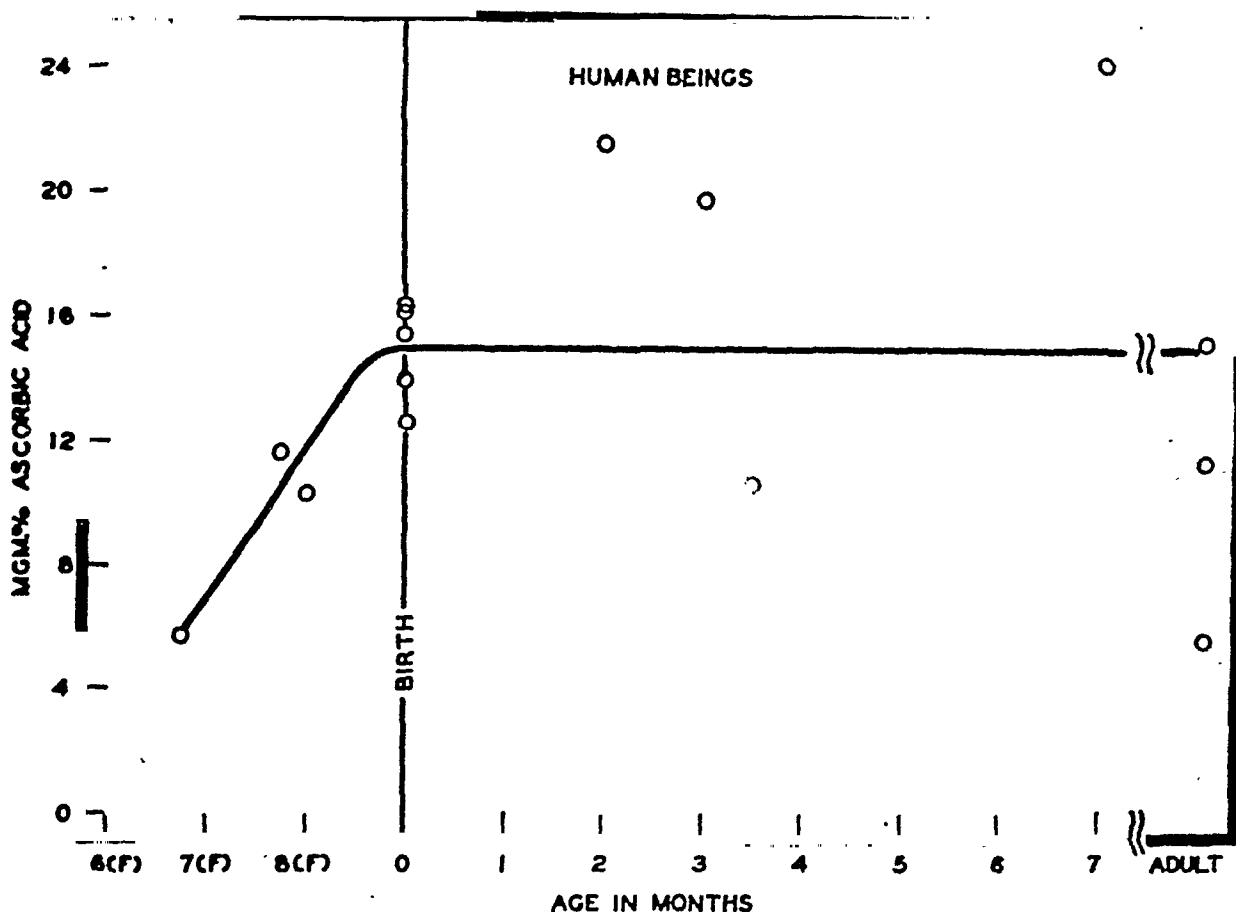
Fig. 2 (Kinsey and Jackson). This graph shows the concentrations of ascorbic acid in the aqueous humor of human beings at various ages.

ent upon the rate of loss of ascorbic acid from the anterior chamber by the flow or leakage process described elsewhere.[4]

Thus, the eventual concentration of ascorbic acid in the aqueous humor may be dependent on (1) the rate of secretion and/or diffusion of dehydroascorbic acid into the aqueous humor, (2) the capacity of the lens to reduce dehydroascorbic acid to ascorbic acid, (3) the relative permeabilities of the blood-aqueous barriers to the oxidized and reduced forms, and (4) the rate of outflow.

Of the factors listed above, the only one

ages, using the techniques devised by Friedenwald and Stiehler for selective transfer of acid and basic dyes by ciliary epithelium and stroma, distribution of the enzyme systems associated with the secretion, and so forth.[5]

Regarding the capacity of the lens at various ages to reduce the dehydroascorbic acid to ascorbic acid, analysis of a 1-day-old rabbit lens showed the glutathione concentration to be 169 mg. percent. This concentration is approximately half that found in the normal adult and, assuming that its rate of re-

newal is at least as high as that in the adult lens, it would be more than sufficient to reduce the small quantity of dehydroascorbic acid transferred into the aqueous humor of the eyes in the animals at this age. It may be significant, too, that the ascorbic-acid concentration of the lens is already at the normal adult level (11 mg. percent).

The third factor already mentioned which influences the concentration of ascorbic acid in the aqueous humor is the relative permeability of the blood-aqueous barrier to the diffusion of ascorbic and dehydroascorbic acids. In the adult, the chief sites of the blood-aqueous barrier are the iris and ciliary body, but in the eye of the newborn the tunica vasculosa lentis network of the hyaloid system must also be considered as part of the blood-aqueous barrier.

It is pertinent to follow the condition of the hyaloid system during the period in which the concentration of ascorbic acid in the aqueous humor is increasing to the level characteristic of the adult eye. The rabbit eye at birth is richly supplied by the hyaloid system. At this time, the ascorbic-acid level in the aqueous humor is the same as that found in the blood. By the 9th or 10th day after birth, although the system has regressed significantly, blood is still circulating through it, and the ascorbic acid concentration of the aqueous humor is still at blood level. By the 14th or 15th day, however, the vessels have disappeared completely, and concentration of ascorbic acid in the aqueous humor is increasing but has not yet reached the level found in the adult eye.

Information now available concerning the time of regression of the hyaloid system in the rhesus monkey is incomplete, being limited to observations made on the eye of a single animal obtained on the day of birth. In this eye, the lesser branches of the hyaloid system were already partially closed. It is possible that the hyaloid vessels of the monkey may continue to function to some degree for several weeks after birth. If this is true, the age at which the hyaloid system regresses in the monkey also seems to coincide with onset of increase in concentration of ascorbic acid in the aqueous humor.

In human beings, the main trunk of the hyaloid artery shrinks considerably during the 7th month of fetal life, and the pupillary membrane begins to atrophy. By the end of the 9th month, the pupillary membrane and the hyaloid artery have practically disappeared.[6] Analysis of the sample of aqueous humor obtained from the youngest human fetus (6¾ months) suggests that at this stage the ascorbic-acid concentration has already begun to rise. Thus, in man also, the time of regression of the hyaloid system parallels the initial increase in concentration of ascorbic acid in the aqueous humor.

The analyses from all the species therefore indicate a reasonably close time relationship between the breakdown of the hyaloid system and the initial rise of ascorbic acid in the aqueous humor. The final (adult) level of ascorbic acid does not, however, coincide with the complete regression of the hyaloid system in all the species. In the rabbit, the delay amounts to about 12 days; in the monkey, possibly as long as 4 to 5 months; and in man, the correlation appears to be relatively closer—of the order of 2 weeks. Direct experimental evidence has been obtained that ascorbic acid exchanges between blood and aqueous humor in the rabbit during the 12-day period following closure of the hyaloid system more freely than it does in the adult eye.[7]

The possible effect produced by variations in the rate of outflow on the concentration of ascorbic acid in the young and adult animal remains to be discussed. Kinsey and Grant[4] have considered the influence of this factor on the distribution of solutes between the aqueous humor and the blood under steady-state conditions and have expressed the relationship mathematically.

If it is assumed that in the adult rabbit eye the major loss of ascorbic acid is by flow, and evidence for this has been obtained,[7] and also assumed that the relative

rate of secretion of ascorbic acid into the posterior chamber is the same for young and adult rabbits, then it follows that the rate of outflow would have to change tenfold to account for the tenfold change in ratio of concentration in the aqueous humor to concentration in the blood, that is, from 20 found in the adult rabbit to 2 as found in rabbits 8 to 10 days old.

While changes in permeability factors of this order of magnitude are frequently encountered, it seems unlikely that any factors known to influence the rate of flow, such as intraocular pressure or changes in width of the angle, would vary to such a degree.

In conclusion, it seems that the observed changes in concentration of ascorbic acid could be accounted for almost entirely by changes in the permeability of the blood-aqueous barrier undergone during this period of development. From the fact that the ascorbic-acid levels in the aqueous humor and blood were indistinguishable during the period in the life of all the species when there is a discrete hyaloid system present, it might be inferred that the presence of this vascular system alone could account for the experimental findings. The subsequent delay in the rise of ascorbic-acid concentration of the aqueous humor suggests that the barrier properties of the iris and/or ciliary body are also changing during the time interval under consideration. It is possible also that simultaneous variations may occur in the secretory rate and perhaps in rate of leakage.

SUMMARY

The ascorbic-acid concentration of aqueous humor has been determined in young monkeys (Macaca mulatta) and in infants of various ages. In the monkey, as was shown previously for the rabbit, the concentration increases from that in the blood to that characteristic of the adult eye during the period 6 weeks to 6 months after birth. In the human being, a similar rise occurs between the 6th and 9th fetal months.

The following factors were discussed to account for the experimental findings:

1. Increased rate of secretion.
2. Capacity of lens to reduce dehydroascorbic acid to ascorbic acid.
3. Variations in properties of blood-aqueous barrier.
4. Alterations of outflow.

The observed changes in concentration of ascorbic acid seem to correlate best with regression of the hyaloid system and subsequent changes in the permeability of the iris-ciliary body barrier between the blood and the aqueous humor.

243 Charles Street (14).

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TRAUMA TO THE HEAD WITH PARTICULAR REFERENCE TO THE OCULAR SIGNS*

PART II.† INJURIES INVOLVING THE HEMISPHERES AND BRAIN STEM; MISCELLANEOUS CONDITIONS; DIAGNOSTIC PRINCIPLES; TREATMENT

ARTHUR B. KING, M.D., AND FRANK B. WALSH, M.D.

Baltimore, Maryland

3. HEMISPHERE AND BRAIN-STEM LESIONS

HEMISPHERE LESIONS

In addition to the temporary neurologic signs produced by intracranial collections of blood, a variety of neurologic defects may remain following injury to the hemispheres and brain stem.

Monoplegia, apraxia, hemianopia, aphasia (sensory and motor), and cortical blindness may follow cortical lacerations produced by indriven bone fragments and foreign bodies. Injury to a major vessel, especially the middle cerebral or one of its larger branches, results in hemiplegia. Signs produced by injuries tend to be pronounced at first and to show great improvement with passage of time.

Lacerations at the base of the frontal and temporal lobes are a common occurrence and produce extensive subpial and subarachnoid hemorrhages. Not infrequently large parts of these lobes are reduced to a hemorrhagic necrotic pulp. While signs of high intracranial pressure are prominent, few localizing symptoms are seen. Convulsions may be severe.

Lowered blood pressure due to hemorrhage or shock may predispose to thrombosis. Often thromboses develop while the patient is conscious. The occlusions may be arterial or venous. Depending upon the extent of the thromboses various symptoms ensue. Coma, asphyxia, and hemiplegia are most often seen. Dural sinuses may become thrombosed and produce tremendous increase in the intracranial pressure. Cerebral paraplegias (superior longitudinal sinus) and proptosis (cavernous sinus) are occasionally seen.

Ocular Signs of Hemisphere Lesions

Apart from conjugate deviations of the eyes which are associated with epileptiform seizures (occurring in a small percentage of cases of head trauma) pronounced deviations of the eyes occur infrequently as a result of injury to the head.

Frontal lobe lesions. It might be anticipated that injury to the frontal lobe would often produce pronounced deviation of the eyes (to the side of a destructive lesion and away from an irritative lesion). Undoubtedly such deviations occur in some instances but they do so rarely and we have not observed them. It is to be assumed that the anterior oculogyric pathways are interrupted infrequently. This applies also to the posterior oculogyric pathways if pronounced conjugate deviation is an accurate criterion.

Prefrontal lobotomy affords an interesting example of frontal lobe trauma. In such cases we have not observed pronounced deviation of the eyes in any instance. Occasionally there has been inabilty to move the eyes on request for a short time following operation but this has been inconstant and seemed to be due to lack of attention.

Pseudohemianopia develops in some instances of excision of a frontal lobe. In some such cases there has been a transitory deviation of the eyes to the side of the removal; also there has been what appeared to be defective perception in the contralateral visual field. This is not a true hemi-

anopia and probably represents only lack of attention.

Lesions of the parietal lobe. Lesions involving the parietal lobe produce sensory involvements predominantly. Among these are sensory fits, loss of postural sensibility, and loss of tactile discrimination in the areas of the body on the opposite side corresponding to the cortical representation.

Stimulation of the angular gyrus produces conjugate deviation of the eyes to the side opposite the stimulation just as in the instance of stimulation to Area 8 of the frontal lobe. Also there may be deviation of the eyes to the side of a destructive lesion. Such ocular deviations are neither as pronounced nor as constant in their occurrence as when the frontal lobe is involved. The ocular deviations associated with lesions involving this secondary center are due to interference with the optic fixation reflexes; that is, they influence the posterior oculogyric pathway.

The angular gyrus is an area which is considered of great importance. It is thought of as a center for word-memory. Lesions situated in this general region produced word blindness (alexia). There are various types and degrees of word blindness. In its purest variety it is fairly well agreed that the angular gyrus region usually is affected.

Henschen's[31] extensive work on this shows, however, that pure word blindness may be associated with lesions situated elsewhere in the cortex. With word blindness there may be an associated hemianopia, and it is recalled that involvement within the parietal lobe may directly involve the optic radiation. It has been suggested that a lesion in the superior portion of the cuneus may produce alexia and that it may originate in involvement of the occipital lobe or as the result of a lesion in the corpus callosum.

Spatial agnosia has resulted from bilateral involvement of the angular gyrus as described by Holmes[32] in traumatic cases. His patients exhibited errors in judgment as regards distances, walking into obstacles in the path, inability to count coins, accommodation retardation, and loss of the blink reflex as well as loss of stereoscopic vision.

Riddoch[33] described such cases when the phenomena observed in Holmes's cases were present only in the homonymous half-fields. Trescher and Ford[34] described a case in which there was loss of object vision in the homonymous half-fields as a result of splitting of the corpus callosum; also in their case there was loss of topographic memory which characterized some of Holmes's cases.

Brain[35] has described such anomalies of vision as are mentioned above in a person whose fields were normal. Defects in integration of visual perceptions at a higher level than the primary projection areas arise from lesions involving the parietal, occipital, temporal, and even the frontal lobes. Our present knowledge regarding the lesions responsible for these abnormalities is incomplete. They have little significance in topical diagnosis other than they arise as a result of injuries in the region of the angular gyrus and posterior to it.

Lesions of the temporal lobe. In this lobe, visual-field defects are the outstanding characteristic. Homonymous sector-shaped defects indicate interruption of the lower portion of the optic radiation where the fibers are fanned out in the forward portion of the temporal lobe. Sector defects and complete homonymous hemianopia with or without sparing of the macula originate in interruptions of the optic radiation at the level of the temporal lobe. In some instances the field defects are not completely congruous, as has been pointed out by Harrington.[36] The suggestion that incongruity of the defects is due to pressure upon or involvement of the underlying optic tract has been mentioned by Traquair[37] in the instance of tumorous involvement.

Occipital lobe lesions. The cortical localization concept of Holmes and Lister[38] was established during World War I on the basis of a study of war wounds, and during World War II has been verified. Other evidence

which supports this localization concept has been obtained from patients who have been subjected to removal of part or all of an occipital lobe.

Occipital lobe lesions may be responsible for deviation of the eyes due to interference with the optic fixation reflexes.

Total blindness results from removal of the occipital lobes. Removal of one occipital lobe results in hemianopia which may or may not be characterized by "sparing" of the macula. It is our concept that the macular fibers do not cross after reaching the geniculate body, and that Verhoeff's[39] explanation for "sparing" is correct in all probability. He has pointed out that interference with the optic fixation reflexes may account for sufficient unsteadiness of fixation so that "sparing" results; in anteriorly situated lesions where "splitting" is encountered the optic fixation reflexes are not influenced.

Posterior injury of the occipital lobes produces central scotomas as shown by Holmes, and later by Greear and McGavic.[40] The central field defects have usually been associated with other field defects.

Homonymous quadrantic defects have come to be recognized as indicative of a radiation lesion but not necessarily a lesion of the occipital lobe. Complete loss of the lower visual fields, or homonymous quadrantic defects in the lower fields, have been observed to result from trauma. With penetrating injuries such loss of upper visual fields must be rare because the injury which produces them in this instance would penetrate dural sinuses and death would occur immediately.

Feigenbaum and Kornblueth[41] described ring scotomas in the visual fields as a result of injury to the occipital lobes. Greear and McGavic described bilateral homonymous hemianopia as a result of war injury. Holmes[42] charted completely congruous homonymous field defects originating in injury to the occipital cortex. From this brief recounting it would seem that the field defects associated with occipital lobe injuries may vary widely; they are congruous and, of course, homonymous.

We wish to draw attention to a group of cases seen in civilian practice which may be compared with cases seen as a result of war wounds. In cases in which air is injected into the posterior horn of the lateral ventricle there may be loss of vision which it would seem obvious must be attributed to involvement of the occipital lobes in large part.

In such cases we have observed almost complete blindness as a temporary phenomenon, bilateral homonymous hemianopia, and homonymous paracentral scotomas. In the cases with which we are familiar the visual defects and associated visual field changes have always cleared in greatest part, usually completely. These cases are comparable with other traumatic cases since trauma, even though elective, initiated the symptomatology. Again, similar to the traumatic cases, the initial loss of visual field is much more pronounced than the final field defects.

It was stated in the first paragraph of this paper that lesions involving the visual association pathways are not considered in any detail in this paper. The subject is extremely complicated and contentious. However, we may point out that alexia (word blindness) and object blindness (mind blindness) are each reported to have arisen as the result of occipital lobe injury. They are closely related affections or different degrees of the same type of involvement.

Convergence and divergence paralysis. We have seen what seemed to be examples of convergence and divergence paralysis in cases of head injury. Convergence paralysis has been observed on several occasions, usually as a late result. Divergence paralysis occurs less frequently. The diagnosis of divergence paralysis invariably had been made with some misgiving.

It is our belief that convergence and divergence palsies resulting from trauma, or from any cause, do not prove or disprove the existence of supranuclear centers concerned with the indicated capacities. All supranu-

clear centers, so-called, are theoretical and have not been demonstrated anatomically; they make possible visualization of associated ocular movements.

Immediately after trauma has occurred to the head, sometimes when it has been mild, there is incoördination in the movements of the eyes amounting to dissociation. Usually as the patient recovers the eyes become parallel, or, less often, muscle palsies develop.

With severe head trauma, divergence of the eyes is commonly observed during the period of unconsciousness. When such divergence is associated with dilated pupils the prognosis is grave.

Observation of injury cases does not clarify the situation as regards cortical control of convergence and divergence. However, it is quite certain that such control exists. Divergence of the visual axes during deep sleep, deep anesthesia, and following trauma supports this concept.

Cortical Blindness

Mention has already been made in this paper of bilateral homonymous hemianopia, which, in the absence of "sparing of the maculas" amounts to cortical blindness in many instances. There are several prerequisites to the diagnosis of cortical blindness. As enumerated by Marquis[43] these are: (1) Complete loss of all visual sensations including loss of appreciation of light and dark; (2) loss of lid closure reflex on exposure to bright light and threatening gestures; (3) retention of pupillary response to light stimulation, and on convergence; (4) normal retinas on ophthalmoscopic examination; (5) normal motility of the eye.

In cases of cortical blindness there may be hemiplegia, sensory disorders, aphasia, and disorientation, and consequently the diagnosis often is difficult. Not uncommonly individuals who are quite blind maintain that they can see; this is known as anosognosia.

Cortical blindness undoubtedly occurs as a result of injury, but it occurs infrequently in its complete form as defined above. In cases of blindness, partial or complete, following injection of air into the posterior horn of the lateral ventricle it seems probable that there is a degree of cortical blindness. In such cases blindness may be the only symptom. The fact that such patients recover in almost all instances is proof that there has not been death of cells. It seems probable that spasm of the posterior cerebral arteries may account for such blindness in many instances.

Visual Hallucinations

We have had little or no experience with visual hallucinations as a result of trauma. Weinberger and Grant[44] concluded that visual hallucinations have no value in topical diagnosis. They found that they were associated with lesions involving the optic pathways at many levels. They concluded that they represented psychologic phenomena involving the total integrative activity of the mind, and depended upon constitutional factors and not on cortical psychic organization. Our experience points to temporal lobe involvement when hallucinations are "formed" and to the occipital lobe when they are sensations, such as lights.

BRAIN-STEM LESIONS

Closed injuries to the brain produce widespread multiple, small hemorrhagic petechias. If the hypothalamus, midbrain, and pons are traumatized, hyperthermia, tonic fits, and respiratory distress are seen. The tonic fits are spontaneous or follow painful stimuli. Their presence gives a grave prognosis since when they appear the injury is rarely survived. Tonic neck reflexes are sometimes present.

Hemorrhages and edema about the aqueduct of Sylvius may occlude it, producing acute hydrocephalus. Many of the incoördinated eye movements and transient cranial nerve palsies which are associated with injury may be so produced. Frequently multiple small hemorrhages in the brain stem

are the only postmortem finding in patients who die as a result of head trauma.

Cerebral edema produces prolonged unconsciousness and many deaths. This is particularly true when the vital centers at the base of the brain are involved. Trauma to the cerebral hemispheres may result in a similar symptomatology as a result of herniation of the temporal lobes through the tentorium and of the cerebellum through the foramen magnum.

Because of such herniation the respiratory centers and other vital centers in the pons and medulla are compressed, thus resulting in prolonged coma or death. Under such circumstances, neurologic findings are the result of a combination of direct pressure, indirect pressure, acute hydrocephalus, and anoxia. Frequently it is quite impossible to state what produces any particular symptom.

Recently Kremer, Russell, and Smyth[45] have described several cases of severe head injury with damage about the aqueduct. They found that ataxia, incoördination, and prolonged loss of ability to speak were outstanding symptoms.

Ocular Signs of Brain-Stem Lesions

Frequently it is impossible to determine the precise site of the lesions which are responsible for incoördination of the eye movements in cases in which there has been injury to the base and presumably injury to the brain stem. It is our belief, however, that injuries to the brain stem are productive of transient ocular muscle palsies in a large percentage of cases of head injury in which recovery occurs.

Ptosis, either unilateral or bilateral, is not an uncommon finding. Certainly it occurs more frequently than definite conjugate deviation of the eyes or pronounced weakness of conjugate movement. In a majority of cases of injury to the brain stem the incoördination of the extraocular muscles is not pronounced. Probably when pronounced paralyses occur with lesions at this level the patient rarely survives.

Usually it is impossible to differentiate between nuclear and intranuclear lesions in such cases on the basis of examination of the eyes. Nuclear lesions involving the third nerve can be predicted with some degree of certainty, certainly not lesions involving the fourth and sixth nerves unless, with the sixth, there is an associated seventh nerve palsy.

Conjugate deviations of the eyes which originate in brain-stem lesions, notably in the pons, tend to be permanent as compared with deviations which originate in lesions of the hemispheres which tend to be transient.

Nystagmus and other involuntary movements of the eyes. Not uncommonly following trauma to the head there are involuntary coördinated movements of wide amplitude which resemble searching movements. These often come on as consciousness is returning. They are transitory and of no localizing significance.

In a small percentage of cases there is jerky nystagmus of wide amplitude seen in individuals who, while conscious, invariably vomit and complain of severe dizziness and unsteadiness. They present the picture of an acute labyrinthitis and usually suffer from fracture of the temporal bone in the region of the semicircular canals. In our cases such individuals usually have exhibited unilateral deafness.

Certainly, when following trauma nystagmus is present in association with deafness, the localization is obvious; there has been fracture of the temporal bone or damage to the vestibular apparatus.

In other injury cases when nystagmus persists the nystagmus probably points to brain-stem damage. Nystagmus which may be dependent on interference with optic-fixation reflexes is a very uncertain affection.

4. MISCELLANEOUS CONDITIONS

FAT EMBOLUS

When head trauma occurs, other parts of the body are often severely traumatized. Particularly when the long bones are fractured,

fat emboli may complicate the neurologic status. The lesions are produced by free liquid particles of fat in the blood stream. These particles plug the capillaries and small veins producing focal areas of necrosis.

The injury which produces fat emboli may be mild or severe. Fractures of bones, jarring of the skeleton, and trauma to the subcutaneous and intramuscular fat and to fatty visci sets liquid fat free. If there are severed veins in the vicinity, the fat may be forced into them. Usually there is a latent period of 48 to 60 hours before the appearance of symptoms, which, however, occasionally appear within 30 minutes.

Microscopic sections of the brain shows capillaries and the smaller vessels filled with fatty globules. Around plugged vessels there is an area of necrosis surrounded by a ring of hemorrhage. All parts of the brain are affected.

Vance[46] reported fat emboli in the lungs and kidney in 102 of 104 fatal traumatic cases. However, fat emboli were severe in only 11 cases and were considered as productive of the fatal termination in three instances.

The earliest symptoms are dyspnea, restlessness, tachycardia, and precordial pain. Then there is insomnia, memory disturbances, disorientation, and delirium. Stupor and coma develop in the terminal stages. As the coma deepens there is rigidity and tonic convulsions. In the terminal stages the muscles become flaccid and there is loss of sphincter control. Death due to respiratory failure supervenes about 1 to 4 days after the onset of coma.

Fat emboli in the retina are observed infrequently, but in all probability they are present more frequently than reported cases would suggest. Certainly they are not usually looked for in cases of trauma, or in fracture cases. Our experience is limited to a single case in which there was no history of trauma to the head. There were no visual symptoms suggesting the presence of retinal fat emboli. The patient, a young girl, had suffered a

fracture of the tibia, and a member of the house staff on doing a routine ophthalmic examination, detected the retinal changes which were observed several days after the accident occurred. Within 2 or 3 weeks the retina had become entirely normal. At no time had there been any reduction of visual acuity.

Retinal fat emboli appear as patches of white semihard exudates situated in the superficial retina about the posterior of the eye. In the single case we have studied the accumulations were circular. Some were almost as large as the disc, others were much smaller. In one instance, an underlying vessel was hidden from view. Most of the patches were well away from the retinal vessels. In our case there was gradual disappearance of the patches without development of scar.

CARDIAC RESPONSES TO INJURY TO THE HEAD AND FACE

Firm pressure on one or on both eyeballs slows the normal pulse rate and frequently reduces the rate of an auricular tachycardia. This response is known as the oculocardiac reflex. Often it is associated with a sensation of faintness and nausea.

It has been assumed that there is a reflex arc connecting the fibers of the ophthalmic nerve with the nucleus of the vagus. Pressure on the eye, or perhaps pain in the eye, or pressure within the orbit, sets up a train of action which ultimately stimulates vagus fibers thereby producing an inhibitory action on the heart, gut, and vasomotor tone. Exact connections between the fifth and tenth nerves have not been demonstrated histologically. The reflex has been observed as a physiologic phenomenon from pressure of the fingers, also as a result of intraocular infections, intraorbital hemorrhages and injections, and blows on the face which produce bruising and edema.

It immediately becomes apparent that the presence of the oculocardiac reflex in an individual who has suffered an injury to the

head may cause confusion as regards the diagnosis. Recently we observed a child who was struck just below the eye with a baseball bat. He was brought to the hospital to have a superficial laceration of the cheek treated.

When he was examined it was noted that he had an enlarged, oval pupil on the side of the injury. The pupil did not react to light either directly or consensually; there was a small amount of blood staining of the lower eyelid and it was thought there might be mild intraorbital hemorrhage. The pulse rate varied from 54 to 60 beats per minute.

He was observed for several hours without any change in his pulse rate, or any change in the abnormal pupil. On the following day his pulse rate had increased to 64 to 68 beats per minute. On the second day after the accident occurred the pulse rate was again within the range of normal for his age, 76 to 80 beats per minute. The child was not unconscious at any time.

Bradycardia seemingly present as an oculocardiac reflex may last for several days. In a child who had been kicked in the face over the lateral wall of the orbit, there was pronounced orbital hemorrhage with proptosis; there was pronounced limitation of all extraocular movements but no paralysis of any muscle. There was slight clouding of consciousness, and complaint regarding headache. There was severe nausea and occasional vomiting. The respirations were 16 to 24 per minute, and the pulse rate was 48 to 56 beats per minute. The patient was up and walking about. The pulse rate persisted essentially unchanged for four days and then periods of normal rhythm (70 to 76) developed.

It seemed as if the sinus node was being either stimulated or released from the control of the vagus intermittently. During this time, the orbital hemorrhage was subsiding and the ocular movements were improving. By the time the heart had resumed its normal rhythm, the orbital condition had almost completely cleared. The child was lucid at all times.

Knowledge regarding the occurrence of the oculocardic reflex is important in evaluation of head injuries. The slow pulse rate suggests increased intracranial pressure due to a subdural or extradural hemorrhage, or cerebral edema. However, the history of injury about the eye, and physical findings limited to the eye and orbit will usually allow one to come to the proper conclusion. In cases of doubt, the patient should be carefully observed in a hospital until there is no question about the diagnosis. It is to be recalled that the state of consciousness is of utmost importance. Usually the pulse rate is not significantly slowed without some impairment in consciousness.

Another phenomenon that we have noted in a few patients with basilar fractures or injuries to the base of the brain is periods of pulsus bigeminus. This may persist in short bursts for several days. Turning or otherwise stimulating the patient will frequently abolish the rhythm. Nurses checking the pulse of such individuals may report 30 to 40 beats per minute since every alternate beat is missed at the wrist.

The mechanism responsible for pulsus bigeminus is not at all clear. It may be related to the oculocardiac reflex. It may be due to abnormal stimuli applied to the hypothalamus. The electrocardiogram shows periods of extra systoles alternating with a normal rhythm. This has suggested that anoxemia was producing the extra systoles but clinically the patients were breathing normally and did not exhibit cyanosis.

We have observed this cardiac arrhythmia for as long as a week after injury. The periods gradually get shorter and shorter with longer intervals between them and eventually they disappear. In the cases we have studied the heart has been found to be normal.

Here again the significance of the cardiac rate must be understood. When it appears as an isolated finding, one is not justified in assuming that the patient is suffering from an intracranial hemorrhage or increased in-

tracranial pressure. The state of consciousness, the respiratory rate, and the temperature will be the best guides in evaluating the requirements for treatment.

ARTERIOVENOUS FISTULAS

Carotid-cavernous sinus fistulas are a relatively frequent sequelae of head injuries. The frequency is probably due to the unique anatomic situation, where an artery is actually surrounded by a venous sinus. This does not occur elsewhere in the body, and it is the only place inside the head where a large artery and vein lie in close approximation. Congenital intracranial arteriovenous aneurysms need not be commented upon here since they are developmental anomalies.

The site of injury producing a carotid-cavernous fistula is usually on the side of the head, about the lateral wall of the orbit or temporal region. Often the injury is so mild that consciousness is not lost. In nearly all cases there is a skull fracture that passes through the cavernous sinus. This may produce a tear in the wall of the carotid artery, or a fragment of bone may be driven into the wall of the artery.

The onset of symptoms is often rapid. The patient may notice a buzzing or humming noise in or behind the eye almost immediately, although it may be delayed. The examiner can easily hear a bruit with a stethoscope, usually loudest just over the eye. Detection of a bruit, even though it is pronounced, does not establish the diagnosis of carotid-cavernous fistula unless there is engorgement of ocular vessels and/or proptosis. The engorgement and pulsating exophthalmos may be delayed. We have on two occasions heard a bruit, one definite but soft, the other booming, in two patients neither of whom had a carotid-cavernous fistula.

Usually the conjunctiva becomes engorged and reddened within a few hours due to overfilling of the veins. In later stages it may become everted over the lower lid and we have observed alarming hemorrhages from such everted and swollen conjunctiva. Blood vessels of the sclera and lids also become overdistended within a short time.

Proptosis is delayed for several days but then proceeds quite rapidly. Following an initial increase, the exophthalmus progresses slowly. It is due to the overfilling of the ophthalmic vein. The globe pulsates synchronously with the heart beat.

Vision is good initially and the fistula may be present for many months before it is seriously affected. If the vision is poor or absent shortly after the injury, an additional lesion in the optic nerve or retina must be present. Ultimately, if the fistula is not closed as the result of operation, the visual acuity becomes low or is lost.

Papilledema in the affected eye is common according to Dandy. It occurs late. This is due to the venous engorgement. Extraocular palsies may be present, either due to direct trauma to the nerves, or due to the aneurysm with its distended veins. These palsies are usually incomplete, and often the motion of the eye is limited as a result of proptosis rather than a nerve palsy.

Pain may or may not be present, and often it is delayed in its onset. Horner's syndrome may occur if the sympathic fibers are interrupted. This is difficult to detect in the late stages.

The condition may persist for many years. We have seen a patient who had a carotid-cavernous fistula for more than 20 years. Proptosis was extreme, and vision almost gone from the affected eye. There was advanced primary optic atrophy. The veins over the lids, forehead, nose, and face were greatly distended and pulsated. The patient remarked that on occasions, these had ruptured spontaneously and that blood had spurted several feet. The hemorrhage was controlled with difficulty.

Dandy[1, 47] states that in 10 percent of cases the proptosis is bilateral. This is due to a persisting circular sinus that unites the two cavernous sinuses. He also remarks

that the proptosis is usually on the same side as the fistula but occasionally is present on the contralateral side. The bruit, however, is always loudest on the affected side.

Rarely the onset of symptoms is delayed for a few months. This is probably because the fistula is small. Besides blunt trauma, we have seen a case produced by a stab wound, in which the knife went through the supraorbital fissure and penetrated the wall of the carotid.

The diagnosis is usually not difficult. A history of trauma, distention of the veins about the eye, proptosis, and bruit are characteristic. Absence of the roof of the orbit may produce displacement of the globe, but the venous distention and the pulsation synchronous with the heart beat are not found. Tumors of the orbit and arterial aneurysms may produce proptosis and some degree of venous enlargement but bruit is absent.

Ligation of the internal carotid artery both intracranially and in the neck "traps" the fistula; it produces a cure in the majority of cases. Where the aneurysm has been present for a long time, it may be necessary to ligate the external carotid artery in addition because of collateral circulation. Ligation of veins in the orbit was at one time the only operative procedure. Now it is done only when venous distention persists after carotid ligations have been performed. In especially persistent cases, Adson[48] has found it necessary to ligate the ophthalmic artery; to cure the proptosis completely, he removed parts of the ophthalmic vein.

INTRACRANIAL BLEEDING

Intracranial bleeding is perhaps the most important complication of an acute head injury, and a fatal outcome may be due solely to bleeding that has resulted from trauma. The suspicion, detection, and evaluation of signs that hemorrhage may produce are highly important because prompt treatment is often life saving.

Blood may escape and collect in the fol-

lowing places: (1) Extradural space, (2) subdural space, (3) subarachnoid space, (4) subpial, (5) intracerebral, (6) intraventricular.

It is unusual for bleeding to develop at only one of these locations but it is common that one site may be the predominant site of hemorrhage while bleeding elsewhere is relatively unimportant.

For example, with a blow on the temporal region, a large extradural hematoma may form. Small subpial and intracortical hemorrhages in the temporal lobe may be produced at the same time but these do not change the clinical picture, or the treatment.

Each of the above subjects will be treated separately but it should be understood that, especially with severe injuries and compound fractures, any or all types of hemorrhage may occur simultaneously.

1. Extradural Hematoma

Bleeding from a ruptured middle meningeal artery or its branches is the usual cause. Rarely bleeding from the other meningeal arteries or bleeding from bone may be vigorous enough to produce a significant collection of blood.

The trauma may be severe or slight. A localized injury to the temporal region, such as a blow from a blackjack, falling on a stone or curb or against a railing or step, is frequently sufficient to shear the middle meningeal artery.

Factors that permit the shearing of the artery are: (1) It is embedded in a groove in the bone so that a minor deformation of the contour of the skull may rupture it, and (2) the artery converges from the bone at right angles which permits easy shearing with small movements of the dura.

It has often been emphasized that a relatively mild injury has been sustained perhaps followed by a brief period of unconsciousness. There is then a lucid period for a varying number of hours followed by a return of drowsiness, loss of consciousness,

Jacksonian convulsions, and perhaps other localizing signs. While this history is not unusual, many cases never have a lucid period, so that deepening unconsciousness and the appearance of fresh neurologic signs are just as important.

The rapidity with which extradural hematomas may form make it an immediate surgical emergency. Usually the bleeding is sufficiently brisk to manifest itself within 1 to 6 hours. Only occasionally do symptoms first occur after 12 hours but we have seen two instances in which there were insufficient symptoms to lead one to suspect extradural bleeding for 3 days and 1 week respectively.

Besides the onset of drowsiness the appearance of facial twitches followed by focal convulsions involving the face and hand are early signs. There may be weakness of the facial musculature or of the extremities on one side of the body but these are always mild. The order of appearance of the weakness is of extreme importance. It is always face, arm, and finally the leg.

Ocular signs are of the greatest importance. Very early one may note sluggishness in the pupillary light reflex on one side. Later inequality develops. The dilated pupil soon becomes fixed to light. Ptosis is occasionally noted. It never is complete. While the dilated pupil is frequently on the side of the hematoma this is not invariable. Usually the patients have become so drowsy and uncoöperative that the ocular movements cannot be adequately tested. Not infrequently there is divergent strabismus. At other times coarse searching-type movements are noted. Papilledema is absent at first but occasionally it develops within 24 hours and usually is present in some degree thereafter. Dr. A. C. Woods and Dr. W. E. Dandy observed *development of papilledema within 3 hours.*

Other signs of increased intracranial pressure make their appearance rapidly. Most prominent is noisy, difficult respiration. By this time, the patient responds only to the most painful stimuli. When both pupils become dilated and fixed, the terminal event is not far distant.

Since many of the signs and symptoms discussed above are not pathognomonic for extradural bleeding, multiple bilateral diagnostic trephinations should be used freely in cases of doubt. The procedure is easily done under local anesthesia and is harmless. It is better to trephine many cases than to procrastinate too long and lose a patient with this easily remedied condition.

2. Subdural Hematoma

This condition varies according to acuteness and age of patient. Each type requires separate description. They are (1) acute, (2) chronic, (a) occurring in infants, (b) occurring in adults. The acute form is almost always found in association with other types of intracranial bleeding, frequently with severe injuries. Even after evacuation the mortality is high. In contradistinction, the chronic variety is almost always found in "pure culture" and the chances for survival following removal are excellent.

Acute. Bleeding into the subdural space after a severe injury may come from several places. The veins passing from the cerebral cortices to the dural sinuses may tear and cause a profuse hemorrhage. Vessels may also be ruptured by indriven bony fragments or during the process of a contrecoup injury.

Frequently acute subdural hematomas are thin. Associated conditions such as subarachnoid hemorrhage, cortical laceration, and cerebral edema occur concurrently, and the clinical picture presented by the patient is not characteristic. When found at operation or autopsy, it is difficult to say which of the conditions produced any given symptom.

Occasionally, however, these hematomas become massive, and cause marked compression of the brain. They may extend from nasion to inion and are not infrequently bilateral. At operation 200 to 300 cc. of blood

may be evacuated from a single side. Death is no doubt directly caused by the bulk of the hematoma. It has been our experience, however, that after the removal of the blood, extensive injury to the brain is almost always uncovered.

Even these massive hemorrhages frequently fail to produce localizing signs. The patient is usually deeply unconscious, often not arousing from the time of the injury. Signs of medullary compression such as difficult and irregular breathing may be the first evidence that the patient is losing compensation. Tonic fits may be seen but Jacksonian convulsions are uncommon unless there is a cortical lesion in addition. In the later stages a mild hemiparesis, or bilateral pyramidal tract signs, may appear.

Eye signs are varied, unreliable, and not characteristic. The usual divergence of the eyes and dilatation of the pupils seen with unconsciousness is common. Sometimes the pupils are small and react sluggishly to light. They may be unequal but rarely markedly so. Since the bulk of these patients are unconscious and cannot coöperate, evaluation of ocular signs due to midbrain and medullary compression are difficult.

Papilledema is extremely rare since patients with significant acute subdural hematomas rarely live more than 48 hours unless treated. In our experience preretinal (subhyaloid) hemorrhages occur in approximately 25 percent of these cases. Almost always there is an associated subarachnoid hemorrhage.

Small subdural hematomas of a few millimeters in thickness found either at operation or autopsy probably produce no special symptoms and are not responsible for the patient's condition.

Chronic subdural hematomas in adults. These collections of blood present quite a different clinical picture from those discussed above. Often it is impossible to connect them accurately with trauma. They occur very rarely below the age of 20 years, except in infancy. It is noted that they are most frequent in the 4th, 5th, and 6th decades of life. They are found 6 to 8 times more frequently in men.

Since chronic subdural hematomas have never been produced experimentally, the sequence of events in their formation and the course they pursue is inadequately understood. It is agreed that the trauma responsible for the initial bleeding is often exceedingly mild and that there may be a latent period without symptoms of from a few weeks to several months. Some authors believe that all the bleeding occurs at the time of injury while others present evidence to show that the hematoma increases its size as time passes. Rarely the mass calcifies and produces symptoms years later.

Sometime during their course, membranes form around the hematoma. The outer is thick and vascularized while the inner is thin. The outer membrane can be easily stripped from the dura but leaves a mass of bleeding points. In our experience the inner membrane can rarely be stripped from the pia without causing considerable damage to the underlying vessels and cortex.

The signs produced by chronic subdural hematoma are exceedingly variable, and they may simulate almost any intracranial condition. There may be the usual symptoms of intracranial pressure as headache, bradycardia, vomiting, drowsiness, and unconsciousness. Dandy emphasized that head pain as distinguished from headache may be a feature. Meningeal signs such as a stiff neck and a Kernig's sign may be present. Evidence of local pressure such as hemiplegia, aphasia, cortical sensory disturbances, and rarely convulsions may be produced. There are no characteristic signs. Lumbar punctures almost always yield normal spinal fluid often under normal pressure. In an adult who has suffered a head injury, and presents obscure signs suggesting brain injury, diagnostic trephinations and ventriculograms should be utilized.

In contrast to acute hematoma, ocular signs are fairly frequent and important. Papilledema may be present but is found in only about 17 percent of patients (Govan and Walsh[49]). It is precisely the same type that is observed in cases of neoplasm. It probably develops late in the course of the disease but sometimes the changes of the nervehead suggest that the papilledema is old. If of long standing, secondary optic atrophy may result. In a few instances pronounced loss of vision has occurred rapidly.

Pupillary changes are important in the diagnosis of subdural hematoma, but frequently the pupils remain normal. A dilated and fixed pupil, or a slightly enlarged pupil which reacts sluggishly to light, suggests a hematoma. Pupillary dilatation was found in only 10 percent of cases surveyed by Govan and Walsh but in about half the series reported by Kennedy and Wortis. Undoubtedly pupillary dilatation results more frequently from extradural than from subdural hematoma. We have observed unilateral dilatation of a pupil in a case of bilateral subdural hematoma.

Incomplete ptosis is relatively common and is almost always unilateral. It is usually on the side of the lesion but may be contralateral. Complete paralysis of the third nerve has not been recorded so far as we are aware. Except for the pupillary paralysis and ptosis the nerve remains intact. Unilateral, and occasionally bilateral, involvement of the sixth nerve is seen in a few cases and is probably due to the generalized increased intracranial pressure. Rarely is the fourth nerve involved. We have seen conjugate deviation of the eyes away from the side of the lesion. Since the deviation was persistent, it was thought to be due to interruption of the supranuclear pathways in the hemisphere contralateral to the hematoma.

Visual field defects are found in a few instances. Maltby[50] described them in 11 percent of his series. The defects were homonymous and contralateral to a clot in all but one instance when it was ipsilateral. We have seen one instance of a homonymous hemianopia for color.

Total blindness with advanced optic atrophy is rarely seen and it follows long standing papilledema. Nelson[51] stressed the ocular signs due to brain-stem compression. Nystagmus, loss of convergence, paralysis and disorganization of gaze were noted. These were thought to be due to lesions about the oculomotor and abducens nuclei and about the posterior longitudinal bundles.

In most instances the ocular signs subside rapidly after evacuation of the clot. The ptosis and inequality of the pupils may disappear in a matter of minutes; likewise do the palsies, aphasia, and visual field defects. The state of consciousness improves rapidly although the patient may be confused for weeks. Papilledema subsides more slowly, often persisting for a month. Visual loss due to optic atrophy is irreversible as are some of the brain-stem symptoms described by Nelson.

Hematomas in infants. Hematomas are fairly common in infants under the age of two years. Here again, trauma is important but the injury may be mild and escape notice. Some authors believe that the bleeding may start during delivery. Among infants, the difference in frequency because of sex is not pronounced as it is in adults. The general state of nutrition seems more important. Rickets and scurvy may well be predisposing causes.

The incidence of bilateral hematoma is much higher among infants. This probably accounts for the relative prominence of signs of increased intracranial pressure and the paucity of signs of local pressure. Tense and bulging fontanels are of the greatest importance and are almost constant. Diagnostic subdural taps through the fontanels should be done in every case where there are signs of pressure. Lumbar punctures are also of extreme importance. In almost all cases there is blood or xanthrochromic spinal fluid. A slight elevation of temperature is present in about one third of the cases.

Convulsions are very common. Govan and Walsh noted convulsions in 91 percent of infants and only 4 percent in adults. Vomiting occurs in about one half of the cases, while drowsiness and irritability are even more frequent. Coma may be the presenting symptom in as many as one fourth the number of infants.

The ocular signs are generally the same as those described in adults, with a few exceptions. The incidence of papilledema is about the same or perhaps less. One important point is the presence of subhyaloid retinal hemorrhages. They are very common in infants and are almost never seen in adults with hematomas. The reason for this is not altogether clear. Govan and Walsh have pointed out the difference in anatomy along the superior longitudinal sinus in infants and adults. In the former the pial veins are almost unsupported as they enter the sinus. This permits easy tearing in the event of trauma and, since the arachnoid is also extremely thin, it is probably torn simultaneously. This permits blood to escape into the subarachnoid space, thereby accounting for the blood in the spinal fluid.

Subarachnoid Bleeding

Blood in the cerebrospinal fluid is a frequent finding in head injuries of more than moderate severity. While it signifies a fair degree of trauma and its presence makes the prognosis somewhat more grave, the bleeding itself rarely produces symptoms or sequelae.

The hemorrhage may produce signs of meningeal irritation, a rise in temperature, and is not infrequently associated with pre-retinal hemorrhages.

If the injury responsible for a profuse subarachnoid hemorrhage is survived, certain late phenomena may occur due to the plugging by the blood of the absorbing mechanism of the cerebrospinal fluid. This produces an acute communicating hydrocephalus, with the usual signs of pressure, papilledema, and cranial-nerve palsies.

When the condition is relieved either spontaneously or by operative measures, the signs and symptoms subside.

Intracerebral Bleeding

The most common form of intracerebral bleeding is multiple petechial hemorrhages. The clinical picture is usually that of concussion and the symptoms are not localizing. We have seen severely injured patients who exhibited divergent strabismus, horizontal nystagmoid movements, alternating dilatation and constriction of one or both pupils and, in the terminal stages, bilateral fixed and dilated pupils. In such cases one cannot be sure whether the signs produced are due to a localized lesion in the brain stem or generalized increased pressure. Even at autopsy this question is not answered. Individuals who survive such injuries may show certain changes attributed to lesions about the aqueduct of Sylvius. These have been discussed previously.

Large collections of blood sometimes form in the frontal and temporal lobes. Should the patient survive the acute phase of the injury, these intracerebral hematomas may produce signs typical of those of any intracranial neoplasm in the same position. Many absorb slowly and leave porencephalic cysts, their presence being asymptomatic. Large intracerebral hematomas are rare complications of head injuries. If they produce signs of pressure, they should be evacuated.

The Eyelids and Conjunctivas and Trauma

It is generally known that ecchymoses develop in the eyelids and conjunctivas as the result of trauma about the orbit which results in a "black" eye, and as a result of fractures in the base of the skull. Similar ecchymoses may occur under other circumstances when their origin is not easily understood.

When trauma is directly applied to the eye and orbit, as, for example, a blow from a fist, there is the development of a "black" eye. Immediately after the blow has been struck a purplish-red color of the eyelids and

extreme redness of the conjunctiva appear. After a day or two, the color changes to purple, then to green, then to yellow, and finally to normal.

Associated with discoloration of the eyelids and conjunctivas there may be dilation of the pupil; usually such a pupil is irregular in shape and sluggish in its response to light. There may be intraocular damage, such as detachment of the retina, tearing of the choroid, dislocation of the lens, or dislocation backward of the optic nerve, but such injuries are uncommon and as a rule a "black" eye is properly regarded as a trivial injury.

When there is a fracture in the anterior fossa extending into the orbit, the blood is said to extend along the torn dura and bone. It becomes visible several hours or even several days after the injury. Often the lower lid contains more blood than the upper and frequently there is "butterfly" distribution of the blood staining. The color is purplish rather than red.

Blakeslee[52] in studying 610 fractures of the skull found eyelid and conjunctival hemorrhage in about 17 percent of the cases. In some instances he observed that blood reached the eyelids when the fracture was situated far posteriorly. In such instances he visualized the blood extravasations as due to the explosive action of the force which had produced the fracture.

In several cases of fracture of the middle fossa, we have observed characteristic blood staining of the eyelids. In cases described by Greear and McGavic there were massive intraocular hemorrhages when bullet wounds were situated far posteriorly; in such cases undoubtedly there were extensive subarachnoid hemorrhages.

Hamilton Bailey[53] made a useful differential diagnosis between "black" eye and hemorrhage into the eyelids and conjunctivas as a result of fracture of the base, and his observations conform largely to ours.

1. In fracture of the base the extravasated blood is limited sharply by the pal-

pebral fascia to the orbital margins, and thus it tends to be circular. In "black" eye there is no such limitation.

2. With fracture of the base the discoloration of the conjunctiva is purplish from the commencement; whereas, with "black" eye it is beefy red. With "black" eye, hemorrhage is in the conjunctiva and the mass of hemorrhage moves when the conjunctiva is moved; in fracture of the anterior fossa the hemorrhage is subconjunctival.

4. With a conjunctival hemorrhage associated with "black" eye there is a posterior limit to the extravasation; whereas, in fracture of the anterior fossa there is no such limit and the hemorrhage tends to be fan-shaped with the handle of the fan toward the iris.

5. With fracture there is a parallelism between the edema and the amount of blood in the eyelids; that is, the greater the edema the greater amount of blood by inspection; with "black" eye with pronounced edema there is relatively little blood.

6. With fracture, the blood in the eyelids almost always is first seen at the medial border of the lower lid and gradually suffuses along the lids. It rarely joins the lesser suffusion in the upper lid at the outer canthus.

7. If the eyelids are everted the conjunctivas in a case of fracture usually are clear; whereas, with "black" eye they are edematous and discolored.

Ecchymoses in the eyelids following fracture of occipital bone. As an unusual example we may cite the case of a woman who fell forcibly into the sitting position. She developed the ocular picture of fracture of the base.

Ecchymoses in the eyelids following cranial operations. We have observed that following many transcranial operations there is pronounced edema of the eyelids and hemorrhages occur in them. The mechanism accounting for such extravasations is unclear. On first thought it would seem likely

that such hemorrhages resulted from taking down of the bone flap, but in many cases this can scarcely apply. The extravasation in many such cases is precisely that which is seen associated with fracture of the base. We have observed such extravasations following prefrontal lobotomy and following a transcranial operation when the subdural space was not entered.

We do not have an explanation for the ecchymoses which occur as the result of transcranial operations in which there has not been gross trauma applied to the skull, and such extravasations seem particularly mysterious when the operative effort has been directed to posterior aspects of the skull. It seems questionable that the explanation concerning fracture of the base, namely disruption of the periosteum, is valid in consideration of the fact that such lid extravasations occur under many circumstances when the base is intact.

PNEUMOCEPHALUS

Following fractures of the skull, air may collect extracranially beneath the galea, or intracranially. Both of these conditions are rare.

Extracranial aeroceles. Fractures through the frontal sinuses or mastoid cells may allow air to escape beneath the galea and strip the scalp from the skull. Slight increases in the intraoral pressure may be sufficient to elevate large portions of the scalp, since it is so loosely adherent to the pericranium.

The spread of the emphysema is limited by the attachment of the galea and consequently does not spread like subcutaneous emphysema elsewhere in the body. Treatment is simple, since only aspiration is required. One should not be misled in the diagnosis.

The soft fluffy tumor in which crepitation can be felt is typical of gas in the soft tissues. Gas gangrene can be easily eliminated since it is practically unknown in the scalp and an infection necessary to produce so much gas would also give rise to alarming systemic symptoms, while pneumocephalus is often asymptomatic.

Intracranial aeroceles. As pointed out by Dandy,[54] air may collect in the subdural space, subarachnoid space, in the brain substance, and in the ventricular system. Subdural collections of air are very unusual. These are small since the subdural space is only potential and considerable pressures are required to expand it. Subarachnoid filling must be accomplished by a break in the membranes in one of the cisterna.

Most cases of pneumocephalus are the results of fractures that pass through the frontal or paranasal sinuses. In these regions the dura is thin and adherent, so that it is easily split. Occasionally breaks in the region of the middle ear and mastoid cells may allow air to escape inside the head. Gunshot wounds, compound fractures, and stab wounds, especially in the occipital region, may produce a fistulous opening, producing pneumocephalus. Besides trauma, ostemas of the skull, syphilis, tuberculosis, and cancer may erode the coverings of the brain. Mild trauma under these circumstances may produce a fistula.

A case in which gas was demonstrated in the orbit and frontal lobe following a puncture wound of the lid by a lead pencil was reported by Slaughter and Alvis.[55] The "lead" apparently was pushed through the orbital roof into the frontal lobe. An orbital abscess followed which was drained with eventual complete recovery. The gas may have been air, or may have been generated by the bacteria producing the abscess.

Courville[56] remarked that the intracranial collections of gas are air less oxygen, since the latter is rapidly absorbed. He also stressed the necessity of having a loose flap of dura producing a valvelike action to trap the air inside the skull.

Symptoms may be present almost immediately following the trauma or may be delayed for months. The reason for the latter is not clear, but since basal skull fractures are very slow to heal, a sudden increase of

intraoral pressure during sneezing, coughing, and so forth, may rupture the overlying meninges and allow the ingress of air.

The complaints of the patient may be mild. Often there may only be a complaint of a "swishing or sloshing" noise in the head. This is almost characteristic of air in the ventricular system. On the other hand, there may be symptoms of increased intracranial pressure, with severe headache, dizziness, nausea, vomiting, hyperthermia, and unconsciousness. If the pressure is prolonged, papilledema develops.

The pressure may be constant or spasmodic. In the latter instances, the temporary rises are brought about by coughing, sneezing, straining, and so forth, and are undoubtedly due to the ball-valve action of the tissues in the fistula. There is severe head and face pain in sneezing, sudden nausea, and even temporary lapses of consciousness.

The diagnosis is usually easy to make. Evaluation of the patient's story of sudden pain and swishing noises in the head are sufficient. Patients with intermittent rhinorrhea are very good candidates for pneumocephalus. X-ray studies will demonstrate the presence of gas inside the skull, and spontaneous ventriculograms have been noted frequently.[57]

Treatment should be conservative in the beginning. The patient should be put at rest and observed. Penicillin and sulfonamides should be given prophylactically since meningitis or intracranial infections are real dangers. If a compound vault fracture is present, it should be treated in the usual manner. Most of the cases are benign and the fistulas soon close. The gas is then rapidly absorbed.

Occasionally symptoms remain, or those of increased pressure progress. In these cases surgery is indicated. The tear in the dura should be closed, with a graft if necessary. The skull fracture may be treated at the same time, by elevation of a depression, removal of loose fragments, and so forth. Treatment should not be long delayed in cases of intracortical aeroceles as persistent pressure may cause considerable cortical damage.

The end results are usually good especially if chemotherapy is started promptly and if operation is not long delayed in cases that do not show rapid absorption of the air.

SUBCUTANEOUS EMPHYSEMA

Air may be forced into the subcutaneous tissues in large amounts following puncture wounds of the chest. There is probably a bellowslike action of the lungs which forces air into subcutaneous tissues through a fistula that has a ball-valve action. Once into the loose subcutaneous tissue, there is almost no limit to where the air may dissect. It is restrained only by the tough attachment of the skin in the palm of the hands and soles of the feet, and by the galea at the edges of the skull. We have seen a patient who within two hours following a closed injury to the chest that produced several fractured ribs, had subcutaneous collections of air over the entire body except the finger and toe tips and the scalp. The eyelids were so full of air that the eyes were swollen shut.

Besides chest wounds, generalized emphysema may follow the puncture of almost any air-containing viscus. Tracheotomy and operation in the nasopharynx may allow the egress of air into the subcutaneous spaces. Brown and Hinton[58] report an instance following the operative resection of the large bowel. They mention cases following rupture of a peptic ulcer and a perforated sigmoid diverticulum.

Localized emphysema of the orbit may follow tooth extractions or operations in the paranasal sinuses. In both these cases the continuity of bone is broken and air is forced into the orbit. Linhart[59] has reported several cases following trauma about the nose or eye. Often this is mild, and not infrequently follows falls or boxing. We have seen it following stab and gun wounds about the eye, also after therapeutic injections about the eye and in the nose.

Air readily finds its way into the orbit when the lamina papyracea of the ethmoid is fractured. Increased intranasal pressure, as produced by sneezing and coughing, forcibly propels more air through the fracture. Thus air reaches the eyelids and the air is behind the septum orbitale.

In such cases, there is a unique combination of signs: proptosis and narrowing of the palpebral fissure. Emphysema of the lids with the air in front of the septum orbitale does not produce exophthalmos or pronounced narrowing of the palpebral fissure.[60]

The diagnosis of subcutaneous emphysema is not difficult to make. The soft swelling of the tissues, with crepitation that can be felt and heard, leaves no doubt about the presence of gas. Both in the generalized and orbital cases, there is usually a history of trauma or operation. X-ray studies of the orbit will demonstrate the air clearly, but fractures of bone are almost never seen.

It is of importance to realize that the firm attachment of the galea limits the upward direction of the air. As pointed out in the section on pneumocephalus, extracranial aeroceles are limited by the attachment of the galea and therefore do not involve the lids and orbit. Likewise air coming from below this attachment will involve the eyes but will not go into the scalp. If both are found two lesions must be present.

Gas gangrene is the only condition that may be confusing. However, patients with this condition do not show the rapid advance of gas in the subcutaneous tissues. In traumatic cases, the symptoms begin at once but, in gas gangrene, there is a delay of hours or days. Also the local condition of the wound, fever, tachycardia, pain, and cerebral signs of intoxication charasteristic of gas gangrene are missing in cases of subcutaneous emphysema.

Treatment is conservative, as far as the emphysema is concerned. Penicillin and sulfonamides should be administered to prevent infection. In the generalized cases, the swelling of the lids usually subsides within 72 hours, while in the localized orbital cases all get well within a week.

DIAGNOSTIC PRINCIPLES AND TREATMENT OF ACUTE HEAD INJURIES

Only the broadest principles can be mentioned here. Patients in shock should be treated for such at once. Then a history should be obtained. Since many patients are unconscious, this may have to be obtained from relatives, witnesses, or police. The type of injury received may be the largest clue as to what is going on inside the head.

The physical and neurologic examinations should be as thorough as possible. The results should be recorded, as changing signs, especially in the state of consciousness, are of the greatest importance. Associated injuries may need prompt attention and should not be overlooked.

It is rare that acute injuries require immediate operation. Since most patients will require careful watching, nurses properly trained are essential. Frequent determination of the temperature, pulse, respiration, and blood pressure are noted. The state of consciousness is most important and any changes should be noted and evaluated. The surgeon should often check on this point himself. The appearance or disappearance of neurologic signs should be watched for and recorded.

Besides these things, the unconscious patient needs constant attention to see that vomitus is not aspirated; that his temperature is controlled, either by keeping him warm if the temperature is subnormal; or by cooling him by fans, ice sponges, and so forth, if it goes about 104°C. An adequate airway must be maintained. An unconscious patient who has difficulty breathing should be suctioned frequently, an anesthesia airway inserted and, if necessary, intubated. Bladder catheterization may be necessary and the bladder should not be allowed to become overdistended.

Certain neurologic signs and symptoms, if present, or if they appear under observation,

require careful consideration since they may signify that a collection of blood of surgical importance may be forming. A steadily deepening unconsciousness, especially after a lucid interval, is very important. A prolonged period of unconsciousness without signs of rousing may be equally significant.

Anisocoria with a sluggish or fixed pupil very commonly means that a large hematoma has formed. This sign may be transient but that does not lessen its importance. The onset of facial convulsions later spreading to arm and leg is a sign of local irritation and often means that an extradural hematoma is present.

Generalized convulsions, especially in children, do not carry the same import. Usually they are produced by a local cortical laceration or blood in the subarachnoid space. "Tonic" or cerebellar fits mean brain-stem injury or compression and carry a grave prognosis. Not infrequently large subdural hematomas producing great increase of intracranial pressure account for this type of convulsion.

The onset of a hemiparesis, sometimes only evident in the face, or the appearance of unilateral clonus and the Babinski sign, may be of surgical importance when they occur in the presence of other symptoms indicating a rapidly rising intracranial pressure.

The respiratory rhythm is often a valuable guide to the state of intracranial compensation. A falling rate usually means increasing pressure. However, an irregular rate, with beginning cyanosis, retraction of the chest, and a honking noise due to a relaxed soft palate means that the medullary centers are becoming embarrassed. Occasionally this is the only sign of failing compensation, and we have seen several instances when this has been due to massive acute subdural hematomas. Diagnostic trephinations should be done promptly in the absence of other signs.

X-ray examinations have little importance in the immediate treatment of acute injuries. Most depressed fractures may be palpated.

The presence of linear fractures may increase one's suspicion that a hemorrhage of surgical significance is present, but operation should neither be delayed because of its absence nor rushed because of this finding. Before depressed and compound fractures and gunshot wounds are subjected to operation, an adequate X-ray examination of the head should be carried out.

The value of diagnostic lumbar punctures is open to question unless infection is suspected. The presence or absence of blood is of academic value, and the pressures are not reliable guides.

Diagnostic trephinations should be used freely in cases of doubt. They may be done under local anesthesia and carry no risk. Openings should be large enough to inspect the dura and cortex thoroughly. A small crown trephine makes excellent inspection holes. Openings should always be multiple and bilateral. Four holes in each side of the head are usually adequate, two about 2 to 3 cm. from the midline; one in the frontal and one in the parietal regions, and two in the temporal region; one in front and the other behind the ear. The ventricular system may be tapped at the same time and the fluid studied. The hemispheres may also be explored with a needle for intracerebral hematomas.

Ventriculograms, encephalograms, and arteriograms may be necessary in chronic cases. Their use during the acute stages of a head injury is not recommended.

Treatment is divided into operative and nonoperative. The bulk of cases falls into the latter classification. Rest, adequate fluids, chemotherapy and antibiotics, and mild sedatives are used. We have had no experience with the regimens of dehydration and repeated lumbar punctures and have not been impressed by the statistics cited by others. Convulsions are controlled with phenobarbital and intramuscular magnesium sulfate.

Operations are reserved for compound

and depressed fractures and hematomas. Compound fractures of the vault should be thoroughly debrided, cortical bleeding controlled, the dura repaired, and the scalp closed. This should be done as soon as shock has been controlled. The same holds true for gunshot and other penetrating wounds of the skull.

Depressed fractures should be elevated promptly. Although the bulk of the cortical damage is sustained at the time of injury, if the condition is not relieved, additional damage may be sustained during the period of edema and later during scar formation. While some neurosurgeons disagree on the necessity for elevation of all depressed fractures, especially those over "silent" areas, the risk involved is so slight it seems all should be repaired as soon as the shock has been controlled.

Linear cracks need no special care, other than that outlined above. When the fracture has passed through the ear or a sinus, the liberal use of antibiotics and chemotherapy is indicated until all drainage has stopped and healing has been completed.

Extradural hematomas when located should be evacuated promptly and the bleeding controlled. Most of these hemorrhages are produced by rupture of the middle meningeal artery. In every case this vessel should be located and traced to the foramen spinosum to be sure that it has not been torn. If the hematoma is evacuated promptly the prognosis is excellent. Frequently, the symptoms disappear within a matter of a few minutes. However, if operation is delayed, pressure on the vital centers may be so severe that unconsciousness persists for days and severe permanent cortical damage results. At times, death ensues despite the relief from pressure.

Subdural hematomas present a somewhat different problem. In the thin acute type, simple irrigation through burr holes is sufficient. If the hemorrhage is massive, it may be well to enlarge one of the openings suf-

ficiently so that the hemorrhage can be thoroughly and quickly evacuated. Any bleeding from torn cortical vessels can be stopped with the cautery at the same time.

Chronic subdural hematomas on the other hand often present a more difficult problem. These, too, can sometimes be evacuated through burr holes and the membranes allowed to absorb. The process may have to be repeated several times. A better method is to turn down a small flap so that the blood can be entirely removed. The outer membrane need not be stripped completely but the incised edges should be carefully cauterized to prevent oozing. Rarely can the inner membrane be stripped completely, and this should not be attempted if it is adherent to the cortex.

The hematomas in infancy can sometimes be cured by multiple aspirations through the open fontanel or by a burr hole placed beneath the temporal muscle. However, if fluid continues to reaccumulate after 3 or 4 taps, or if membranes are present, a small bony flap has proved satisfactory for the complete removal of the hematoma and at least part of the membrane.

Subarachnoid hemorrhages should be treated conservatively. The nuchal rigidity and fever produced by the blood may lead to confusion with meningitis. A diagnostic lumbar puncture will clear up this difficulty. Repeated drainage of the cerebrospinal fluid in an effort to draw off the blood has not seemed worth while.

Intracerebral hematomas of significant size are rare. If they present symptoms, they should be tapped and the blood drawn off.

Recently, some authors have advocated total removal of badly lacerated temporal and frontal lobes shortly after the injury. They point out that an internal decompression is obtained, and that convalescence is shortened by the removal of the mass of necrotic tissue. This seems a rather heroic measure, and in our hands has not been very successful.

In summary, operative intervention is only occasionally required in the treatment of head injuries, and is directed toward the evacuation of collections of blood and the repair of compound fractures. Subtemporal decompressions for increased intracranial pressure have questionable value.

12 West Read Street (1).

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SOME OBSERVATIONS ON MIOTICS*

EDWIN B. DUNPHY, M.D.
Boston, Massachusetts

The fact that so many different miotics are in use is perhaps an indication that the ideal one has not yet been found. During the past 15 years, tremendous strides have been made in our knowledge of the pharmacodynamics of the intraocular muscles, but there are still many gaps in our understanding of how miotics act and why they sometimes succeed in controlling increased intraocular pressure and more often fail to do so.

Therefore, it may be worth while to evaluate some of the miotics currently used, beginning with a brief review of the pharmacologic background.

PHARMACOLOGIC BACKGROUND

Although the possibility that chemical substances might mediate nerve impulses was suggested as far back as 1877 by Dubois-Reymond,[1] it was not until 1914 that Dale[2] brought forward his theory of the parasympathomimetic action of acetylcholine on the autonomic nervous system, and postulated the existence of an esterase to account for its brief duration and its breaking down into acetic acid and choline.

The classic experiments of Loewe[3] in 1921-1922 established the first proof of the release of chemical agents by nerve impulses and the fact that these substances act on smooth muscle causing it to contract. Due to the work of Feldberg,[4] Dale,[5] Chang and Gaddum,[6] and others it has become accepted that stimulation of parasympathetic nerves causes the liberation of acetylcholine at the myoneural junction. In similar fashion most sympathetic nerves act through the medium of epinephrine, the notable exception being those to the sweat glands.

The theory of nerve impulses being transmitted by acetylcholine at the myoneural junctions has been challenged recently by Nachmanson,[7] who suggests that this substance is responsible only for conduction. However, his views have not received universal acceptance.

Englehart,[8] in 1931, showed that impulses, passing along the short ciliary nerves, liberated a substance in the aqueous which had the properties of acetylcholine. This was absent when the ciliary ganglion had been removed beforehand. It was found to be greatly increased when the eye had been previously exposed to light, but it was absent in the dark-adapted eye, even after eserine had been instilled to destroy the cholinesterase.

The present belief is that acetylcholine exists in the tissues in an inactive, nondiffusible form. The nerve impulse changes this to an active and diffusible form which acts immediately on the hypothetical effector cell, but is thereupon quickly destroyed by cholinesterase. The inactive form persists as long as parasympathetic nerves remain intact.

The ciliary body has plenty of it except when the postganglionic fibers are cut. As the nerves degenerate, the acetylcholine disappears from the tissues but, as Cannon[9] has shown, the cells formerly innervated by the parasympathetic fibers then become abnormally sensitive to acetylcholine. This increased sensitivity to acetylcholine can develop within 24 hours. Its mechanism is not clearly understood.

CLASSIFICATION OF MIOTICS

We may divide miotics into two broad groups:† (1) Those which act directly on the effector cell in the iris muscle, and (2) those which act passively by inactivating or de-

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† Since this paper was written a new group of miotics which block sympathetic stimulation adrenergic receptors has been introduced into ophthalmology by Christianson and Swan.

stroying cholinesterase and thus permitting the unregulated production of acetylcholine which stimulates the effector cell to activity.

Those in the first group are, for the most part, drugs closely related to acetylcholine, and merely supplement the normal stimulation which this chemical gives to the sphincter muscle of the iris. They are mecholyl, charcolin, and furmethide. Pilocarpine, an alkaloid, acts in similar fashion, and, like the others, is effective after nerve section and complete degeneration. Histamine also acts directly on the muscle and is a very powerful miotic, but it causes too much irritation to be of practical value.

The second group, which destroys cholinesterase and thus allows the uncontrolled production of acetylcholine, is probably the most powerful but not necessarily the most desirable. Examples of this group are eserine, neostigmine, the fluorophosphates, and a relatively new compound, tetraethyl pyrophosphate.

Miotics may be discussed under three main headings. (1) Their effect on the musculature of the iris and ciliary body. (2) Their effect on the vascular supply of the anterior segment and on the blood-aqueous barrier. (3) Their effect on the intraocular pressure.

I. Effect on musculature of iris and ciliary body

In general, any miotic, when dropped into the conjunctival sac, affects the iris sooner than the ciliary body, probably because it reaches the iris first and in higher concentrations. Thus miosis begins before any spasm of accommodation takes place.

The degree of miosis and accommodative spasm depends entirely on the intraocular concentration of the drug and the individual quantitative response. Some miotics produce relatively more cyclotonia in relation to miosis than others. We must always remember in comparing one miotic with another that usually the same degree of miosis can be accomplished by either, provided an ad-

equate concentration is brought to bear on the iris.

Factors affecting the intraocular concentration are the size of the drop used, the vehicle emyployed, the method of instillation, the permeability of the corneal epithelium, the physical properties of the drug, and its relative affinity for water or fat. With so many variables it is obvious that direct comparisons of one miotic with another must be carefully controlled to have any value.

The following observations on the various miotics are based on my own experience, and that of others.

Pilocarpine. The miosis produced by 1-percent to 2-percent pilocarpine is prompt and efficient, but lasts only for a day. In these same concentrations, pilocarpine usually causes a slight, but not unpleasant, stimulation of the ciliary muscle, and this fact has been made use of by some ophthalmologists in recommending the use of 0.25-percent solution before reading for certain young asthenopes with subnormal accommodation. I have found this useful on occasions.

However, certain individuals may react rather violently to pilocarpine, as little as 0.5-percent solution causing a marked miosis and ciliary spasm, but these are exceptions. On the whole I feel it is the most satisfactory miotic and can be used in much higher concentrations than was formerly thought possible.

For maximal miosis in glaucoma a 4-percent solution is frequently employed, and it can be used as high as 10 percent if the HCl salt rather than the nitrate is employed, since the former has greater solubility. The pH must be kept at 5 to 6 to avoid precipitation of the alkaloid. Long-continued use, even in moderate concentrations, occasionally causes a follicular conjunctivitis and the production of pigment synechias, but in my experience this is extremely rare. Pilocarpine is superior to eserine in this respect.

Acetylbetamethylcholine (mecholyl) is

poorly absorbed through the cornea and has very little effect on the normal pupil in anything less than 15-percent solution. I have attempted to remedy this by the addition of zephiran (1:3,000 solution) as a wetting agent, but without success. However, as Adler[10] has pointed out, the situation is different in a glaucomatous eye with high tension, where a 10-percent solution will constrict the pupil readily.

This apparent sensitivity to mecholyl in glaucoma is interesting. It may be that the choline esterases are interfered with in this disease as suggested by Friedenwald[11] and hence mecholyl is more effective than in normal eyes. Swan's[12] explanation is that the corneal-epithelial barrier is disturbed in cases with elevated tension and this enhances absorption.

Adler and Scheie[13] found that, although mecholyl in less than 15-percent solution had no effect on the normal pupil, a 2.5-percent solution sharply constricted the tonic pupil of Adie's syndrome. From this observation and from experimental work on cats, they concluded that the site of the lesion in tonic pupils is in the third nerve somewhere between the ciliary ganglion and the nerve endings in the sphincter muscle, and that the lesion partially destroys these fibers. Hence the pupil becomes permanently sensitized to acetylcholine and will respond to small concentrations of mecholyl which ordinarily would have no effect.

It has been my experience that in the dilated atrophied pupil of an old blind, glaucomatous eye, a 10-percent mecholyl solution will constrict the pupil moderately; whereas, in the dilated pupil of a complete third-nerve paralysis the same drug will have no effect. In the former case there has been damage to the postganglionic nerve-fiber endings in the sphincter muscle with some sensitization, but, in the latter, the preganglionic fibers are probably involved, hence no sensitization.

In glaucomatous eyes mecholyl usually causes more stimulation of accommodation than pilocarpine, but not as much as some of the other miotics. Since this drug is partially destroyed by cholinesterase upon reaching the aqueous, its action is brief, the miosis persisting for two hours only. Therefore, for practical purposes it should be used with one of the cholinesterase inhibitors, usually neostigmine.

A word of warning should be given on the use of mecholyl by retrobulbar injection, a method occasionally employed in acute glaucoma and in cases of sudden obstruction of the central retinal artery. I have seen three near-fatalities by this method of administration. Although the dose in each case was considered a perfectly safe one, the patients reacted very badly to it, going into circulatory collapse. It should never be given subconjunctivally unless there is, ready and waiting, a sterile syringe containing 1/100 gr. atropine. Mecholyl by injection is also contraindicated in asthmatics for fear of bronchial constriction.

Carbaminoylcholine (carcholin). This drug, formerly called Doryl, is another choline ester which is probably the most toxic and the most potent of the group. It has the advantage of not being destroyed by cholinesterase. Its miotic action is therefore prolonged, provided it is properly administered.

O'Brien and Swan[12] brought out the important fact that this drug is poorly absorbed through the cornea. Carcholin is of low surface-tension activity with high affinity for water, and low lipoid affinity—such drugs are poorly absorbed in aqueous solution since they tend to remain in their vehicle.[14] O'Brien and Swan[12] recommended the instillation of 1.5-percent solution of carcholin in an aqueous solution of zephiran (1:3,000) which reduces the surface tension of the cornea, possibly injures the corneal epithelium, and thereby enhances absorption.

In a more recent communication Swan[15] found that 1.5-percent suspension in anhydrous petrolatum penetrated best of all. By

this method carcholin has a relatively higher affinity for the corneal epithelial barrier than for its vehicle, and therefore passes through readily.

The accommodation is definitely stimulated by carcholin, O'Brien and Swan[12] finding an average of 1.18 diopters of false myopia produced by one drop of the above concentration as compared to an average of 0.5 diopter produced by 2-percent pilocarpine.

Furfuryltrimethylammonium iodide (furmethide) is a fairly recent drug, which is a strong parasympathetic stimulator, and which is not destroyed by cholinesterase. When used in 10-percent solution, its miotic action is prompt and it produces a moderate degree of cyclotonia. According to Owens and Woods,[16] it is more effective than mecholyl and prostigmin in acute primary glaucoma, especially in late cases, and is slightly more effective than pilocarpine (2 percent) in chronic primary glaucoma. Although I have not made any critical comparisons of this drug with other miotics, my impression is that it possesses no special virtues over 2-percent pilocarpine, and, furthermore, it often causes more blurring of vision than the latter.

The second group of miotics consists of the anticholinesterase drugs.

Physostigmine (eserine) is probably the best known of these, although neostigmine, a synthetic alkaloid, has practically identical qualitative actions so that the two drugs may be considered together. In addition to rapid and intense miosis, they often cause a severe accommodative spasm. After their use, the accommodation remains in a hyperexcitable state for many hours. Long continued use of eserine may cause a follicular conjunctivitis. I have not observed this with neostigmine.

Eserine has a tendency to take on a pink color due to oxidation. To delay this the pH should be adjusted to 4 to 5. Many patients complain of smarting following instillation. The irritating quality of this drug must be due to something intrinsic since the

degree of irritation usually bears a direct relation to the concentration irrespective of the pH. It is usually employed in 0.25- to 0.5-percent solutions. Neostigmine, which is much less irritating, is used in 3-percent or 5-percent solution.

Di-isopropyl fluorophosphate (D.F.P.) Leopold and Comroe,[17, 18] and McDonald[19] have determined the effects of this interesting compound on normal and glaucomatous eyes.

D.F.P. is a very powerful miotic and has many undoubted advantages. Its prolonged action obviates the necessity of frequent instillations, and sensitivity is extremely rare. However, the unpleasant symptoms from the strong cyclotonia preclude its use in many patients. Detachment of the retina[20] and activation of a quiescent uveitis[21] have been ascribed to it, although personally I have not encountered such complications.

In spite of its unpredictability, I have found it most successful in cases of glaucoma associated with aphakia and I believe it to be the drug of choice in these cases. This does not mean that all aphakic cases are successfully controlled by it since many factors are involved.

It is an interesting fact that the unpleasant symptoms of ciliary spasm and congestion of the eyeball frequently seen after D.F.P. instillation are usually absent or minimal in cases of aphakic glaucoma. Leopold and Comroe[17] have advanced a theory to account for the lack of ciliary spasm. They suggest that a lens with intact zonular fibers must be present for the pain of ciliary spasm to develop. However, this would not account for the lack of vasodilatation in these cases.

The following theory might explain the absence of both factors. The vitreous is known to be very rich in cholinesterase. Brückner[22] has shown that in certain animal eyes its concentration is four times greater in the vitreous than in the aqueous. Following cataract extraction, the barrier between the posterior chamber and the vitreous is

usually disrupted and the vitreous often bulges forward into the anterior chamber.

Thus, it is possible that, in aphakics, there is so much cholinesterase present in the aqueous that it is not all destroyed by the one drop of D.F.P. usually instilled. If so, the remainder might exert some control on the acetylcholine formation and thus the whole effect of D.F.P. would be tempered down with a consequent reduction of the unpleasant symptoms.

Tetraethyl pyrophosphate (T.E.P.) is a colorless liquid of low volatility which is the active ingredient of the insecticide hexaethyl tetraphosphate which was used in Germany during the recent war. T.E.P. is highly toxic and produces marked miosis in animals and man. Pharmacologic studies have shown that it is a very efficient inhibitor of cholinesterase, being more effective in this respect than either D.F.P. or eserine. It is even more unstable than D.F.P. and, like the latter, must be dispensed in peanut oil.

The miotic and antiglaucoma activity of T.E.P. has been investigated by Grant[23] of the Howe Laboratory of Ophthalmology. His studies indicate that in normal human eyes T.E.P., 0.1-percent solution in peanut oil, produces rapid miosis (in 7 minutes), spasm of accommodation, eye pain, and brow ache. The accommodation returns to normal after 4 days, but a relative miosis may persist for 2 to 3 weeks with a progressive relaxation as the days go by. In some of the eyes a slight transient engorgement of the conjunctival vessels occurs. There is no local discomfort at the time the drops are used, and slitlamp examination shows no evidence of damage to the corneal epithelium. In no instance have systemic symptoms been noted.

Grant has studied the effects of T.E.P. on 15 patients with chronic primary or secondary glaucoma. In most instances T.E.P. did not reduce the tension in eyes in which it could not be reduced by other miotics. There were 1 or 2 exceptions, but in general this was true.

II. EFFECT ON THE VASCULAR SUPPLY OF THE ANTERIOR SEGMENT OF THE EYE AND ON THE BLOOD-AQUEOUS BARRIER

It is well known that after the instillation of certain miotics the conjunctival and ciliary vessels may become engorged. This is characteristic of the derivatives of acetylcholine, such as mecholyl and carcholin, which cause it quickly, and even more characteristic of the anticholinesterase drugs, particularly D.F.P., in which the congestive action is delayed.

In the case of D.F.P., engorgement of the iris vessels may occur, as I have often observed by slitlamp examination. I have not noted this to the same degree with other miotics. This is sometimes accompanied by the appearance of cells in the aqueous when 0.2-percent solution is used. There is never any tendency to formation of posterior synechias. It is an interesting fact that these congestive features never appear until 10 to 24 hours after instillation of the drug. They can, of course, be eliminated by atropine which blocks the action of acetylcholine on the effector cell.

This delay in the appearance of the vasodilator effects is difficult to explain. Perhaps the accumulated acetylcholine cannot be absorbed by the tissues and thus causes vasodilation, first of the iris vessels, with the congestion gradually spreading to the anterior ciliary and the conjunctival vessels. All these congestive features usually disappear in 2 or 3 days as the eye becomes accustomed to the drug.

There is considerable evidence to prove that most miotics have a profound effect on the blood-aqueous barrier, and on the osmotic pressure of the aqueous.

Swan and Hart[24] showed that, in rabbits, instillations of mecholyl, carcholin, and eserine all caused a significant increase of the protein content of the aqueous. Pilocarpine did not. Studies with intravenous inulin, a large molecule polysaccharide, demonstrated that this substance, which does not ordinarily pass the blood-aqueous barrier

in rabbits, passed freely into the aqueous after instillations of eserine, carcholin, and mecholyl, but not after pilocarpine. Similar studies made with intravenous dyes such as sodium fluorescein showed that after eserine, carcholin, or mecholyl instillations, the dye appeared in the anterior chamber 4 to 8 minutes before it appeared in the control eye.

More recent experimental work by Leopold and Comroe,[18] by Scholz,[25] and by von Sallmann[26] indicates that D.F.P. also produces a marked change in capillary permeability to flourescein and a definite increase of protein in the aqueous. This change in the permeability of the blood-aqueous barrier is probably of marked significance in changes in the intraocular pressure.[27]

III. EFFECT ON INTRAOCULAR PRESSURE

It has long been felt that miosis is not the only factor which reduces the tension of the eyeball, since the miotic drugs have been known to accomplish this in cases in which the iris angle appears gonioscopically to be completely blocked by adhesions and even in cases of complete aniridia. Therefore, other possibilities must be considered.

The vasodilator effect which all miotics possess to a greater or less degree is probably a most important one. Because of this vasodilator factor intraocular pressure tends to rise slightly after instillation followed by a fall as the other factors become operative.

This was shown years ago by Wessely[28] who noted that eserine dropped into a rabbit's eye gave a marked dilatation of the vessels of the iris and ciliary body, also that the protein in the aqueous was increased and that entrance of intravenous fluorescein into the anterior chamber was facilitated. Eserine also caused an increased tension in rabbits a few minutes after the pupil had become miotic. This lasted 15 minutes, dropping back to normal and then becoming subnormal.

Clinically, we see certain cases of glaucoma in which the tension rises following the use of miotics and remains elevated. I have seen it occur once after eserine, 6 times

following D.F.P., and once with T.E.P. I have never seen it following pilocarpine. It has been reported rarely with carcholin and with mecholyl.

Let us consider the various possible factors which might tend either to reduce or increase the introcular pressure following the instillation of miotics.

ACTION OF MIOTICS

Factors tending to reduce tension	*Factors tending to increase tension*
1. Mechanical freeing of the angle.	1. Vasodilatation of iris and ciliary body with increase in their volume.
2. Contraction of longitudinal fibers of ciliary muscle on the scleral spur, opening up Schlemm's canal.	2. Cyclotonia causing lens to push iris root forward.
3. Reduction of blood flow to ciliary processes by ciliary spasm.	
4. Changes in permeability of blood aqueous barrier and the iris vessels.	

It can be seen that the action of miotics on the intraocular pressure is a complex one and represents a struggle between antagonistic forces. Sugar[29] has suggested the use of a vasoconstrictor drug, such as neosynephrin (1 percent), along with the miotic as a logical means of combating excessive vasodilatation and cyclotonia, and thus insuring a predominance of the pressure-reducing effects. He advises this only in shallow-angle glaucomas, and in acute congestive attacks, to reduce the chances of inadvertently raising the pressure.

In the six cases in which I have observed a rise of tension after D.F.P., and the one in which this occurred following T.E.P., all the eyes had very shallow chambers. I, therefore, have been following the advice of Sugar in all cases of shallow-chamber glaucoma whenever D.F.P. is used, and have used neosynephrin (1 percent) along with it.

Kronfeld,[20] a few years ago, attempted to correlate the responsiveness to miotics with the gonioscopic findings in various types of glaucoma. His conclusions were that:

1. In shallow-angle glaucoma, both in the

chronic and in the congestive phase, miotics were successful if not more than three-fourths of the angle was closed off by synechias.

2. In glaucoma associated with delayed reformation of the anterior chamber, miotics were often successful in reducing the pressure, provided the peripheral anterior synechias were filamentous in nature and not too solid.

3. In glaucoma associated with exfoliation of the lens capsule, miotics were notoriously inefficient.

In all other types of glaucoma no correlation was found.

In my own experience, very little correlation exists between the gonioscopic picture and the response to miotics in any type of glaucoma, the possible exception being that associated with exfoliation of the lens capsule. This type is seldom controlled by miotics. Even in the shallow-angle, iris-block type with few synechias, there are many cases that will not respond. In some patients both angles will look exactly the same, yet one eye will respond to miotics and the other will not. There are too many other factors beside the miosis to permit correlation.

What, then, is the value of miotics in the treatment of glaucoma?

1. Certainly in acute congestive attacks they are of inestimable value in bringing the tension under control before surgery is attempted.

2. In chronic simple glaucoma a few patients may be carried along successfully for years on miotics alone. I think this is rare, but perfectly possible, in both the shallow-angle and the wide-angle types, if treatment is instituted early.

3. They are often very helpful after operations which are only partially successful.

4. They are indicated after cyclodialysis as an aid in maintaining an open cleft.

Their danger lies in our placing too much reliance on them. Patients are apt to grow careless in using them and, therefore, should be frequently observed if on a miotic regime.

In most instances the beneficial effects of miotics are not sufficiently prolonged to postpone surgery indefinitely.

DISCUSSION

When all is said and done, an ophthalmologist's choice of a miotic is based on his own experience. Without wishing to appear too dogmatic I would like to state what my experience has been. In acute glaucoma I want to use a drug that will bring the tension under control quickly. For this I usually employ the synergistic combination of mecholyl (20 percent) and neostigmine (5 percent) every 15 minutes for an hour or two, until the tension comes down to normal, and surgery can be performed. Equally good results may be accomplished by similar use of a combination of pilocarpine (4 percent) and eserine (0.5 percent). I am a little fearful of D.F.P. in these acute congestive cases.

In chronic simple glaucoma I depend on pilocarpine (1-percent to 4-percent solution, 2 to 4 times daily) to control the pressure. If this is ineffective, I usually suggest operation and waste no more time with other miotics, particularly when the patient shows well-defined field changes.

There are exceptions of course. A patient on whom surgery is contraindicated for any reason, or one on whom surgery has been performed without complete success, deserves further trial with some other miotic. In these instances I may try the combination of pilocarpine and neostigmine, or D.F.P. (0.05 percent) solution. In using the latter I combine it with 1-percent neosynephrin in all cases with shallow angles.

I have found carcholin (1.5-percent suspension in anhydrous petrolatum) valuable in patients who develop sensitivity to other drugs.

In glaucoma associated with aphakia, I use D.F.P. (0.1 percent) solution as my first choice. I may use adrenalin borate (2 percent), particularly if the pupil appears blocked by vitreous.

In glaucoma secondary to uveitis I do not use miotics in active stages, but treat the

patient with atropine and adrenalin borate. However, in mild chronic cases with white eyes and no tendency to synechias, I often use pilocarpine. In old cases with the iris plastered to the lens, pilocarpine may be helpful. I am inclined to avoid strong vasodilating drugs in glaucoma secondary to uveitis.

In glaucoma associated with exfoliation of lens capsule, in hemorrhagic glaucoma, and in buphthalmos, I spend little or no time using miotics, but proceed to other measures.

CONCLUSIONS

1. In spite of an enormous amount of work done on the subject we are still not certain just how miotics lower the tension. Clinical experience and experimental work suggest a combination of miosis and an opening up of the blood aqueous barrier with changes in the osmotic relationship.

2. Some drugs produce more vasodilatation and cyclotonia than others, although their miotic effects may seem to be equal.

3. These vasodilatating and cyclotonic actions of miotics are probably of considerable importance in determining their effect on the intraocular pressure.

4. The combination of 1-percent neosynephrin with a miotic should be a rational procedure in glaucomatous eyes with shallow angles, especially when the miotic has strong vasodilating and cyclotonic actions.

5. Although we are learning more and more about the iris angle through gonioscopy, we are still not in a position to predict just what type of glaucoma will respond to miotics.

6. Generally speaking, miotics are valuable in early cases of both acute congestive and chronic simple glaucoma in bringing the tension under control while evaluating the patient for proper surgical procedure. They are also extremely helpful after operations which just miss being 100-percent successful. Although miotics alone may carry a few glaucoma patients along satisfactorily for years, they must be considered an adjunct to, rather than a substitute for, surgery.

243 Charles Street (14).

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NASAL CONTRACTION OF VISUAL FIELDS IN GLAUCOMA

Wiktor Arkin, M.D.

Warsaw, Poland

Some of the factors which may contribute to the pathologic processes in glaucoma have not, as yet, been satisfactorily elucidated. One of these factors is the nasal contraction of the visual field which is, in my opinion, one of the important signs of this disease.

CIRCULATION THEORY

In many monographs, this phenomenon is explained by the theory of Arlt and Rydel.[1] Their theory, which seems to have more probability than others, is based on the fact that circulation of the blood is poorer in the temporal parts of the retina, since the vessels that go out of the optic-nerve disc to this region have a longer course than those which run to the nasal part. The temporal vessels describe a long circle, while the nasal ones go straight to the periphery.

Moreover, it must be remembered that the disc (the exit of the vessels and nerve fibers) is situated eccentrically at the nasal side and not in the center of the retina.

Wegner[2] found, when producing experimental anemia of the retina (pressing the eye), that the nasal half of the visual field disappears first, and only later, the temporal half. I could not confirm this phenomenon either in others or in myself. The visual field darkened equally on both sides and, as the pressure increased, suddenly ended in total blindness.

Another weak point in the circulation theory is the fact that macular vision is preserved for a long time after peripheral vision is impaired. Since both the macula and periphery depend for their nutrition on the small vessels, it would seem logical to assume that, if pressure exerted on the vessels was the exclusive decisive factor, macular and peripheral vision would be equally impaired.

One explanation offered for this difference in the rapidity of visual impairment is that, in the region of the macula, the vessels are deeper and are, therefore, better protected against pressure. Yet, one must consider the observations of Jacobson and Gamo Pinto[3] who found that the greatest loss of visual field corresponded to the deepest cupping of the opposite side of the disc.

ARGUMENTS AGAINST THEORY

There are a number of arguments that can be presented in refutation of the theory of Arlt and Rydel.[1]

1. In arteriosclerosis, the visual fields, unlike those in glaucoma, show a uniform contraction, although, in this disease, there is also disturbance of the circulation of small blood vessels.

2. Tangent-screen studies of visual fields in glaucoma always demonstrate that the loss of the visual fields is in connection with the blindspot. This would seem to indicate that the pathologic condition first affects the nerve fibers. It would seem logical to assume that, if pressure on the vessels was primary, the peripheral parts of the retina would be affected since it is they which suffer first from a circulatory disturbance. In this case, contraction of the visual field would proceed from the periphery and would have no connection with the blindspot.

3. The presence of an annular scotoma coming directly from the blindspot would seem to indicate that there is direct pressure on the nerve fibers.

4. In arteriosclerosis, atrophy of the retina and secondary atrophy of the optic nerve make a hollow cup of the disc that is easily distinguished from glaucomatous cupping.

IMPAIRMENT OF NERVE FIBERS

Such arguments as have just been presented would tend to show that the contraction of the visual field is immediately connected with the impairment of the nerve fibers on the margin of the disc (and it is interesting to note in this connection that Arlt and Rydel[4] indicated that the temporal nerve fibers going out from the disc describe the same circle as the blood vessels).

HYDROSTATIC PRESSURE

APPEARANCE OF DISC

According to Fuchs,[5] excavation of the disc can be ascertained only by the curving of the vessels on the brim of the disc, because the nerve fibers are transparent and invisible.

However, if one studies the appearance of the disc during the period of already visible but not yet complete excavation, the cupping can be distinguished by the shadow cast by the overhanging brim. The disc itself has a grayish color, and the vessel trunk with all its capillaries is depressed on the nasal margin. Where the disc is not yet excavated, it has a rosy color.

Examination with the modern electric ophthalmoscope can also rule out the possibility that one margin of the disc is elevated. Such an examination gives the impression that the temporal portion is excavated to its edge, while in the nasal portion, the excavation does not reach the margin.

Fuchs[5] discussed this finding and acknowledged that even when cupping had taken place, nerve fibers remained on the nasal portion of the disc.

ANATOMY OF POSTERIOR REGION OF EYE

These facts would seem to establish the great probability that cupping of the disc begins on the temporal margin. In order to arrive at an explanation for this, it is necessary to have in mind the structure of the posterior region of the eye and particularly the course of the optic nerve and the place where it enters through the sclera.

The optic nerve enters the eye obliquely creating an acute angle with the nasal wall of the eye and an obtuse angle with the temporal part. This anatomic fact has significance in that it divides the internal pressure of the posterior wall of the eye.*

This pressure, which has a perpendicular direction, can be subdivided into two components: (1) that going along the nerve but not pressing on the nerve fibers (fig. 1A),

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* It must be remarked that the interpretation herein presented depends upon the existence of a flow through the nerve. Really such a flow exists, although it is very slow. Therefore, the law of Dascel does not apply.

and (2) that going perpendicular to the nerve which presses the temporal nerve fibers against the margin of the disc (fig. 1B) and pushes the nasal nerve fibers away from the margin (fig. 1C). Physics teaches us that pressure in a curved pipe is greater on the convex than on the concave wall.

It can be justly remarked that, since the optic nerve is not a pipe, such an analogy cannot be made. This contradiction is, however, more apparent than real.

Fig. 1 (Arkin). Direction of the internal pressure of the posterior wall of the eye. (A) That going along the nerve but not pressing on the nerve fibers. (B) That going perpendicular to the nerve and pressing the temporal nerve fibers against the disc. (C) That pushing the nasal nerve fibers away from the margin.

CUPPING OF THE DISC

The disc, as is known, is not a flat surface but has a small hollow known as the physiologic excavation. The physiologic excavation does not reach the margin of the disc, but it is always distinctly marked, being sometimes even in the shape of a funnel.

Glaucomatous cupping of the disc is the consequence of the enlarging and depressing of the physiologic excavation. How often in doubtful cases of glaucoma, when other symptoms are not sufficiently evident, does one seek diligently for any alteration in the physiologic excavation.

When intraocular pressure is pathologically increased, the two components of that pressure already described press immediately and with a distinct difference on the lateral walls of the physiologic excavation.

As soon as the physiologic excavation becomes a pathologic one, the difference in these two components of the intraocular pressure, following the laws of hydrostatics, constantly increases.

ANATOMY OF THE OPTIC NERVE

One other factor must also be considered. When any portion of the optic nerve from the brim to some transversal section (fig. 2) is examined, it is seen that, because of the oblique course of the nerve, the length of
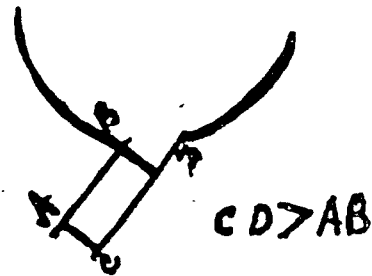

Fig. 2 (Arkin). A transversal section of the optic nerve shows that, because of the oblique course of the nerve, the length of the temporal part of the section is greater than the length of the nasal part.
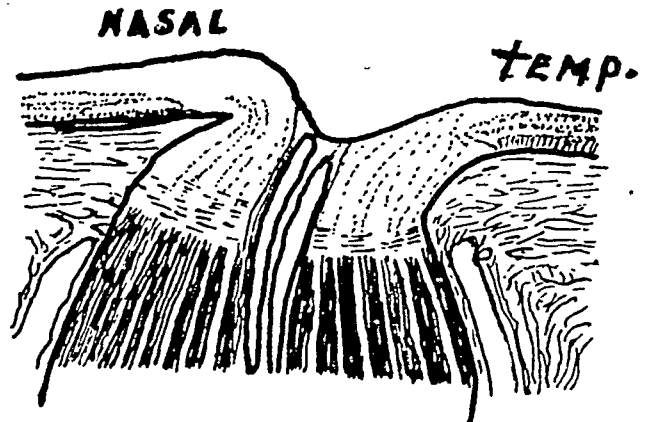

Fig. 3 (Arkin). The bulk of the nerve is greater on its nasal side (after Fuchs).

the temporal part of the section is greater than the length of the nasal part. It follows, therefore, that the bulk of the nerve is greater on its nasal side (fig. 3).

Arlt and Rydel[6] and Fuchs[7] made casual mention of these observations but gave no proper explanation for them.

It is in keeping with the laws of hydrostatics to postulate that a difference in the extent of nerve-fiber accumulation would produce a difference in the degree of resistance of the eye walls. The temporal wall, with fewer nerve fibers, would yield more quickly to increased intraocular pressure and would also show greater excavation than

the nasal wall. An automobile tire under excessive pressure always blows out on the convex side.

ANATOMY OF THE VASCULAR TRUNK

When one considers that the vascular trunk with all of its principal vessels is at the nasal wall of the excavated disc, it would seem to contradict the theory of a different pressure and different resistance on the nasal and temporal sides of the disc. This contradiction is only apparent, not real.

Thus far, only the difference in pressure on the lateral sides has been explained. But the vascular trunk has a central position. None of the vessels except the small macular ones pass over the temporal margin of the disc. Rather, the majority pass over the nasal, superior, or inferior, brim of the disc. When the tissue of the nerve becomes atrophic and hollow, the trunk bends in this direction.

Another factor that must be explained is why, in some cases, there is a contraction of only one-fourth of the visual field (notching of the visual field—symptom of Ronné).

Proponents of the circulation theory attempt to explain this by saying that it is because there is only one artery—superior or inferior. The "hydrostatic" theory herein advanced explains it by saying that it is due to the difference in the resistance of the upper temporal and lower temporal margins of the disc caused by a difference in their structure. Some authors have reported a difference between the size of the superior and inferior walls of the excavation.[3]

Finally, it is necessary to explain why the macular vision remains intact longer than the peripheral. The shorter course of the vascular and nerve supplies of the macula and therefore its better nutrition would seem to retard the decay of the macular vision. The same phenomenon is observed in optic-nerve atrophy deriving from other causes.

CONCLUSION

I admit that the theory herein presented is only an attempt, as is the blood-circulation theory, to explain the nasal contraction of the visual field in glaucoma, and it by no means excludes the circulation theory.

However, the circulation theory explains *only one factor—that its poorer blood supply* put an additional burden on the temporal part of the retina.

The theory I am presenting takes into account not only the existence of a different hydrostatic pressure but also the existence of a different degree of resistance on the nasal and temporal sides of the disc. It would seem, therefore, that the circulation theory and my "hydrostatic" theory complete each other.

SUMMARY

The cause of nasal contraction of the visual field in glaucoma has never been satisfactorily explained. The best known theory is the blood-circulation theory.

I submit as additional considerations the oblique course of the optic nerve, which makes the length greater at the temporal part of the retina, and the consequent difference in the pressure acting on opposite sides of the physiologic or pathologic excavation, as well as the discrepancy in tissue resistance on the nasal and temporal margins of the disc.

Targowa Street, W. 15.

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CONGENITAL CATARACTS*

A SURVEY OF THE VARIOUS TYPES OF OPERATION

CECIL H. BAGLEY, M.D.

Baltimore, Maryland

There has always been some question as to the best method of removing congenital cataracts. To evaluate the various surgical procedures, we have studied the operations performed on 87 eyes with congenital cataracts. The operations were performed at the Wilmer Institute between October, 1943, and November, 1947, by the members of the full-time staff, the visiting staff, and the house staff. In all the cases the cataracts were present at birth or were noted shortly thereafter; the study includes both mature and immature cataracts. The average follow-up on the cases was 9.4 months. The longest period of observation was 4 years.

Similar statistical studies have been made by Horay,[1] Klare,[2] Kiss,[3] Chechik-Kunina,[4] Falls,[5] Owens and Hughes.[6] Owens and Hughes surveyed the operations on congenital cataracts performed at the Wilmer Institute between 1925 and October, 1943. Our data have been analyzed similarly to the method used by Owens and Hughes. This was done so that comparisons can be made of the results in the more recent years with the results in earlier years. The cases were analyzed to determine what effect the preoperative and operative factors had on (1) the final visual outcome, and (2) the occurrence of postoperative complications.

ASSOCIATED OCULAR DEFECTS

The first preoperative factor to be considered was the presence or absence of associated ocular defects. In 32 eyes (36.8 percent) the congenital cataracts were associated with other ocular defects, such as nystagmus, microphthalmos, strabismus, and congenital coloboma of the uveal tract. When strabismus was considered a congenital defect, the operation had been performed on the nonfixating eye.

Table 1 shows the occurrence of these various congenital defects in our group of cases. It was found that the presence of as-

TABLE 1

OCULAR DEFECTS ASSOCIATED WITH CONGENITAL CATARACTS

Nystagmus	9
Strabismus	9
Microphthalmos	2
Microphthalmos+strabismus+nystagmus	5
Microphthalmos+strabismus	1
Microphthalmos+nystagmus	1
Strabismus+nystagmus	1
Strabismus+coloboma of iris	1
Strabismus+nystagmus+aniridia	2
Coloboma of iris+coloboma of choroid	1
Total	32

sociated ocular defects was the most important factor in determining the final visual outcome.

Table 2 shows the relationship of the final vision to the presence or absence of associated ocular defects. Of 47 cases with no associated ocular defects in which the final vision was known, 70.2 percent obtained a final vision of 20/70 or better, while only 12.8 percent had a final vision of less than 20/200. On the other hand, in 13 cases with associated ocular defects in which the final vision was known, 30.8 percent obtained a final vision of 20/70 or better, while 38.4 percent obtained a final vision of 20/200 or less.

AGE AT OPERATION

One of the most controversial points in the treatment of congenital cataracts is the

* From the Wilmer Ophthalmological Institute of The Johns Hopkins University and Hospital.

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TABLE 4

RELATIONSHIP OF TYPE OF OPERATION TO FINAL VISION IN EYES WITH NO ASSOCIATED OCULAR DEFECTS OPERATED ON WHEN PATIENT WAS FOUR YEARS OF AGE OR MORE

Type of Operation	Number with Known Vision	Final Vision		
		20/70+	20/100–20/200	Less than 20/200
Single or Repeated Needlings	5	1 (20.0%)	3 (60.0%)	1 (20.0%)
Needling with Subsequent Lavage	17	13 (76.5%)	3 (17.6%)	1 (5.9)
Linear Extraction	11	11 (100.0%)	0	0

TABLE 5-A
COMPLICATIONS

Associated Ocular Defects	Number of Cases	Vitreous Loss	Anterior Chamber Hemorrhage	Irido-cyclitis	Capsular Remains	Retinal Detachment	Cortical Remains	Lens Sensitivity	Glaucoma	Vitreous Opacities
None	55	13 (23.6%)	2 (3.6%)	1 (1.8%)	1 (1.8%)	1 (1.8%)	3 (5.5%)	1 (1.8%)	0	0
Present	32	4 (12.5%)	0	0	2 (6.3%)	0	1 (3.1%)	1 (3.1%)	2 (6.3%)	1 (3.1%)

TABLE 5-B
COMPLICATIONS

Age at Operation (years)	Number of Cases	Vitreous Loss	Anterior Chamber Hemorrhage	Irido-cyclitis	Capsular Remains	Retinal Detachment	Cortical Remains	Lens Sensitivity	Glaucoma	Vitreous Opacities
Less than 4	33	6 (18.2%)	1 (3.0%)	0	3 (9.1%)	1 (3.0%)	1 (3.0%)	1 (3.0%)	2 (6.1%)	0
4 or more	54	11 (20.4%)	1 (1.9%)	1 (1.9%)	0	0	3 (5.6%)	1 (1.9%)	0	1 (1.9%)

TABLE 7-A

RELATIONSHIP BETWEEN NUMBER OF OPERATIONS AND ASSOCIATED OCULAR DEFECTS

Associated Ocular Defects	Number of Cases	Number of Operations			
		One	Two	Three	Four
None	55	23 (41.8%)	22 (40.0%)	9 (16.4%)	1 (1.8%)
Present	32	18 (56.2%)	8 (25.0%)	3 (9.4%)	3 (9.4%)

TABLE 7-B

RELATIONSHIP OF NUMBER OF OPERATIONS TO AGE OF PATIENT

Age at Operation (Years)	Number of Cases	Number of Operations			
		One	Two	Three	Four
Less than 4	33	13 (39.4%)	9 (27.3%)	8 (24.2%)	3 (9.1%)
4 or more	54	28 (51.8%)	21 (38.9%)	4 (7.4%)	1 (1.9%)

TABLE 8

RELATIONSHIP OF NUMBER OF OPERATIONS TO TYPE OF OPERATION

Type of Operation	Number of Cases	Number of Operations			
		One	Two	Three	Four
Single or Repeated Needlings	13	9 (69.2%)	2 (15.4%)	2 (15.4%)	0
Needling with Subsequent Lavage	28	0	19 (67.9%)	6 (21.4%)	3 (10.7%)
Linear Extraction	20	10 (50.0%)	7 (35.0%)	2 (10.0%)	1 (5.0%)
Intracapsular	11	11 (100.0%)	0	0	0
Broken Capsule	7	5 (71.4%)	1 (14.3%)	1 (14.3%)	0
Extracapsular	8	6 (75.0%)	1 (12.5%)	1 (12.5%)	0

TOTAL NUMBER OF OPERATIONS

Table 7-A shows that there was no significant relationship between the number of operations performed and the presence of associated ocular defects. Table 7-B is a similar study of the number of operations required when the cases are divided according to the age of the patient at the time of operation.

It shows that the age of the patient at time of operation had no significant effect upon the number of operations required to remove the congenital cataract satisfactorily.

The number of operations required to remove the congenital cataract completely in the various methods of operation are shown in Table 8. This table presents an interest-

TABLE 6

RELATIONSHIP OF COMPLICATIONS TO TYPE OF OPERATION

Type of Operation	Number of Cases	Vitreous Loss	Anterior Chamber Hemorrhage	Irido-cyclitis	Capsular Remains	Retinal Detachment	Cortical Remains	Lens Sensitivity	Glaucoma	Vitreous Opacities
Single or Repeated Needlings	13	1 (7.7%)	0	0	1 (7.7%)	0	3 (23.1%)	1 (7.7%)	0	0
Needling with Subsequent Lavage	28	7 (25.0%)	2 (7.1%)	0	0	0	0	0	1 (3.6%)	0
Linear Extraction	20	2 (10.0%)	0	0	1 (5.0%)	0	0	1 (5.0%)	1 (5.0%)	0
Intracapsular	11	2 (18.2%)	0	0	0	0	0	0	0	1 (9.1%)
Broken Capsule	7	3 (42.8%)	0	1 (14.3%)	0	0	1 (14.3%)	0	0	0
Extracapsular	8	2 (25.0%)	0	0	1 (12.5%)	1 (12.5%)	0	0	0	0

TABLE 9-A

RELATIONSHIP BETWEEN NUMBER OF HOSPITAL DAYS AND PRESENCE OF ASSOCIATED OCULAR DEFECTS

Associated Ocular Defects	Number of Cases	Days in Hospital								
		Six or less	Seven	Eight	Nine	Ten	Eleven	Twelve	Thirteen	Fourteen or more
None	55	2 (3.6%)	0	3 (5.5%)	4 (7.3%)	2 (3.6%)	5 (9.1%)	10 (18.2%)	6 (10.9%)	23 (41.8%)
Present	32	3 (9.4%)	1 (3.1%)	1 (3.1%)	0	2 (6.3%)	3 (9.4%)	4 (12.5%)	4 (12.5%)	14 (43.7%)

TABLE 9-B

RELATIONSHIP BETWEEN AGE AT OPERATION AND NUMBER OF HOSPITAL DAYS

Age at Operation (years)	Number of Cases	Days in Hospital								
		Six or less	Seven	Eight	Nine	Ten	Eleven	Twelve	Thirteen	Fourteen or more
Less than 4	33	2 (6.1%)	1 (3.0%)	1 (3.0%)	1 (3.0%)	2 (6.1%)	2 (6.1%)	2 (6.1%)	3 (9.1%)	19 (57.5%)
4 or more	54	3 (5.6%)	0	3 (5.6%)	3 (5.6%)	2 (3.7%)	6 (11.1%)	12 (22.2%)	7 (12.9%)	18 (33.3%)

TABLE 10

RELATIONSHIP OF NUMBER OF HOSPITAL DAYS FOR PATIENT TO TYPE OF OPERATION

Type of Operation	Number of Cases	Hospital Days per Patient								
		Six or less	Seven	Eight	Nine	Ten	Eleven	Twelve	Thirteen	Fourteen or more
Single or Repeated Needlings	13	4 (30.8%)	1 (7.7%)	0	1 (7.7%)	1 (7.7%)	0	1 (7.7%)	1 (7.7%)	4 (30.8%)
Needling with Subsequent Lavage	28	1 (3.6%)	0	1 (3.6%)	1 (3.6%)	0	2 (7.1%)	3 (10.7%)	2 (7.1%)	18 (64.3%)
Linear Extraction	20	0	0	1 (5.0%)	2 (10.0%)	2 (10.0%)	1 (5.0%)	3 (15.0%)	4 (20.0%)	7 (35.0%)
Intracapsular	11	0	0	0	0	0	2 (18.2%)	5 (45.4%)	1 (9.1%)	3 (27.3%)
Broken Capsule	7	0	0	0	0	0	3 (42.8%)	2 (28.6%)	0	2 (28.6%)
Extracapsular	8	0	0	2 (25.0%)	0	1 (12.5%)	0	0	2 (25.0%)	2 (37.5%)

ing contrast between the cases operated on by the method of linear extraction and those operated upon by the method of needling followed by a subsequent lavage.

Naturally in all the cases in which needling was followed by subsequent lavage, 2 or more operations were performed. However, in 50.0 percent of the cases in which a linear extraction was used only one operation was necessary.

The use of the linear extraction, therefore, reduces the total number of operative procedures necessary and thereby greatly decreases the anesthetic and operative risks. Table 8 shows that only one operation was required in 69.2 percent of the cases in which the method of single or repeated needlings was employed. However, when this method of operation was used, the final visual result was poorer than the results obtained after linear extraction or needling followed by subsequent lavage.

NUMBER OF DAYS IN HOSPITAL

Table 9-A shows there was no significant relationship between the number of hospital days per patient and the presence or absence of associated ocular defects. Table 9-B shows a similar lack of correlation between the age of the patient at time of operation and the total number of hospital days per patient.

However, Table 10 shows that the method of operation had an important relationship to the total number of hospital days per patient—64.3 percent operated upon by needling followed by subsequent lavage spent 14 or more days in the hospital, while only 35 percent operated upon by the method of linear extraction spent 14 or more days in the hospital. The method of linear extraction is therefore superior in this respect because it has significantly decreased the number of hospital days per patient.

COMMENT

A comparison of our results with those reported by Owens and Hughes is interest-

ing. In our cases the operations have been performed since October, 1943, while those reported by Owens and Hughes were performed before October, 1943. In the earlier series associated ocular defects occurred in 55.8 percent, but in our series similar associated ocular defects were present in only 36.8 percent, indicating that in the more recent years, operations have not been performed on many eyes having gross defects that would have been subjected to operation in the past.

In the early series, Owens and Hughes found better visual results when the operation was performed on patients over 2½ years of age. In the more recent series, the number of patients operated on at an early age is smaller. To obtain a large enough group to make a similar comparison, it was necessary to separate those cases operated upon when the patient was under 4 years of age from those operated upon when the patient was over 4 years of age. The comparison of the visual results of these groups confirmed the results of the early study by showing that the operative results were superior when the operation could be delayed.

The analysis of the operations performed since October, 1943, confirms the earlier experience that the method of single or repeated needlings does not give as good final visual results as linear extraction or needling followed by subsequent linear extraction.

From our data the most striking point in favor of the linear extraction is the reduction in the total number of operations necessary to remove the cataract completely. Owens and Hughes found similar results in their analysis. They reported that the percentage of cases requiring subsequent operations was essentially the same in the group having the single operation of linear extraction as in the group having the double operative procedure of discission followed by linear extraction.

In our series 50.0 percent of the cases having the single, primary operation of linear

extraction required only one operation to remove the cataract completely. The use of the simple linear extraction not only cuts down the total number of hospital days per patient, but greatly reduces the anesthetic and operative risks of removing congenital cataracts.

The Johns Hopkins Hospital (5).

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APHAKIA*

ALFRED COWAN, M.D.
Philadelphia, Pennsylvania

The purpose of this paper is to consider briefly and to stress again some of the salient features concerning the optical management of aphakia.

CHANGES IN APHAKIC EYE

The removal of the crystalline lens system changes the eye into an entirely different optical instrument. Using the constants of the normal, simplified schematic eye of Gullstrand, the power is reduced from 59.74 diopters to 43.08 diopters, a difference of about 16.6 diopters for air. This produces a principal point refraction of about 12.6 diopters of curvature hypermetropia.

The two principal points of the normal eye which were 1.505 mm. and 1.631 mm. behind the cornea now coincide at the vertex of the optical zone of the cornea. The nodal points which lay 7.13 mm. and 7.256 mm. behind the cornea in the lens containing eye are now replaced by a single point 7.8 mm. behind the cornea.

The direction of the visual axis, therefore, is changed and the eye must turn in a different direction to obtain an image at the fovea. The anterior principal focal distance is 23.214 mm. instead of 16.74 mm. in the normal eye. The size of the retinal image by the aphakic eye to that of the lens-containing eye is in the proportion of 23.21:16.74, about 1.38×. It would be formed 31.014 mm. behind the cornea, that is 7.014 mm. behind the retina of the aphakic eye; a refractive change of about 4 diopters for each 3 mm. of elongation instead of about 3 diopters for each 1-mm. difference in the normal eye, but the proportion of 4:3 does not hold precisely unless the correcting lens is placed at the anterior principal focus of the eye.

REFRACTION OF APHAKIC EYE

The lens that would correct this error and bring forward the image of a distant object so that it would be formed on the retina, must be of such dioptric power and denomination that the distant object would be placed (optically) at the far point of the eye which lies about 79.43 mm. behind the cornea. If this lens were situated at the anterior principal focus of the eye, it would have a power of about +9.75 diopters and the retinal image would be 38 percent larger

than the image in the normal eye. Of course, the spectacle lens is always set closer than 23 mm. from the cornea.

If it were placed at about 14 mm. in front of this schematic aphakic eye, it would have to have a power of about +10.7 diopters and, while the retinal image would not be so great because of the lessened distance, it would still be about one-third larger than that in the normal, lens-containing eye.

The size of the retinal image in aphakia depends on the refraction of the eye before removal of the lens. The image in the previously myopic eye will be larger than in the previously emmetropic eye because a convex lens of less power will be required to correct it. The image will be smaller in the eye that was hypermetropic before operation. But in every case of aphakia the retinal image is larger than before extraction of the crystalline lens and it is due to this enlargement that better than average normal visual acuity is frequently obtained in aphakia.

EYE DEVOID OF ACCOMMODATION

Besides these changes, the eye is now devoid of any accommodation whatever, and this loss is not unimportant because, even in aged persons, there is some power of accommodation, and be it ever so slight it helps in the adaptability of the eye. Properly corrected for distance and no accommodation, the vision becomes noticeably blurred from 4 meters in.

Also after removal of the crystalline lens, especially a senile lens, the eye becomes hundreds of times more sensitive to violet and ultraviolet light than before. Often there is some degree of erythropia after cataract operation, especially in those patients whose pupils have been enlarged by iridectomy. Cyanopia may occur immediately after extraction and last several weeks. These conditions are always transient.

In addition to the changes mentioned, regardless of the skill of the surgeon and the healthy success of an extraction of a senile cataract, there remains, in nearly every case, a more or less mutilated eye.

UNUSUAL NEW VISION

The wonder is why all of these elderly persons who have been operated on for cataract are not confused and, to a certain extent, disappointed in their entirely new kind of eye. It seems only reasonable that many find it hard to accustom themselves to it. The ophthalmologist, therefore, in treating a patient with aphakia after extraction of senile cataract, must always bear in mind that he is treating an elderly person who has just had his sight restored, but by the use of a strange, new optical instrument.

An unusual kind of vision is provided, possibly more acute than ever before, but with larger images, different aberrations, a changed pupil, and lessened focal depth. The patient must accustom himself to strong glasses with all their faults, a smaller field, and the probable image distortion with a newly acquired astigmatism.

Often it will be seen that the patient will find it difficult, at first, to fixate an object so that it will lie exactly on his new visual axis in order for it to be imaged at the fovea. While with most of these phenomena nothing can be done except to explain them away, some can be refined out or softened with carefully chosen and adjusted glasses. The optical management of aphakia is usually difficult for the younger man and often for the experienced ophthalmologist, too.

OPTICAL MANAGEMENT OF APHAKIA

All the accessory effects of the correcting glass before any ametropic eye are exaggerated in the case of aphakia corrected by a convex lens of around 10 diopters. The focal distances and the location of the lens itself are measured from its principal planes, and the position of the principal planes depends on the shape and thickness of the lens. Even though the finished lens has the same equivalent power, unless it is

of the same shape and thickness as the trial lens, the vertex power, and therefore the effectivity of the spectacle lens, will not be the same.

In low-power lenses, the difference in effectivity is so slight it may be disregarded, but in strong convex lenses it is important. For example, an 11-diopter, equal sided, biconvex lens 7-mm. thick has a vertex power of about 11.12 diopters. If this lens were replaced by a meniscus lens with—3-diopter back surface and +14-diopter front surface, and its back surface in the same plane, the effective power would be about 11.88 diopters—a difference of about 0.75 diopter. The same rate of change is also produced in the cylindric component.

IMPORTANCE OF VISUAL AXES

Uninformed opticians are under the impression that the pole of the spectacle lens (the so-called optical center) should coincide with the center of the pupil. With ordinary low-power lenses and normal eyes this may be done without notable error. But we know that, properly, the pole of the lens should coincide with the visual axis, which does not usually pass exactly through the center of the pupil.

In the case of displaced, mutilated, irregular, or multiple pupils the visual line may not go through the pupil at all. It may even pass through an opacity. In the case of a 10-diopter lens, in which a decentration of 1 mm. produces a prism of 1 diopter, proper centering in binocular aphakia is very important.

If the lenses are alike or nearly so, the conjugate movements of the eyes can bring them into such parts of the lenses that the apparent displacement and distortions are in the same direction for the two eyes; but if they are improperly adjusted with regard to the visual axes or if there is a material difference in the strength between the two lenses or if they contain strong cylinders with marked angular difference between

their axes, the prismatic effect is unequal as soon as the eyes turn from looking through the poles of the lenses. This prismatic effect, particularly in vertical and oblique directions, may be enough to cause the patient a great deal of discomfort.

TILTING OF LENSES

The tilting of these lenses is also important. Roughly about a 0.12-diopter cylinder is produced for every diopter of the given lens power with a tilting of 20 degrees, so that in looking at this obliquity through a 10-diopter lens there will be produced the equivalent of a 1.25-diopter cylinder with axis perpendicular to the direction of the movement of the eye. With a fixed spectacle glass, looking obliquely starts the moment the eye turns from looking straight forward. It is easy to conceive how, in looking obliquely through these lenses, a cylindric component at one time can be increased by a whole diopter while on looking along the opposite direction the same amount can be neutralized out.

AMOUNT OF REFRACTIVE ERROR

In the correction of any form of ametropia it is important first of all to determine the most nearly approximate refraction; but it is of equal importance that the finished spectacle lens produce as closely as possible the same effective power as that of the trial lenses. The refractionist therefore should give careful consideration to such controllable factors as the flexure of the lenses, the style of bifocal, and the best adjustment and position of the spectacles before the eyes. The importance increases, of course, with the amount of the refractive error.

In order to procure an effective power in the finished spectacle lenses which approximates that of the trial lens combination, the ophthalmologist whose equipment consists of old-fashioned double convex and double concave spheric trial lenses must either prescribe lenses that nearly duplicate the shape

of his trial lenses or the spectacle lenses must be carefully computed and ground with such back-front curves that they will have the same effectivity.

If the lens contains a cylinder, the closest duplicate of the double convex cylindric trial lens combination will have one side spheric and the other toric. For example, a +10D. sph. ⊃ +2.0D. cyl. ax. 180° should have one side a +5.0D. sph. and the other side a +5.0D. sph. ⊃ +2.0D. cyl. ax. 180°. But a double convex lens is not a good form even in a low power.

A good form lens of about 10 diopters is one which might be started from either about +14 diopters in front or about −3 diopters in back. Variations of 2 or 3 diopters in back-front combination will not make a great difference providing the back surface is concave.

At best the field is bound to be restricted through such a strong convex lens and all the faults besides the prismatic effects toward the periphery must be accepted. It is practically and theoretically impossible to eliminate the astigmatism of oblique pencils and other serious faults of a convex spectacle glass of around 10 diopters, especially if it contains a cylindric component.

APPROXIMATION OF EFFECTIVITY

An approximation of the effectivity can be obtained by arranging the lenses in the trial frame to resemble the shape of the finished lenses. Compared with the thickness and index of refraction of a biconvex lens of +10 diopters having an effective power of 10.08 diopters, two equal-sided lenses, +13 in front and −3 in back, will have an effective power of around +10.5; a +10-diopter meniscus with −3 back will have an effective power of +10.55 diopters.

Plano-trial lenses (every trial lens should have a plane surface) can be arranged so that they will conform to the finished spectacle lenses with negligible difference. Take a case, for example, in which by the ordinary

procedure of manifest refraction the final combination is +11 diopters.

Simply replace the single +11-diopter lens with two lenses, one −3 diopter with concave surface toward the eye as close to it as possible or at the exact distance the spectacle lens will be placed, and in front, in apposition to the plane surface of the concave lens, place the plane surface of a +14-diopter convex lens.

After testing subjectively for small differences with quarter- and half-diopter additions and subtractions, suppose the final result totals +10.5 diopters; order the lens ground with +13.5 diopters in front and −3 diopters in back.

The advantage of a meniscus over a flat lens is that, optically, it lies farther away from the eye than its actual position. This is good in hypermetropia because, for distance vision, the farther away from the eye the correcting lens the weaker its power must be and the larger the retinal image.

Suppose, for example, the result by the usual method is a sphero cylinder, +11D. sph. ⊃ +2.0D. cyl. ax. 180°. Ordinarily this combination will consist of a +11-diopter spheric lens in the rear cell and a +2-diopter cylinder in the front cell of the trial frame. Replace these lenses with a −2-diopter cyl. ax. 90°, concave surface toward the eye and as close as the spectacle lens will be and, in front of this with curved surface in front and plane surface behind and in apposition to the front, plane surface of the cylinder, a +13-diopter sphere.

In this way we have transposed the combination from +11D. sph. ⊃ +2.0D. cyl. ax. 180° to +13D. sph. ⊃ −2.0D. cyl. ax. 90°, its numerical equivalent.

This combination will, of course, not have the same back power and it will be necessary to add quarter or half diopters to both sphere and cylinder to find the difference. The axis, having been carefully determined in the first stage, will remain. If after the refinement by subjective tests

the final result is +12.5D. sph. ⊃ −2.0D. cyl. ax. 90°, order the lens to be ground as written. It is a good form.

By this procedure no computation is necessary nor need any allowances for shape or distance be made, provided the spectacle lenses are placed at the same distance from the eyes as were the trial lenses.

A change in distance of only 1 mm. away from the eye is likely to make a noticeable difference in effectivity in such strong lenses and this should be determined by pushing the lenses closer or pulling them away slightly when the patient returns to have them checked. If, by doing this, any improvement can be made one way or the other, have them readjusted.

PRESCRIBING BIFOCALS

These better forms can be obtained in fused bifocals in which the segments will be placed in the front spheric surface. If one-piece bifocals are preferred they can be ground with segment on the −3-diopter back surface in the case of spheric lenses. The spherocylindric lenses can also be made in one-piece bifocals but they must be specially ordered because the segment must be incorporated in the front spheric surface.

The advantages of cement bifocals should not be overlooked. Cement bifocals are optically good and will often be found useful and economical, especially for the first glasses when it is likely that the correction may have to be changed in a short while.

The segment of any of these bifocals should be so cut that the base is down, to neutralize somewhat, but more particularly not to exaggerate, the strong prism, base up, already in the lower part of the distance glass. For this reason flat-top segments are fundamentally wrong in any bifocal with convex distance lens.

Also, too often it is forgotten that the ordinary reading distance is nearer 14 inches (2.75D.) than 13 inches (3.0D.). If the media are clear and the visual acuity good, there is no reason ordinarily for stronger reading additions than 2.75 diopters. This will give a greater range and usually prove more satisfactory than additions of +3 or +3.25 diopters, which are so frequently prescribed in aphakic corrections. Stronger additions for near are justifiable, however, when the visual acuity is low, especially with monocular vision.

MONOCULAR APHAKIA

The correction of monocular aphakia (one eye normal with good visual acuity) is impractical, not only because of the diplopia due to the aniseikonia and to the prismatic effect of the difference between the glasses, but also because the patient has two different optical instruments, one dynamic with more or less active accommodation and normal adaptability and the other static.

It has been claimed that binocular single vision from infinity in to 10 inches has been obtained by the use of a contact glass for persons with monocular aphakia, even for young persons with accommodation in the normal eye sufficient for all ordinary distances.

If the retinal images are made equal in size it is possible to superimpose one on the other, but perfectly for only one distance at a time. But even then, mere equalization of the retinal images is not sufficient to produce single binocular vision. It is hard to conceive how this is physiologically possible with such a pair of eyes. But it is equally hard to explain accommodation for near vision in aphakia as has sometimes been reported.

The same reasoning regarding a contact glass can be applied to the usefulness of minifying glasses with the added disadvantages of their unsightliness and small field. While these devices may enable a patient to obtain a sort of binocular vision, it cannot possibly be good and might cause considerable discomfort, nevertheless if a patient seems to be comfortable with such a

quality of vision there is no reason why it should not be given.

In monocular aphakia, immature cataract in the other, the eye chosen for correction will, of course, be the one with the better visual acuity. In many instancs, however, the patient will prefer the use of the lens-containing eye even though the visual acuity cannot be brought up to that of the aphakic eye.

In monocular aphakia (only the aphakic eye functioning) the proper power and shape of glass and its position before the eye are important, but this is a simple matter compared with the correction of a pair of aphakic eyes.

CORRECTION OF BINOCULAR APHAKIA

It is in the correction of binocular aphakia that the greatest care must be taken to observe the characteristics of the eyes and to utilize the power, shape, and adjustment of the lenses to the best advantage of the patient. It is sometimes very difficult for an elderly person to coördinate two aphakic eyes, providing they do coördinate.

For this reason, probably in many instances the patient who submits to the removal of the cataract in the second eye is often disappointed after the second operation. This is especially true if there is a material difference between the refractions of the two eyes.

To the mind of the layman it is logical to suppose that two eyes are better than one, so much better that he is willing to risk a second operation even though a good result was obtained by the first. But it seems that most ophthalmologists also think the same way.

Often after combined operation, the amount of light which enters the eye through the enlarged pupil is so much greater than that to which the patient is accustomed that it causes considerable glare. This excessive light, particularly the selective nature of it, is likely to prove very annoying for some time following the operation, and protection is often desirable. For this purpose dark glasses may be given for those times when the occasion warrants. They should never be ordered for permanent, constant use. For obvious reasons light shades are just about useless. When dark glasses are given they should be dark enough to serve their purpose.

The provision of the best optical correction for aphakia requires special skill, experience, and a knowledge of the scientific principles involved, but also it must be constantly borne in mind, as already stated, that we have also to treat a patient that frequently is a more or less perplexed, elderly person who, by means of a serious operation, has just recently been given an entirely new kind of vision.

1930 Chestnut Street (3).

NEWER CONCEPTS IN THE CLASSIFICATION OF THE GLAUCOMAS[*]

H. SAUL SUGAR, M.D.

Detroit, Michigan

With the introduction of gonioscopic and chamber-angle depth observations into recent considerations of ocular hypertension, it has become obvious that many of the older ideas about glaucoma need modification. These changes have been sufficient to require a broader concept of the etiology, course, and even of the treatment of the various ocular conditions which have in common an elevation of intraocular pressure.

The term *glaucoma* does not apply to a particular ocular disease entity but rather denotes only the presence of increased intraocular pressure. Thus, glaucoma may be one of the manifestations of a large group of ocular diseases which may be called *the glaucomas*. From the viewpoint of what constitutes an increase in intraocular pressure and, therefore, glaucoma, it must be considered as that pressure which the individual eye cannot tolerate without some damage to its integrity.

Let us consider the classification of the glaucomas as a framework for the various concepts to be discussed.

Von Graefe[1] distinguished four clinical varieties of glaucoma; namely, acute glaucoma, absolute glaucoma, secondary glaucoma, and "amaurosis with excavation of the disc" (chronic simple glaucoma).

The classification in general use today is more elaborate but actually differs little from von Graefe's. It may be divided into three groups:

I. Primary or idiopathic glaucoma
   A. Congestive glaucoma (inflammatory, incompensated)
      1. Acute
      2. Chronic

   B. Chronic simple glaucoma (noninflammatory, compensated)
II. Secondary glaucoma
III. Hydrophthalmos

Absolute glaucoma is the end stage of any of the glaucomas and need not be included in any classification.

The weaknesses of this classification lie in the lack of etiologic connotation and in its failure to provide a cubbyhole for all the clinical varieties of glaucoma.

One of the things which started my dissatisfaction with this classification was my inability to classify properly the type of glaucoma which occasionally follows instillation of mydriatic drugs in patients with shallow anterior chambers and without previous ocular hypertension. Here the patient shows no evidence of vascular congestion, but the tonometric reading may be well over 60 mm. Hg (Schiøtz). The condition is acute but not congestive; so it does not fit into either the acute congestive glaucoma or the chronic noncongestive glaucoma cubbyholes, although the latter is where many men have placed it.

A review[2] of a series of 45 patients with acute glaucoma was made to determine whether the presence or absence of congestion was a justifiable criterion in the classification of glaucoma. The results of the study indicated that 95.4 percent of the 24 cases precipitated by mydriasis (mydriatic drugs or darkness-dilatation) were free from congestion at the onset. Of the 7 with acute episodes precipitated by accommodative effort, 80 percent started without congestion. In the group of 18 cases precipitated by vascular engorgement, presumably involving the vessels of the ciliary body, 53.3 percent were congested from the onset.

It appeared, then, that in a majority of cases of acute glaucoma, the onset was not

associated with congestion, but, after a varying period of time, the eye suddenly became congested, due, probably, to the presence of histaminelike metabolic products resulting from the poor nutrition and hypoxia associated with the interference with the blood supply by the high intraocular pressure.

Congestion is only a phase into which an eye with acute glaucoma may or may not enter, depending on the precipitating factors and the duration and height of the increased intraocular pressure. Therefore, the descriptive terms congestive and noncongestive and their synonyms were eliminated from the diagnosis and only appended after it as follows:

Acute glaucoma, noncongestive phase
Acute glaucoma, congestive phase
Simple glaucoma, noncongestive phase
Simple glaucoma, congestive phase

Another weakness in the generally used classification is its tendency to give the impression that the various primary glaucomas are various stages of the same disease so that one clinical picture may change to another and then even revert back to the original type. Beginning with Raeder,[3] in 1923, there has come a separation of the two primary glaucomas of adult life into two separate entities, based on the depth of the chamber angle. This has been amply confirmed by gonioscopic evidence and by provocative mydriasis.[2]

One confusing consideration is how to classify acute glaucoma which remains unrelieved by treatment. This is still acute glaucoma which has entered a chronic phase. The term acute glaucoma is used to designate a specific entity and should be used as the diagnostic term, even though the words "chronic phase" may be appended.

The classification which I wish to present is based on an attempt to continue the time-honored terms *primary* and *secondary* glaucoma and yet maintain an etiologic viewpoint.

My first attempts at classification of the glaucomas considered only chronic simple glaucoma as primary since this was considered the only condition whose relation to any other ocular disease was not known. Since acute glaucoma results from a known anatomic cause, it was classified as secondary.

Following this classification it was only a step further to avoid the terms primary and secondary entirely and simply to classify each type of glaucoma according to its causal relationships. But because we do not yet know the cause of the most important glaucoma—chronic simple glaucoma—and because of usage, I have reverted in teaching to the use of the terms primary and secondary.

The primary glaucomas, according to my present concept, are those which do not follow other ocular disease. In this group are included the idiopathic chronic simple glaucoma cases and those cases caused by anatomic and developmental anomalies. The latter are subdivided into the congenital glaucomas and acute (narrow-angle) glaucoma which depends on both an anatomic predisposition[4]—a narrow angle usually associated with high hyperopia—and the normal continuous growth of the lens with increasing age, together with such physiologic angle-narrowing factors as accommodation, dilatation of the pupil, and congestion of the ciliary body.

The classification of the glaucomas in Table 1 is suggested on the basis of the definition of primary glaucomas just presented.

A consideration of the diagnostic clinical features of each of the glaucomas would be beyond the space available in this paper. However, a consideration of the important ones, especially those which present a diagnostic problem and those about which newer concepts have arisen, will serve to describe the desired material.

GLAUCOMA SIMPLEX

By far the most important of the glaucomas is the classical glaucoma simplex. The usual patient with early glaucoma simplex has no symptoms until changes in the visual fields bring the condition to his attention. Occasionally some fogginess of vision and

TABLE 1

A CLASSIFICATION OF THE GLAUCOMAS

I. PRIMARY GLAUCOMAS

A. Chronic simple (normal angle width) glaucoma { noncongestive phase / congestive phase (rare)

B. Glaucomas caused by anatomic and developmental anomalies
  1. Congenital glaucomas
    (a) Hydrophthalmia
    (b) Glaucomas associated with aniridia or with neurofibromatosis
  2. Juvenile glaucoma. (Only those cases related to developmental anomalies belong here.)
  3. Acute (narrow-angle) glaucoma—due to anatomic plus physiologic angle-narrowing factors which lead to mechanical obstruction of trabecular spaces by iris. This includes the acute glaucoma associated with microcornea
    (a) Noncongestive phase—including "dilatation glaucoma"
    (b) Congestive phase—classical "acute congestive glaucoma" and the recurrent form called "chronic congestive glaucoma" in the older classification

II. SECONDARY GLAUCOMAS (Each may be subdivided into a noncongestive and a congestive phase; some never enter the congestive phase.)
  A. Secondary glaucoma due to mechanical blockage of the trabecular spaces
    1. Obstruction by iris
      (a) Acute secondary glaucoma due to lenticular intumescence
      (b) Acute secondary glaucoma due to dislocation of the lens into the anterior chamber
      (c) Glaucoma following operation for cataract—*aphakic obstructive* glaucoma—due to delayed reformation of the anterior chamber
      (d) Glaucoma associated with essential progressive atrophy of the iris
      (e) Glaucoma associated with retrolental fibroplasia
    2. Obstruction of the trabecular spaces by particulate matter
      (a) Glaucoma capsulare
      (b) Pigmentary glaucoma
      (c) Glaucoma due to obstruction by lens particles
      (d) Glaucoma due to tumor growth
      (e) Glaucoma due to cellular debris associated with active or healed iridocyclitis
  B. Secondary glaucomas due to lack of communication between the anterior and posterior chambers
    1. Secondary glaucoma due to seclusion of the pupil
    2. Secondary glaucoma due to total posterior synechia
  C. Secondary glaucomas probably due to overproduction of aqueous as a result of irritation of the ciliary processes
    1. Glaucoma associated with posterior dislocation of the lens so that latter touches ciliary processes
    2. Cyclitis and anterior choroiditis
  D. Secondary glaucomas due to obstruction of venous drainage
    1. Experimental and clinical glaucoma due to vortex-vein obstruction
    2. Secondary glaucoma in pulsating exophthalmos
  E. Secondary glaucomas due to newly proliferated anastomotic vessels involving the Schlemm's canal mechanism in rubeosis iridis (diabetic and arteriosclerotic) and following occlusion of the central retinal vein
  F. Secondary glaucoma resulting from trauma
  G. Secondary glaucoma associated with epidemic dropsy
  H. Secondary glaucoma associated with choroidal angiomatosis

diminished accommodation bring him to the oculist. Less frequently, colored halos around lights and headache are complained of. In the later stages the patient complains of night blindness, contraction of the visual fields, or even interference with macular vision.

Objectively, the ocular findings in simple glaucoma depend on the stage of the disease. The earliest findings are a slight ocular hypertension and changes in the pericecal visual field, usually manifested as a vertical increase in the size of the blindspot. As the

disease progresses, the field changes increase slowly so that various characteristic changes, such as Bjerrum's sign and Roenne's step, occur. Excavation of the optic disc begins at the temporal side of the disc. As the disease progresses, the excavation of the disc increases concurrently with contraction of the field, until only a central zone about 10 degrees in diameter remains.

If allowed to continue untreated, the tension usually remains between 30 and 45 mm. Hg (Schiøtz); and the central field is finally lost. In this state of absolute glaucoma, the

eye may remain painless and pale or may, rarely, after a considerable time, suddenly enter a congestive state, in which the conjunctival vessels become injected, the eye painful, and the tension high. In fact, the suddenness of the onset and the symptoms may be the same as in an eye with acute glaucoma which has entered the congestive phase.

The few eyes with early simple glaucoma which have been studied in the laboratory show no abnormalities. The late stages of unoperated simple glaucoma show only the effects of increased intraocular pressure.

The diagnosis of early simple glaucoma depends on routine tonometric studies. Tactile tension estimations are so notoriously inaccurate that they cannot be termed a useful subsitute for the instrumental measurements.

The experience of the residents in ophthalmology at the Detroit Receiving Hospital serves to emphasize the value of routine tonometry. In March, 1947, when the present glaucoma clinic at that institution was started, there were about 18 active glaucoma patients, all in an advanced stage. Routine tonometry on all eye-clinic patients of 40 years of age or over led to an increase of glaucoma patients during the first nine months to 118, a high proportion of which were in the earliest stages.

Gonioscopically, the chamber angle is normal in depth in simple glaucoma, although one occasionally finds cases of simple glaucoma in which the chamber and the angle are relatively shallow. The shallowness is coincidental, since the factors leading to relative shallowing of the chamber are present in persons of the age group affected. In the late stage of simple glaucoma in which sometimes a congestive phase appears, peripheral anterior synechias may form.

The slitlamp findings in simple glaucoma are entirely negative except in the later stages when congestive episodes may have occurred. Then the evidences of congestive and atrophic changes are seen.

The provocative tests, including the water test and pressor-congestion test,[7] are of considerable help in the diagnosis of early cases of simple glaucoma, especially when the tonometric readings are 28 to 30 mm. Hg (Schiøtz) or when the tonometric readings are lower but the history or clinical findings are suspicious. The provocative tests are significant only when positive.

In the more advanced stages, the diagnosis is made on the basis of the visual fields, the tension, and the appearance of the nerve-head.

PRIMARY ACUTE GLAUCOMA

The second of the glaucomas in importance is primary acute (narrow-angle) glaucoma. It is not difficult to diagnose in the full-blown congestive phase but the differentiation, in the noncongestive phase, from simple glaucoma and, in the congestive phase, from the secondary glaucomas, is usually difficult, and of much more than academic importance.

The actual onset of the noncongestive phase of acute glaucoma is hardly noticed by the patient. Blurring of vision may be noticed, especially among the younger patients. Sometimes the onset is associated with colored halos, or slight pain in the head or in the eye. These mild symptoms usually last a half-hour to two or three hours and then subside entirely, only to recur at varying intervals, becoming more frequent and lasting longer as time goes on, each attack leaving the anatomic conditions more favorable for further attacks. The circumcorneal injection associated with these episodes is slight, if any.

Occasionally the patient finds relief from his symptoms by the use of hot or cold applications, by looking at a bright light for several minutes, or by sleep.

Ultimately, one of the mild episodes will persist longer than usual, and suddenly the patient will experience marked diminution in vision, photopsia, swelling and redness of the conjunctiva, and pain in the head and the eyes, often so severe as to cause nausea and vomiting.

The sudden change in symptoms often

awakens the patient from sleep and occurs without any precipitating factor, it being an aggravation of the previous mild symptoms. It is induced by a sudden congestion of the globe, probably as a result of the accumulation of tissue metabolites within the eye when the blood supply and drainage of the intraocular fluid is impeded due to the high intraocular pressure. At any rate, the sudden aggravation of symptoms is attributable to the combination of high intraocular pressure and increased permeability of the vascular walls.

In some cases, the first mild noncongestive episode of acute glaucoma is followed by the congestive phase. Of course, if treated early with miotics, even the congestive phase subsides rapidly, and if the patient does not use miotics as a prophylactic measure it will likely recur, the disease passing again through the noncongestive phase. What has been previously called the prodromal stage of acute glaucoma is in reality the noncongestive phase of the disease.

In many patients with episodes of primary acute glaucoma, there is a history of onset of the condition following nervous shock. Many authors for this reason attribute primary acute glaucoma to a nervous cause. Actually the neurovascular factors are important only as the precipitants of the angle-blocking mechanism.

Objectively, the tension may not be different in the noncongestive and in the congestive phase. It is usually very high in the latter, since the additional vascular congestion adds to the mechanical obstruction of the angle.

. Shallowness of the anterior chamber is typical of this type of glaucoma and is its predisposing anatomic cause. For this reason the nonglaucomatous fellow eye of a patient who has had an episode of primary acute glaucoma may be classified as preacute glaucoma. The same term may be used to describe the interim of normality between episodes of primary acute glaucoma in either the noncongestive or the congestive phase.

Shallowness of the anterior chamber in this form of glaucoma is usually associated with high or relatively high hyperopia, especially during the patient's early adult life.

When vascular decompensation occurs, it produces not only chemosis of the conjunctiva but edema of all the ocular tissues. The corneal epithelium is so involved that details in the fundus are obscured. Blebs and vesicles appear on the cornea. The cornea loses its sensitivity. In the noncongestive stage, even in the presence of very high tension, the cornea is not edematous, and arterial pulsation is easily seen in the fundus.

The pupil is dilated in both phases of acute glaucoma but is irregular in the congestive phase. The dilatation, when it is not in itself the actual etiologic factor in the onset of the disease, is probably due to slight stretching of the eyeball and to the pressure effect on the nerves.

In rabbits, if a needle is inserted into the anterior chamber and the pressure increased, the pupil dilates, and it contracts when the pressure is decreased.

Barkan[8] suggested that the vertically oval shape of the pupil is due to anatomic narrowness of the angle above. Undoubtedly, in the congestive phase the blood supply to a few of the nerve fibers to the sphincter is affected irregularly, and irregularity of the pupil results.

The iris in the congestive phase becomes muddy and discolored. Some of the iris vessels become visibly distended. If the congestive phase persists any length of time, fine posterior synechias may form.

The nervehead in the noncongestive phase is normal. In the congestive phase, it is red but not excavated. If repeated attacks occur or if an attack persists, the disc becames rather rapidly excavated.

Biomicroscopy reveals abnormalities only in the congestive phase or after the eye has suffered the effects of long-standing pressure as in simple glaucoma. Edema of the epithelium, blebs, and vesicles are seen in the congestive phase. The contents of the anterior chamber and the vessels of the iris are difficult to see clearly in this phase. Chemi-

cal studies are of no etiologic significance but show only the results of the vascular changes.

In the noncongestive phase, gonioscopy reveals the contact between the iris and the trabecular wall. In the congestive phase, closure of the angle must be presumed, since the cornea is usually too cloudy for visibility.

In a person in whom a congestive attack is relieved spontaneously or with miotics, floating particles of pigment, irregularity of the pupil, occasional fine posterior synechias, and pigment on the posterior corneal surface are seen. Slight persistent pericorneal injection may be present. If a patient is seen for the first time after such an attack, the tension in the eye is usually below normal and an erroneous diagnosis of acute iritis may be made.

When the congestive phase of acute glaucoma has been allowed to exist without treatment, the eye eventually becomes blind and enters the stage common to all glaucomas, namely, absolute glaucoma. The eye remains injected, the episcleral veins remain dilated, vesicles form on the cornea, and the iris remains muddy. Pain persists. Gradually, the vascular system adjusts itself somewhat, and the eye often becomes less painful.

SECONDARY GLAUCOMAS

Of the secondary glaucomas, those due to obstruction of the trabecular spaces by iris deserve consideration as a group. They have the same mechanism as primary acute glaucoma. This is most obvious in the acute secondary glaucoma due to lenticular intumescence which not only has the same mechanism but has the same clinical picture except that only one eye is usually involved in the process; that any refractive error, even high myopia, may have been present; and that an intumescent cataract is present. An anterior chamber of normal depth in the fellow eye is an important differential sign. I have never seen a primary acute glaucoma with a normally deep anterior chamber in the fellow eye.

Secondary glaucoma following cataract operation has been proved clinically to be due to obstruction of the trabecular spaces by iris only since my preliminary report on the gonioscopic findings in 1940. It is important not only as proof for the fact that obstruction of the trabecular spaces can cause a rise in the intraocular pressure in human beings, but in the differential diagnosis from other glaucomas occurring coincidentally in an eye which has had surgery for cataract.

In this type of glaucoma, the obstruction of the trabecular spaces usually results from delayed reformation of the anterior chamber due usually to failure to obtain tight wound closure.

The clinical picture varies considerably, depending on whether it occurs early or late after the operation. When it occurs early, the eye is usually congested and painful, and may be mistaken for a postoperative inflammatory process. Late onset may be free of congestion and lead to symptom-free loss of vision as in glaucoma simplex.

The diagnosis depends on gonioscopy. The etiologic factor may be relieved surgically by the cyclodialysis operation in both the congestive and the noncongestive phases.

The secondary glaucomas due to obstruction of the trabecular spaces by particulate matter are of several types, depending on the obstructing material. The diagnosis in each depends on gonioscopic examination of the chamber angle. The type, designated as glaucoma capsulare,[9] is associated with the exfoliation of the zonular lamella of the lens capsule. It is impossible, in this group, to be certain whether the capsular debris or the pigment granules deposited in the trabecular spaces, or both, are the cause for this type of glaucoma.

A second type of secondary glaucoma associated with a marked deposition of pigment in the trabecular spaces, without capsular exfoliation, is a form of glaucoma which has recently been described as an entity. It has been designated as *pigmentary glaucoma.*[10]

It was observed in two young myopic individuals with degeneration of the pigment epithelium of the iris and ciliary body. The pigment was deposited as a dense trabecular pigment ring in the trabecular spaces and as Krukenberg spindles on the posterior cor-

diagnosis is more probably correct. In this case, the treatment is exactly the same as that for simple glaucoma, both medically and surgically.

The secondary glaucoma associated with cyclitis or anterior choroiditis is probably
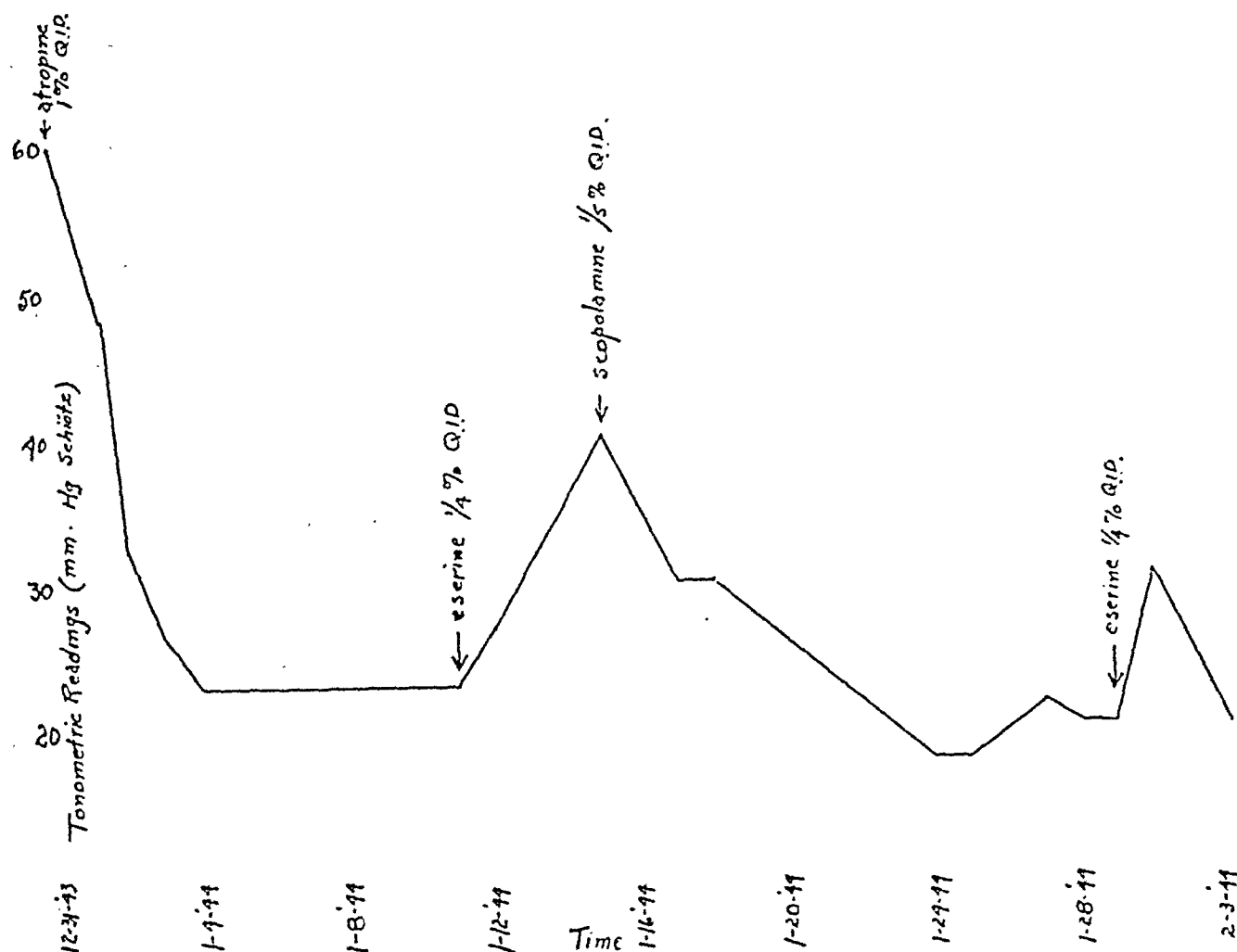
Fig. 1 (Sugar). Graphic representation of the effect of cycloplegics and miotics in the treatment of cyclitic secondary glaucoma.

neal surface as well as on the anterior iris surface. It differs from chronic simple glaucoma clinically in its response to mydriasis by significant elevation of the intraocular pressure.

Secondary glaucoma due to obstruction by cellular debris in the angle is difficult to differentiate from simple glaucoma when the antecedent iridocyclitis is completely inactive. Only the history of a previous iridocyclitis and the gonioscopic and biomicroscopic findings suggest the possible cause. If the condition is and remains unilateral, the

due to an overproduction of aqueous and is usually temporary, lasting only as long as the irritative inflammatory process persists in a relatively quiet form.

It is interesting that early in these inflammatory processes, when the eye is congested, the intraocular pressure is usually lower than normal, as in ordinary acute iritis. This is presumably due to a general vasodilation involving the iris and ciliary body.

As the inflammatory process appears to subside, and the eye becomes relatively paler or completely white, the intraocular pres-

sure rises. Deposits on the posterior corneal surface increase, even though evidence of increased protein in the aqueous may decrease or even be biomicroscopically absent.

The diagnosis is important in that the intraocular pressure responds favorably to atropine or scopolamine and not usually to miotics, as the following case shows.

Case report. S. V., a 25-year-old man, was first seen by me on December 31, 1943. He had been entirely well until July, 1943, when he began to notice fogginess of vision, first in the left eye and later in both eyes.

Examination revealed a bilateral chronic granulomatous iridocyclitis. The visual acuity was: R.E., 20/30; L.E., 20/20. The tonometric readings were: R.E., 21 mm. Hg (Schiøtz) ; L.E., 60 mm. Hg. Both eyes were rather pale. Atropine (1 percent) was instilled into the left conjunctival sac three times daily. The response to cycloplegics was favorable, to eserine unfavorable as shown in Figure 1. The tension stayed normal from February 3, 1944, until a recurrence of the iridocyclitis appeared in June, 1946. This episode responded to scopolamine.

One other secondary glaucoma will be considered since some new thoughts concerning it have appeared. This is the secondary glaucoma associated with rubeosis iridis and following occlusion of the central retinal vein.

From the viewpoint of mechanism both of these are exactly the same.[11] The chamber angle early is open and shows the same newly formed vessels lining the angle and penetrating the angle wall. Later the angle becomes blocked by adhesion between the iris root and the trabecular wall.

The earliest case of this type I have seen was in a patient with one blind, painful, glaucomatous eye with diabetic rubeosis iridis, in whose other eye very localized small areas of rubeosis became evident near the pupil border and in a portion of the angle as the tension rose in that eye to 36 mm. Hg (Schiøtz). The angle was entirely open. The newly formed vessels lining the small areas of the angle could be seen penetrating

the trabecular wall, presumably to anastomose with Schlemm's canal.

The occurrence of this condition in an eye with poor nutrition and hypoxia, as a result of severe vascular disease, suggests a causal relationship. The formation of newly formed vessels is stimulated, causing anastomoses with Schlemm's canal and in some way destroying its usefulness.

The treatment of this form of glaucoma is cyclodiathermy for the pain, or enucleation. The presence of the newly formed vessels may lead to spontaneous hemorrhages (hence the term hemorrhagic glaucoma). When surgical treatment is attempted, these vessels nearly always preclude success. I have recently seen a case of hemorrhagic glaucoma associated with rubeosis in a diabetic girl, aged 23 years. I know of no other such case in so young an individual.

Occasionally one finds a combination of two forms of glaucoma in the same patient. This has been described as mixed glaucoma.[11] Mixed primary acute glaucoma and glaucoma capsulare occur. Simple glaucoma and secondary glaucoma following central vein occlusion have appeared together. There may even appear a superimposition of primary acute glaucoma coincidentally on the background of a simple glaucoma.

Summary

A new classification of the glaucomas based on clinical evidence is suggested. The classification is arranged so as to include the same groupings into primary and secondary glaucoma which usage has made universal.

The diagnostic features of those forms of glaucoma where newer concepts have appeared are presented.

Emphasis is placed on routine tonometry in all patients 40 years of age or over to make early diagnosis of glaucoma simplex possible, since it is the most important ocular disease in relation to blindness, and one whose ravages can be prevented to a large extent by early recognition.

1108 Stroh Building (26).

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SIGHT RESTORATION IN A SCHOOL FOR THE BLIND*

PURMAN DORMAN, M.D.
Seattle, Washington

Restoration or improvement of diminished vision is a different problem today from the one it was formerly. As is true in many other fields, conditions change. The diagnoses of pathologic conditions of the eye may remain the same, but the number of children within the various age groups who have eye afflictions is changing, thankfully, for the better.

As a marked example of percentage changes, the new cases entering schools for the blind approximated 3 percent last year due to gonorrheal ophthalmia neonatorum; whereas, 6 percent of new cases of this condition were noted in 1941; but contrast that with 28 percent in 1907! Other eye conditions will not respond with such remarkable speed, although a review of the eye records of pupils in schools for the blind throughout the country allows us to gain an excellent grasp of the many causes that now produce diminished vision.

I am indebted to the Committee on Statistics of the Blind for the information that the total number of pupils in schools and classes for the blind in America is 5,400. Of these, the records of about 3,700 children were studied for the school year 1945-46 when it was found that approximately 15 percent of the children are now blind because of cataracts which are largely of prenatal origin.

Discussion of sight restoration should include all phases of the handicapped individual's life and should not be limited to corrective eye treatment of pupils already enrolled in schools for the blind. It may be well to consider the subject under three categories: (1) prenatal care, (2) actual visual improvement, and (3) psychologic adjustment.

PRENATAL SIGHT RESTORATION

This grouping may be challenged by saying that it is a preventive classification but for the individual the end result by any name is the desired objective. The youngster who may have vision "restored" by an operation

of any form, or by any sort of medical treatment is no more fortunate than the youngster who did not lose vision because his parents did not transmit the visual fault that is considered as a "prenatal" cause.

Those prenatal causes, such as syphilis or the acute eye infections known as ophthalmia neonatorum transmitted from the birth canal, have decreased nearly 40 percent and 25 percent, respectively, within the past 10 years. Such advances are due partly to the greater vigilance of the health officers and partly to the general education that is definitely and steadily being absorbed by all parents, by workers for the blind, by teachers, and by the general public.

It is important that this educational process be continued ceaselessly by varied means. Only by general education has it been possible to pass state or federal laws that emphasize maternal and infant care. Not only should we strive to have more babies live but also to have more babies see.

Medical research now helps by considering in a special category the congenital cataracts of babies born from mothers who had German measles during the early months of their pregnancy. Only since 1941, when a severe epidemic of rubella in Australia infected many expectant mothers with the result that their children showed a greater frequency of these congenital cataracts, has the entire condition been considered a separate entity.

The suggestion has been made that, in order to prevent such congenital malformations in the future, the prospective bride be required to indicate on application for a marriage license whether she has had German measles, just as, at the present in some states, it is required to have a physical examination for syphilis.

Restoration of sight should unquestionably include study of the prenatal causes of blindness. To add to the knowledge of what caused the blindness and how it might have been prevented is the biggest job of all and the one that gives the greatest amount of satisfaction.

IMPROVING VISION

The second division, that of actual visual improvement, would be an oft repeated story, were the operations to be listed, what they were, why they were done, and on whom.

The school for the blind in the state of Washington, for which I am the admissions consultant, had a survey and a thorough review, in 1942, by the American Foundation for the Blind. As a result of this examination of everything that pertained to the school, with the exception of the finances, many changes were made.

Several children were operated upon for cataracts or for other conditions to improve their vision. Some have been improved sufficiently to be removed from the school. However, the greatest improvement was gained by a number of children as a result of having been better fitted with glasses because of more frequent examinations or because special lenses, such as telescopic magnifiers, have been prescribed.

The survey not only opened the eyes of some of our youngsters but our eyes as well. It stimulated us to look around at other schools for the blind and showed that other schools had similar weak points. For example, it was found in our school, as well as in others, that some children were admitted without a preliminary or previous eye examination. Sometimes children did not have eye examinations yearly, or did not have more frequent eye examinations when progressive eye conditions, such as high myopia, were noted.

Today, all children whose parents desire that they be admitted to the school for the blind are examined by an eye physician before the child is admitted to the school. In addition, the entrance eye examination reports are passed upon by the admissions consultant who is also the consultant ophthalmologist of the Blind Division, Department Public Welfare (incidentally a Board certificated man), who may deny entrance to any prospective youngster who is not blind.

All children are again examined by the

school ophthalmologist shortly after their entrance and again routinely yearly, even including those who have no eyes at all.

RETURNING SIGHTED CHILDREN TO THEIR HOMES

After review of our own past mistakes and our attempted corrections, we noted not only the faults relating to the medical needs but we perceived a weakness in our program covering the educational needs of the blind as well as the partially seeing child. We found our school well equipped and well developed for educational instruction along tactual methods. But the partially seeing pupils too often had been placed in the same classes as the blind, without regard to the better or more recent educational procedures or without regard to the utilization of visual media now available.

In spite of the acceptance of these partially seeing children, special educational facilities had not been provided. The partially seeing child had not had sufficient lighting for his greatly reduced eyesight. There had been an erroneous conclusion that the educational needs of the partially seeing and the blind were sometimes similar, sometimes identical—a conclusion manifested by certain types of vocational training that had been given to partially seeing students of the high-school age groups.

We found several children included in the school for the blind who had practically normal vision at the time of the independent, disinterested survey. Some eyes showed no reduction of vision, no intraocular or extraocular pathologic condition. The reasons for admittance of these children were: they were home-problem children; there was a mistaken recommendation made—sometimes by an optometrist and sometimes by a general practitioner; there was a broken home; or there was a suspected willful blindness in the child because a relative was blind, sometimes from some remote cause.

The attendance of these children at the school for the blind was easily remedied. What was not easily changed were the emotions, the attitudes, the living habits, the acceptance of the highly protective environment of the school, and the confusion that goes with returning these youngsters to their homes, sometimes against the will of their parents. This emotional shock of learning a second time that they are not wanted undoubtedly will have certain mental repercussions later.

A remarkable utilization of community resources was achieved when partially seeing as well as blind children participated in several play ventures with normal neighborhood children. Such activities included hikes, "wienie" roasts, and other youthful encounters dear to children everywhere. It was necessary for the superintendent of the school to initiate some of these activities, but after she realized that there had been isolation from neighborhood children, such problems ceased to exist.

Some children had been accepted by the school before a complete examination had been made by a competent ophthalmologist, before any corrective treatment had been attempted. It was obvious that the school accepted responsibility for which it was not prepared, and also that competent medical and adequate educational treatment had been delayed.

Our study revealed certain possibilities of improvement of the sight of the visually handicapped child by surgery, glasses, or some form of medical treatment. We endeavored to gain closer coöperation with our competent, associated eye physician so that whatever remaining vision the child had was maintained, safeguarded, and protected. But, what was more important to the youngster, he had more efficient use of his small amount of vision.

Two children, whose vision was improved from 2/200 to 10/200 by eye surgery undertaken after the survey showed the possibilities for such improvement, believed they should no longer read Braille, that they were not "blind children"—as indeed they weren't! They believed their better vision was adequate for all visual tasks of a seeing

person. Such visual improvement was not great as measured by our standards, but was sufficient for them to obtain an entirely new outlook on life, a new vision and acceptance of work, far beyond their previous abilities. Life for them was not blind, life was seeing.

In addition to the medical or surgical treatments, a re-allocation of the educational groups was done. Fifty percent of the children were kept in the same school but greater emphasis was placed upon visual methods rather than upon tactual procedures. Some children who had an absolute visual loss could not be changed. Ten percent of the remaining sighted children were placed in sight-saving classes, and about the same number were reconsidered for educational placement after corrective treatment had been done.

It was apparent that insufficient attention had been paid to the partially seeing youngster. Not enough attention had been devoted to each individual child so that he could gain full and complete value from the bit of sight that remained. Too often the youngster was given a routine treatment, was not considered as an individual. No one had attempted to probe the depths of personal differences nor to elicit the heights of personal abilities, which sometimes rose to an undreamed of level.

PSYCHOLOGIC ADJUSTMENT

The last phase of sight restoration is often not classified as such, for there actually is no physical change. There is created no actual physical improvement. It is open to no statistical review. The changes in the person, however, are every bit as valuable and create just as much in the final review as if the person had received more vision. I am referring to the psychologic improvement within the mind of the individual.

Instead of permitting an unseeing child to remain huddled in the corner, our school for the blind has taken him out and put him into direct competition with children possessed of all five senses. For example, one boy, after receiving artificial eyes, could not believe that seeing people on casual inspec-

tion would think that he, too, was like them. He was told time and again that no one knew he had artificial eyes. No. He must have that point proved for himself, by himself.

Wearing both eyes, he went into a men's haberdashery, the best one in that city, and asked for a blue tie. He examined a few ties carefully and then asked for a different darker shade. After looking over the second group of ties, he said that none of them seemed to be the correct shade, that he would search elsewhere for a slightly different color, then left the store.

That experience, a few years ago, was all the boy needed. Now he wears his artificial eyes and is making an excellent social adjustment, just as he is making a satisfactory living by selling books. Almost as much has been accomplished as though more vision had been given.

One girl won her sectional high school oratorical contest—in spite of the fact that she had no eyes. Another boy attends a high school in the same town where the school for the blind is located. He competes with sighted students throughout the day, but his lessons are read to him at night. His grades are entirely acceptable. He goes with the high school athletic teams and attends every game, home or afield. He plays a large horn, marches in all the parades, and is accepted by his fellow students.

This boy has encountered only one minor difficulty—that of marching in parade and drill formation. Even that point was solved by running a fine piano wire from his belt to his adjoining companions. He was forced to that solution one day when his companions turned a corner. He didn't turn, but continued marching straight ahead. Now, when his companions turn a corner, now when the world turns a corner, he turns too, confident of success.

Sight restoration can be of still greater, more widespread benefit than it is today when we realize its full import, its greatest possibilities.

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NOTES, CASES, INSTRUMENTS

"TO BALANCE" LENSES

C. Keith Barnes, M.D.
Fort Worth, Texas

The patient was a 14-year-old, auburn-haired, white girl. She gave the history of having pierced the left eyeball with sharp scissors several months previously. The eye was hopelessly damaged and was enucleated elsewhere with the implant of a 16-mm. metal ball into the bulbar fascia. The ball extruded, and was replaced. It extruded again. The original surgeon had suffered a heart attack and was unable to continue with the case, so an interne replaced the ball. In all it extruded five times in less than a year's time.

The socket was markedly shrunken and drained a purulent material constantly. The patient was able to insert only an infant-size prosthesis and, because of the cosmetic disfigurement, preferred to wear a gauze eye-pad. She avoided social activity and felt her disfigurement keenly. She presented herself with the hope that her condition could be corrected.

Eye examination revealed a normal right eye and orbit. A moderately contracted left socket contained a large amount of creamy pus. The skin of the left eyelids, orbital margins, and cheek was badly excoriated. After cleansing the orbit an extensive spider-shaped scar was seen posteriorly in the center of the socket with arms radiating to the cul-de-sac in all directions. The pus oozed from a small ostium in the center of the scar.

Brief exploration at once revealed a small black foreign body which on removal proved to be the end of a 3-cm. fragment of black silk. Saline irrigations of the socket and a bland ointment for the skin were advised. Within a few days the discharge had stopped.

Operation. Since the socket would not accept a satisfactory prosthesis, it was decided to restore it to adequate size with a mucous membrane implant. The girl was nervous and uneasy after her numerous orbital manipulations, but preoperative sedation and local anesthesia were adequate.

The arachnoid scar was dissected out along all of its ramifications, leaving the anterior orbital tissue soft and distensible but lacking much membranous surface. A lateral canthotomy was thought necessary.

The remains of the bulbar fascia were located and the cavity was dilated to adequate size with a large hemostatic forceps. A 16-mm. glass sphere was introduced into the bulbar fascial space and the opening was closed with a 3-0 plain catgut purse-string suture. Bits of surrounding fibrous tissue were imbricated across the purse-string to bury and strengthen the closure.

Hot wet packs were inserted into the socket while the graft was prepared. This was obtained from the lower lip, which throughout was held strongly stretched. An area, 2.5 cm. by 3.5 cm., was outlined and removed in full thickness with a Graefe knife.

The edges of the lip defect were undermined and closed with interrupted black silk sutures; the lip healed rapidly and uneventfully although most of the sutures loosened and were unknowingly swallowed with the food.

The deep face of the graft was carefully denuded of all bits of fat, and the graft was stretched over a prepared and waxed sterile elliptical piece of cardboard cut to size. A small hole had been punched through the center of the cardboard stent to permit possible drainage. The stent was inserted so that the two raw, dry surfaces were apposed. A vaseline gauze pack was snugly forced into the socket. A pressure bandage was applied for 10 days.

At the end of this time the pack was re-

moved, the silk suture clipped, and the stent gently withdrawn. There was considerable foul discharge but, upon cleansing, the graft was seen to be in situ and healthy. The socket was filled with penicillin ointment and the largest possible perforated plastic conformer was inserted. The conformer extruded over night, so it was replaced by a smaller one.

Outcome. The socket healed uneventfully except for one heavy adhesion which had formed under the canthotomy; this adhesion was severed and an effort made to hold the raw surfaces apart with a larger conformer. This failed, so a second graft of mucous membrane was secured from the right cheek, and attached to a stent, and the lateral cul-de-sac was thereby reëstablished.

The resultant socket was healthy and of adequate size but somewhat irregular in shape. Prostheses taken from stock were unsatisfactory, so a special plastic prosthesis was made with an irregular flange trimmed to fit the fornices. After numerous attempts, the prosthesis makers did a beautiful job in matching the opposite eye, and I readily agreed that they had created a masterpiece.

Refraction. The "good" eye was then refracted, with the intention of advising glasses as a protective measure regardless of the optical needs. However, she did need a moderate correction. With the prosthesis, the trial frame, and the right prescription in place I studied her cosmetic effect carefully.

The artificial left eye had a slightly prominent, staring effect, which was found by trial and error to be reduced to normal by a −4D. sph. This, however, made the interpalpebral fissure appear a trifle too short. By trial and error again, it was found that a +2D. cyl. ax. 90° gave the illusion of lengthening the fissure correctly. From the side view her appearance was satisfactory except for a slight retraction of the upper lid.

It was believed that boldness in frame style would draw attention to the frames rather than the eyes, so a gayly decorated frame popular with the teen-age group was selected, a style being found which had a temple to conceal her slight lid retraction.

Result. The result was highly gratifying to all concerned. The young woman has taken a new lease on life, attending parties and public functions with a restored and delightful self assurance. A number of new friends still do not know that she wears an artificial eye, and older friends congratulate her.

DISCUSSION

I have abandoned the custom of prescribing "to balance" lenses before prostheses. I seek instead the prescription which will create the most natural illusion in front of the prosthesis and insist that the opticians grind the lenses as ordered.

Sunken prostheses can be "brought forward" by application of plus spheres. A prominent or staring prosthesis can be minified and recessed by a minus sphere. A palpebral fissure which does not match its fellow can be lengthened, shortened, widened, or narrowed by the use of appropriate cylinders at appropriate axes.

The lateral or profile appearance can be markedly enhanced by a judicious choice of frames and temple positions. The retracted upper lid can be concealed by a high temple. Poor lateral motion of the prosthesis can be minimized by a centrally placed temple. A retraction of the trochlear area can be improved by an oblique cylinder. Prism is justified to elevate a sagging prosthesis.

As a general rule, plastic frames do more to create a cosmetic illusion, particularly if they are fairly massive and have strong color or accents. The frame width should usually be kept more narrow than one would customarily use, since the concealment effect is better.

Probably many hundreds of cases would lend themselves yearly to this cosmetic consideration. One patient with von Recklinghausen's disease and profound distortion of the left orbital area was similarly pleased by a careful choice of glasses. He needed a

minor correction for the right eye, so a pair of very massive frames carrying moderately tinted lenses was chosen. A special left temple was decided upon because of his deformity, and he was given both psychologic and cosmetic benefit. Since the left eye was useless, bulging tissues were minified by a minus sphere.

Blind, staphylomatous eyes can be made less obvious by minus spheres. Blind shrunken eyes can be tried with plus spheres. Tinted lenses can be used where needed without detracting from the effect. It is possible to put a light shade over the "good" eye and a somewhat darker shade over the other with hardly noticeable effect.

I claim no originality for these thoughts; they have all been suggested and tried by others. However, investigation has shown that many ophthalmologists have never considered nor even heard of these simple cosmetic aids. I feel that results can be so gratifying that this small detail deserves studied consideration in every suitable case. Let us abandon the "to balance" prescription!

921 Neil P. Anderson Building (2).

A MODIFIED TECHNIQUE OF TARSORRHAPHY*

M. SARWAR, M.B.B.S.
Oxford, England

The value of tarsorrhaphy in indolent corneal conditions, in muroparalytic keratitis, and in plastic surgery needs no mention. The standard technique of tarsorrhaphy both as described in textbooks and practiced involves a loss of tissue (freshening of the lid margins—Wheeler; cutting out planned areas of tarsal plate—Elschnig) and, unless this removal of tissue is carried out fully, the tarsorrhaphy fails. This loss of lid tissue in temporary tarsorrhaphies is a great disadvantage because of the lid deformities that are sometimes caused.

TECHNIQUE

I have been able to modify the technique slightly, so that there is no taking away of tissues and no chance of failure. I have been practicing this technique with success for over three years. I hope it will appeal to other colleagues and will be given a fair trial.

The instruments required are: (1) 2-cc. hypodermic syringe and needles for infiltration; (2) lid clamps; (3) Beer's knife; (4) black silk (4-0) on No.-3 needles; (5) short length of 1-mm. rubber tubing; (6) needle holder and forceps.

Preparation. The skin of the lids is prepared in the usual way. The lashes may or may not be cut; it is an advantage not to cut them.

Anesthesia. Local anesthesia of conjunctiva is obtained by 4-percent cocaine or any other substitute (anethaine, and so forth). Both the lids are then infiltrated with a suitable infiltration anesthetic. I usually use Novatox. For median tarsorrhaphy and complete tarsorrhaphy, a few drops should also be injected along the medial wall of the orbit.

Operation. With the usual aseptic precautions, one of the lids is held in the clamp firmly. I usually start with the lower lid first. The gray line is then defined, and an incision made along it, separating the tarsal plate from the skin and orbicularis. The length and site of this incision will depend on the length and site of the lid occlusion required. The separation of the tarsus is carried out to about one third of its width; that is to about 3 mm. from the margin (fig. 1). The clamp is now applied to the other lid, and a similar splitting of the lid is done.

A continuous mattress suture is now inserted, biting the pretarsal tissues (fig. 2). The suture is drawn tight, but the ends are left free. This brings the two tarsal plates together at their edges and covers the eye.

The free, lash-bearing edges of the lids are now sutured together with interrupted mattress silk sutures (fig. 3). These sutures

are drawn through 3-mm. lengths of the rubber tubing and tied tight (fig. 4).

The lids are now cleaned and dressed with penicillin Tulle Gras. The dressing is
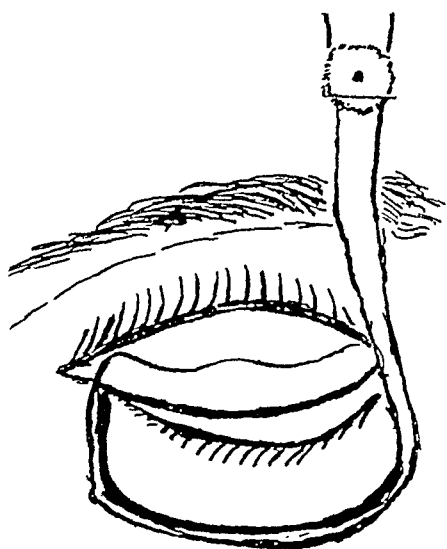
Fig. 1 (Sarwar). Holding the lid firmly in the clamp, an incision is made and the separation of the tarsus is carried out to about one third of its width.
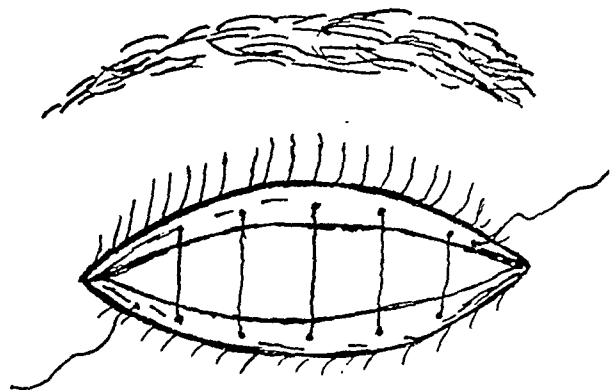
Fig. 2 (Sarwar). A continuous mattress suture is inserted, biting the pretarsal tissues.

changed in 48 hours, when the continuous pretarsal suture is pulled out. The new dressing is left on for 6 days, and the skin stitches are removed at the end of that period.

Postoperation anatomy. The lash-bearing margins of the two lids are directed anteriorly. The orbicularis fibers of the two lids are united together by fibrous tissue; the union is about 2-mm. wide and is along the whole length of the operated area.

DISCUSSION

The operation is very simple to do and requires very few instruments. The lid clamps can be dispensed with if not readily available.

It does not involve removal of any tissues —a point of considerable importance in temporary tarsorrhaphy.

It does not interfere with the anatomy of the tarsus—another important point in temporary procedures. When a temporary tarsorrhaphy is undone, the skin and tarsus
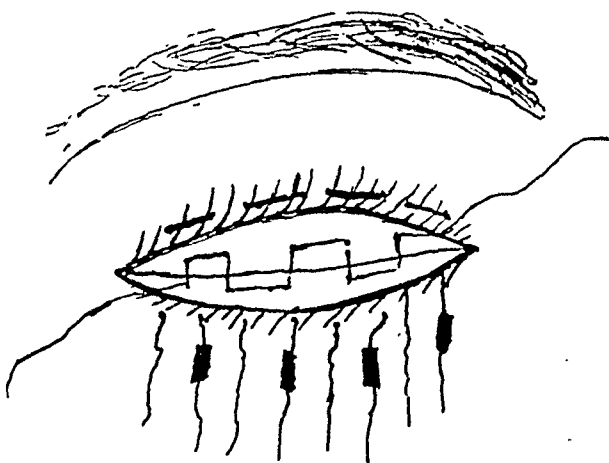
Fig. 3 (Sarwar). The free, lash-bearing edges of the lids are sutured together with interrupted mattress silk sutures.

Fig. 4 (Sarwar). The sutures are drawn through 3-mm. lengths of rubber tubing and tied.

unite together again in their natural state, with no residual deformity of lid margin.

The union of the two lids is by connective tissue and about $\frac{1}{2}$ to 1 mm. behind the lash-bearing area, the two rows of lashes diverging from the line of union, and curving up and down respectively. The cosmetic effect

in a total tarsorrhaphy, although strange, is not unpleasant as with the more usual procedures. For the same reason the cosmetic effect is definitely superior in partial tarsorrhaphies, the eye acquiring a "dreamy" look, rather than the "tampered with" appearance of the usual procedures. The presence of the lashes hides the scar of union, too.

The greatest advantage, however, is the permanence of the procedure. It is, permanent because the union is a fibrous one between the orbicularis muscle fibers, and there is no tension on the skin.

In cases of muroparalytic keratitis, the lid sutures should not be tied too tightly, or else the already atrophic skin might die and slough away, causing a scar.

USE OF PRIVINE-ANTISTINE DROPS IN OPHTHALMOLOGY*

RAY K. DAILY, M.D.,

AND

LOUIS DAILY, JR., M.D.

Houston, Texas

This is a combination of two drugs,[†] Privine and Antistine.

Privine is chemically a naphthyl-methyl-imidazoline hydrochloride. It is a crystalline colorless substance soluble in water and in saline solution. The solution is stable and is not decomposed by exposure to light or air. Its pharmacologic properties were described in 1941 by Meier and Müller.

Instilled into the conjunctival sac it produces a vasoconstriction similar to that of adrenalin; it lasts longer and there is no secondary vasodilatation. The blanching of the conjunctiva sets in rapidly, lasts about 2 to 3 hours, and then slowly recedes; it acts

principally on the small conjunctival vessels. The effect on the larger vessels and on the ciliary and episcleral vessels is less pronounced.

It is a sympathetic stimulant and produces a slight widening of the palpebral fissures through contraction of the musculus tarsalis superior. It also produces a perceptible pupillary dilatation by its effect on the dilator pupillae. The mydriasis is noticeable only in dim light and in eyes with blue irises. In daylight and in brown eyes the mydriasis is uncertain. It disappears in several hours and does not cause dazzling. The pupillary reactions, accommodation, and corneal sensitivity remain normal.

The effect on the intraocular pressure is insignificant. Bürki[2] in the report of his clinical investigations states that he did not see a single case of a rise in intraocular pressure. Fanta[3] of the Lindner Clinic found a few cases in which the instillation was followed by a brief and insignificant increase in tension.

Antistine, a synthetic antihistaminic drug, is a crystalline, white odorless powder, the chemical formula of which is phenyl-benzyl-aminomethylimidazoline. Its sulphate, used for the ophthalmic solution has a pH of 6.9. It is prepared in an isotonic buffered solution with the following formula—antistine sulphate, 18.75 gm.; sodium carbonate anhydrous, 2.66 gm.; potassium chloride, 27.75 gm.; boric acid, 46.50 gm.; distilled water, 3,750 cc.

Bourquin[1] reported on the use of this solution in 37 cases of various types of conjunctivitis and scleritis. He found that its instillation relieved photophobia, itching, and lacrimation, and was of value in giving symptomatic relief, although it had no permanent effect on allergic conditions.

A combination* of 0.5-percent Antistine with 0.025-percent Privine has been used by us in about 100 cases of various types of conjunctivitis.

Its vasoconstricting effect and its calming action on blepharospasm make it useful in a number of conjunctival and corneal diseases. The effect varies in different patients, both as to intensity and duration. Its instillation produces a short transitory smarting sensation. One patient with keratoconjunctivitis sicca, on whom it was tried, complained that after the instillation of the solution the eyes burned for a considerable period of time, but that the eyes were very comfortable for some time afterward.

The solution is particularly suitable for cases characterized by conjunctival congestion. It is used gratefully by patients who complain of burning, itching, photophobia, lacrimation, or dryness, a sensation of sand in the eyes, fatigue and blurring of vision, particularly in the evening.

In most of these patients the objective data are not commensurate with their subjective symptoms. In many cases there is no objective pathologic condition; the conjunctival scrapings are negative for microörganisms; the lacrimal passages are normal; the refractive error is corrected.

In some cases there is a mild subacute or chronic conjunctivitis with moderate redness and swelling of the palpebral and fornix conjunctiva. Occasionally, there is more pronounced conjunctival hyperemia and infiltration with a few follicles. In such cases instillation of Antistine-Privine drops every four hours brings prompt subjective amelioration. The alleviation of subjective complaints is superior to that obtained from the instillation of weak zinc sulphate, resorcin, or mercury oxycyanide, the medicaments which usually give transitory relief to such patients.

Since Antistine-Privine solution may be used indefinitely, it is a useful addition to our list of medicaments for chronic conjunctivitis. It is appreciated by patients with allergic conjunctivitis, who complain of photophobia and lacrimation. In eczematous keratitis, it is said to reduce the inflammatory symptoms by decongestion of the conjunctiva, and to diminish the corneal vascularization with a salutory effect on the visual outcome.

The solution may be combined with astringents in chronic conjunctivitis, or with silver preparations in acute conjunctivitis. In scleritis and episcleritis the bulbar congestion is reduced, and the patient gets a sense of subjective improvement, but the effect is not as pronounced as it is in conjunctivitis. It is also useful for the relief of postoperative discomfort due to persistent conjunctival hyperemia.

In persistent conjunctival irritation following trauma, burns, and chemical injuries, the instillation of the drops causes a blanching of the conjunctiva, and gives the patient a sensation of relief. In combination with local anesthetics, such as pontocaine or holocaine, it reduces the conjunctival irritation frequently produced by these anesthetics. This is an advantage when repeated applications are necessary, as in taking tension curves. It can also be used in place of adrenalin instillations in surgical procedures.

SUMMARY

The combination of Antistine-Privine drops is a valuable addition to our therapeutic armamentarium. Instilled into the conjunctival sac it produces a rapid decongestion of the conjunctiva, which is agreeable in a number of conjunctival conditions.

Medical Arts Building (2).

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ACCIDENTAL CYCLOPLEGIA BY JIMSON WEED

LUCIAN BAUMAN,* M.D.

Washington, D.C.

The solanaceous plant, Datura stramonium, also known as Jimson weed, stink weed, Jamestown weed, is widely distributed in the United States and in many parts of the world. Containing mainly hyoscine, it has been used since the earliest times for its systemic effects. Tradition has it that this was the drug given to the person delivering the oracle in the Temple at Delphi.[1]

During the summer and fall small children playing in the gardens and woods are attracted by this large weed and its fruit, and, mistaking it for some edible fruit, eat it in relatively large amounts. Although there are many reported cases of either accidental or criminal poisoning by ingestion of stramonium every year, there are only seven reported cases of accidental cycloplegia in the world literature during the past 50 years; 3 in the United States,[2,3] 1 in Cuba,[4] 1 in France,[5] and 2 in French Morocco.[6] All occurred in adults.

It is my suspicion that there are many more cases of sudden unexplained cycloplegia (and mydriasis) that are caused by parts of the leaves and seeds of the Jimson weed getting into eyes.

CASE REPORTS

The following cases occurred in children.

* Of the resident staff, Department of Ophthalmology, Gallinger Municipal Hospital.

Case 1.† A very intelligent, 11-year-old girl was recently brought into the eye clinic of Gallinger Municipal Hospital because of sudden loss of vision in the right eye. The girl stated that while playing in the nearby woods the previous afternoon she had kicked at some tall weeds and that the large pods on the plant had burst showering her head with seeds. In shaking them off something had gotten into her right eye. That evening she complained to her grandmother who thereupon found and removed a small black seed from the eye.

The next morning the patient noticed the blurred vision in the right eye and her grandparents noted the dilated pupil. She was brought to the clinic that afternoon. The child brought a segment of the weed complete with pods and the grandfather volunteered the information that the plant was very common in the vicinity and was known as the Jimson weed.

Ocular examination revealed mydriasis and cycloplegia of the right eye. Within 48 hours the pupil and accommodation had returned to normal.

Case 2. Three weeks previously, a 12-year-old boy had been examined. The same type of condition was presented, and it followed the same course. Here, no explanation could be obtained of the phenomenon, the parents stoutly maintaining that no eye drops were ever in the house. The strongest suspicion now points to the Jimson weed as being the offender.

2601 16th Street, N.W. (9).

† Service of Dr. William D. Foote.

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SOCIETY PROCEEDINGS

Edited by Donald J. Lyle, M.D.

INDICATIONS AND RESULTS IN KERATOPLASTY

Dr. Harold G. Scheie reported the results obtained from 22 corneal transplant operations performed at the Hospital of the University of Pennsylvania. Nineteen of the eyes were followed through convalescence and the statistics presented were obtained from these, although it was realized that the number was too small to be of statistical significance. The cases were classified according to Castroviejo's prognostic grouping from Group I, the most favorable, to Group IV, the least favorable.

Three criteria were used to judge the success or failure of the operation: (1) clarity of the graft, (2) improvement in visual acuity, and (3) benefit to the patient.

Six eyes operated were of Group I, including those having a central corneal scar from old keratitis, keratoconus, and one having central scars from interstitial keratitis. All of the patients in Group I obtained clear grafts and improved visual acuity which was very striking in three. When improvements did not result, amblyopia ex anopsia or central scotomas offered the explanation.

The criterion of actual benefit derived from the operation by the patient offers an even more critical and possibly more practical way of evaluating corneal transplantation. In spite of clear grafts and visual improvement in all, only 4 of the 6 patients used the operated eye, thus deriving benefit from the procedure. The astigmatic error varied from 2 to 5 diopters.

Only 3 of the 4 patients in Group II have completed their convalescence. Two of these 3 have clear grafts. All have rather remarkably improved vision, but only 2 of the 3 obtained real benefit from the operation, the third not using his operated eye.

There were only 2 patients in Group III. The first patient had been suffering from recurrent corneal ulceration with severe discomfort for three years. He had reached the point where he preferred enucleation of the eye rather than further discomfort.

The involved area of the cornea was central. A corneal graft was done which remained clear and has made him more comfortable. There was no visual improvement, however, because of a complicated cataract which had been present before operation. He should have a good eye following the extraction.

The other patient had central scarring from an old keratitis, but the lens had been subluxated by a former injury, and was cataractous. A transplantation was done in the hope of giving him a clear cornea before cataract extraction, but the graft became opaque, and he has definitely been made worse by the operation.

Group IV included 8 patients with severe corneal conditions such as epithelial dystrophy, severe corneal degeneration as a result of interstitial keratitis, extensive mustard burns of the cornea, and one recurrent ulcerative keratitis with calcareous degeneration.

Only 1 of these has a clear transplant, and 3 obtain significantly improved vision. However, from the standpoint of benefit to the patient, 4 of the 8 have been dramatically improved either visually or through alleviation of symptoms. The most dramatic was that of a soldier with bilateral severe mustard burns of the cornea. Only 1 patient, who developed an iris prolapse with eventual loss of his eye, was made worse by the procedure.

Taken as a whole, visual improvement

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was obtained in 65 percent of patients. Fifty percent of the grafts remained clear. From the standpoint of benefit to paients, 56 percent of the patients were benefited by the operation. Thirty-one percent were unimproved and 10 percent were made worse, although this is difficult to say since their vision had been hand-movements and light perception respectively before operation. Since 8 of the patients operated were in Group IV, the overall figures are not displeasing.

The indications followed for corneal transplant were:

1. Favorable conditions of Group I and Group II are preferred, but whenever a patient has a chance of some visual or symptomatic gain and nothing to lose, corneal transplantation can justifiably be done.

2. Vision should be less than 6/60.

3. Hesitation is advised in unilateral involvement.

4. A one-eyed patient should be operated only if his eyesight is of no practical value to him.

Discussion. Dr. James S. Shipman: I would like to congratulate Dr. Scheie on this excellent and very honest presentation of a most interesting subject. Indeed the picture of keratoplasty, as given here tonight, is very different from that we see given to the public too often in the newspapers. I think it is too bad that the subject cannot be presented to the public, through the newspapers, in its true light.

The actual cases as presented here tonight are evidence of the excellent technique followed by Dr. Scheie. Indeed they are very convincing for the circular type of transplant.

One of the cases presented here tonight happens to be that of a patient on whom I did a corneal transplant about six years ago. At that time we used the double-bladed knife of Castroviejo and obtained a square graft. In this case everything went well until about a week after operation, when the patient developed a secondary glaucoma. This

was eventually controlled with miotics. I notice that Dr. Scheie encountered this complication only once in his series of 20 cases.

The patient of whom I speak had presented a most severe case of interstitial keratitis. A short while after operation he developed a marked increase, and overfilling, of old corneal vessels. As a result of this, the corneal graft went on to complete opacification. We had given this patient numerous X-ray treatments recently with the hope of blocking off the corneal vessels, and had planned to try a second transplant. I am very happy to see that Dr. Scheie has done this, and I hope that his results are satisfactory. I also hope that he will do a similar operation on the other eye which is less scarred and vascular and offers a better prognosis.

Indeed after seeing the cases presented here to night I feel that Dr. Scheie is to be complimented on his beautiful technical results, and I am sure that, with more favorable cases, the visual results will be better.

Again I wish to say that this paper has been most instructive and enjoyable.

Dr. W. E. Fry: There are a number of interstitial keratitis cases at the Overbrook School and, in breaking down some of the statistics in regard to them several years ago, the general outlook was poor in regard to corneal surgery. Many of the patients showed evidence of severe anterior uveitis and, when the fundus was visible, showed optic atrophy.

There is one point that I think might be added to the discussion, and that is we probably do not know the full story in regard to how the transplant acts as a foreign body in the cornea. The reason why I make the statement is this—one youngster with an interstitial keratitis on whom I did a transplant on both eyes had a 6/9 vision in one eye following surgery, and has maintained this vision for over one year. Six months later I did the second eye with exactly the same technique with no complications whatsoever. The result was a partially opaque cornea

and 6/60 vision. I cannot explain the difference. I wish Dr. Scheie would explain it to me. I think there is something we do not know in regard to the way in which we select our donor material.

Dr. Hunt: It has been my privilege to look at all of these cases that Dr. Scheie has done, I believe, and follow them through, and while the procedure is not technically too difficult, anyone who is not prepared to do very thorough and meticulous after care should not attempt the operation.

I believe Dr. Scheie mentioned there were some 60 complications in this series. From his discussion, I think we can evaluate this as being a practical, useful procedure that should be tried in favorable cases.

Dr. Louis Lehrfeld: The oldest case of corneal transplant that I have on record is one dating back to the year 1940. This case was one of keratoconus in which the transplant was regarded as quite successful. The patient's vision was partially restored by the transplant. The patient, who was seen by me and my associate only a few weeks ago in the clinic, now has keratoconus recurring in the transplant itself. I mention it, because I think that those who are now doing the transplants should keep in mind the fact that mere transplantation of a good cornea to take the place of an old one does not necessarily change the fundamental pathology underlying keratoconus. That does not mean necessarily that one should be discouraged in doing this type of operation for keratoconus or for any other cause.

The essayist has suggested to you various types of corneal lesions for which he would propose to do a corneal transplant. Of course, it has been said facetiously and I have heard the remark passed many times at conventions, that when you get good transplant results it might have been possible to get similar results by doing something else instead of the transplant. I would like to encourage further experimental work in transplants because the future holds much for it. Despite the fact that there are many dis-

appointments and many unusual cases of improvement, I feel that in the future many more cases, even in Groups III and IV, will be successful.

Dr. Harold G. Scheie (closing): I wish to thank all of the discussors. Vascularization of the transplanted cornea is the biggest problem with which we have to deal. The explanation for this vascularization has always been obscure, but might be derived from the experience of the general plastic surgeon who finds that skin transplanted from one individual to another apparently takes well for approximately three weeks. After this time it exfoliates and is lost, not being tolerated by the recipient's tissues.

It is at about this same time interval that eyes on which corneal transplantation has been done become red; the graft tends to become cloudy, and blood vessels invade the cornea. This reaction and vascularization is less severe in corneas where vessels have been minimal preoperatively.

On the other hand, if the cornea was heavily vascularized beforehand, the eye seems to do well for about 2 to 3 weeks, then becomes inflamed and the graft rather rapidly vascularizes. The transplants, as a result, become opaque in a rather large number of cases. The reaction of the recipient to tissues from another of the same species might well correlate with the number of preexisting vessels into the recipient bed, the tissue responses being greater where vascularity is excessive.

SOME OBSERVATIONS ON MIOTICS

DR. EDWIN B. DUNPHY of Boston (guest speaker).

This paper appears in full on page 399 of this issue of the JOURNAL.

Discussion. Dr. Francis Heed Adler: I think we are all very appreciative of the able way in which Dr. Dunphy has covered this entire field in both the theory and practical use of miotics. The point he brought out about mecholyl is evidence that the increased pressure in glaucoma damages the post-

ganglionic fibers so that the myoneural junction becomes sensitive to cholines.

Dr. Scheie has previously reported the experimental production of sensitivity to mecholyl in cats by artificially raising the intraocular pressure for short periods of time. It is generally supposed that such sensitization does not occur until nerve fibers have degenerated and, if this is so, one would hardly expect mecholyl to be of use in an acute glaucoma when the attack has lasted only an hour or so. Actually, it seems to be effective in this condition, and this, combined with Dr. Scheie's experiments, suggests that it is not necessary for nerve degeneration to take place in order to produce sensitivity.

Dr. Irving H. Leopold: This paper represents one of the best summaries of miotic therapy in glaucoma and of pharmacologic data on miotics.

I was very interested in Dr. Dunphy's discussion about T.E.P. triethyl-pyro-phosphate. In 1934 there was an epidemic of diarrhea and peripheral palsies in the inhabitants of one of the islands of the West Indies, and for a long time they were perplexed as to the etiology. It was then found that these individuals were eating or working with Jamaica ginger, and I believe one of the compounds which was extracted from the ginger was tri-ortho-cresyl phosphate. This was found to have marked anticholinesterase activity by some Swedish workers just a few years ago. It may be that this drug or one of its derivatives also might merit evaluation in ophthalmology.

Dr. Dunphy considered the question of synergism of cholinergic and anticholinesterase drugs. It is interesting to consider the effect of combining two anticholinesterase drugs such as eserine and D.F.P. It can be shown that eserine blocks the action of D.F.P.

A series of animals were injected with D.F.P., and the minimal lethal dose of D.F.P. that will kill about 50 of every 100 animals was determined. If another series

of the same animal were given a sublethal injection of eserine, it was found that the previously used dose of D.F.P. no longer killed those animals. In other words, eserine had protected the animals from the lethal action of D.F.P.

The same phenomena can be demonstrated in the eye by instilling a drop of eserine in one eye of an individual, wait until the maximal miotic effect has occurred, which usually takes about 15 minutes, and then instill a drop of D.F.P. in each eye. The eye which has received eserine comes back to preinstillation size in about 2 to 3 days. The eye which has received D.F.P. alone remains miotic a week or two, the usual length of time for the D.F.P. miotic effect.

Now what about the reverse effect, that is if D.F.P. is used before eserine? The sublethal dose of eserine is determined. That is the intramuscular dose that just fails to kill. Animals are given an injection of D.F.P. in a similar sublethal dose. Following this the previously determined sublethal dose of eserine is injected. The eserine injection now results in the death of most of the animals.

In other words, D.F.P. does not prevent the action of eserine. Actually, when eserine is given after D.F.P. there is a combined effect.

One of the experiments that interested me was the one that employed the ingenious method of instilling eyedrops in the dark. The observation that D.F.P. did constrict the pupil of the dark-adapted eye does not mean that D.F.P. has a direct effect on iris musculature, but simply that even the dark-adapted eye produces acetylcholine that can be preserved when D.F.P. ties up the cholinesterase.

This was certainly a very enjoyable paper.

Dr. I. S. Tassman: I would like to make one or two remarks in connection with Dr. Dunphy's observation, particularly regarding the increase in intraocular pressure following the instillation of these miotics, and also regarding the effect on the vessels. I have under observation at the present time at

Wills Hospital one case in which we noted an increase in the intraocular pressure following the instillation of mecholyl and neostigmine and, in addition, the lens in the affected eye was pushed so far forward that the anterior chamber was almost entirely obliterated.

I also recall another case in which we observed an increase in the intraocular pressure following the use of D.F.P.

It is interesting to speculate as to the mechanism by which the intraocular pressure is lowered by these drugs. As was pointed out, I think also that there are certain differences in the action of these various drugs when they are employed in certain combinations. This is probably true of those in the adrenergic group, as well as those belonging to the cholinergic group. Some time ago, I think Dr. Cogan published an article in the *Archives of Ophthalmology* which had something to do with the dual intervention of the ciliary body. In that paper I believe Dr. Cogan referred to the use of these miotics. In another article, I believe it was by Myerson and Thau, speculation was made as to the possibility of an overaccumulation of the esterases with oncoming age to explain the occurrence at that age of presbyopia.

A fair amount of progress has been made since the work of Loewi and Englehart, Cogan and others, but the mechanism is still quite complex, as Dr. Dunphy pointed out, and as yet not fully understood. I think that Dr. Dunphy should be congratulated for this very comprehensive, interesting, and practical paper. It has been a great pleasure to hear it.

Dr. Edwin B. Dunphy (closing): I was very much interested in what Dr. Leopold said about the eserine and D.F.P. combination.

There is very little for me to say, Mr. Chairman, except to thank you again for your invitation.

M. Luther Kauffman,
Clerk.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

March 1, 1948

Dr. Daniel Kravitz, *president*

VISUAL FIELD STUDIES IN NEURO-OPHTHALMOLOGY

Dr. Max Chamlin discussed this subject during the instruction period.

PUPILLARY ABNORMALITIES ASSOCIATED WITH INTRACRANIAL LESIONS

Dr. Abraham Rabiner said that a neurologic examination is never complete without careful study of the pupils. A dilated pupil may be the only clue as to the hemisphere affected by subdural hematoma or other type of expanding intracranial lesions. That abnormal pupillary responses to light may be the only objective evidence of central nervous disease syphilis has long been known. The Horner syndrome often localizes the pathologic process at the cervical cord level. This occurs also in lesions of the medulla and of the lung apex.

The wide-open, staring eyes and dilated pupils of the panicky individual may be compared to the exophthalmos in the goiter patient. The mechanism controlling pupillary innervation is highly labile. The autonomic nervous system may be regarded as the neural apparatus determining the instinctive somatic reactions to each bit of life experience. All stimuli producing emotional reactions travel through the sensorium up the spinal cord or through the other perceptive pathways to the brain stem, the basal ganglion structures, and the cerebral cortex and also travel with the vascular tree.

It seems obvious, therefore, that it is not justifiable to speak only of centers where lesions produce a Horner syndrome. It is, more accurate to think of pathways conducting stimuli that are either interrupted or stimulated. Such stimuli may be of a structural organic nature but often are psycho-

genic. Life itself and its kaleidoscopic events frequently affect the nervous system and amongst other symptoms produces alterations in the appearance and reactions of the pupil.

ALTERATIONS IN EXTRAOCULAR MOVEMENTS RESULTING FROM INTRACRANIAL LESIONS

DR. E. JEFFERSON BROWDER said that the aneurysms arising from the intracranial portion of the internal carotid artery, those budding from the arteries comprising the circle of Willis, and those of the basilar artery and some of its branches, often impinge upon and produce dysfunctions of the third, fourth, and sixth cranial nerves. Other aneurysms not adjacent to those nerves may produce extraocular palsies secondary to rupture into the cerebral subarachnoid space or into the cerebral substance, with massive clot formation.

Dr. Browder said that an analysis of the symptomatology and abnormal physical signs with particular reference to extraocular palsies indicates that six different syndromes may be recognized:

1. The syndrome of rupture of the aneurysms of the internal carotid artery as it traverses the cavernous sinus or the carotid-cavernous fistula.

2. The syndrome of the aneurysms of the second part of the sigmoid of the internal carotid. The intracranial epidural fusiform aneurysms.

3. The syndrome of the aneurysms of the subdural portion of the internal carotid artery.

4. The syndrome of the aneurysms at the bifurcation of the internal carotid artery and those of the posterior communicating artery.

5. The syndrome of intrancranial hypertension resulting from aneurysmal rupture (spontaneous subarachnoid hemorrhage and/or intracerebral hematomas).

6. The syndrome of fusiform aneurysms of the basilar artery.

While it is recognized that all abnormal features must be given consideration in any

example of intracranial aneurysm, a correct interpretation of the disturbance in the ocular mechanism plays an important role in the localization of such a lesion.

MONOCULAR AND BINOCULAR PALSY OF GAZE

DR. ALFRED KESTENBAUM said that horizontal palsy of gaze or palsy of lateral parallel eye movements is characterized by impairment of the lateral gaze movement while the convergence movement of the eyes is preserved. The types of lateral gaze movement are:

1. Command movement, movement on a command, such as: "Look to the right!" This is also known as schematic movement.

2. Optically elicited movement; that is, movement toward a seen object. This is also known as follow movement.

3. Compensatory eye movement on head rotation due to a labyrinth reaction. This is also known as vestibular movement.

Horizontal gaze palsy may involve the lateral rectus of one eye and the medial rectus of the other eye to the same degree. This is known as the congruous form of gaze palsy. The incongruous form of gaze palsy may affect one of the two muscles to a different degree or the medial rectus alone.

Dr. Kestenbaum then cited a series of his own cases and cases taken from the literature which illustrated the following types of congruous gaze palsy.

1. General palsy of lateral gaze in which all main types of movement are abolished.

2. Bielschowsky type of gaze palsy in which labyrinthine countermovement is preserved, while the other types of movement are abolished.

3. Oppenheim's type of gaze palsy in which vestibular movement and follow movement are preserved and schematic movement is abolished.

4. Isolated lesion of schematic movement in which vestibular movement and follow movement are preserved, only schematic movement being abolished.

In these types of congruous gaze palsy,

the medial rectus of the one eye and the lateral rectus of the other eye are involved to the same degree, and the convergence movement is normal.

Incongruous gaze palsy was observed in the following forms:

1. Foville's syndrome. The right eye cannot be adducted in lateral gaze but it can be adducted on a convergence impulse; the left eye cannot be abducted and shows paralytic squint. This proves that in addition to the lesion of the posterior longitudinal bundle, along which run the lateral gaze impulses, the abducens nucleus or abducens nerve is involved.

2. Intranuclear gaze palsy. Adduction of the right eye is more disturbed than abduction of the left eye; convergence is normal. The lesion is usually considered to be in the left posterior longitudinal bundle between the level of the sixth-nerve nucleus and that of the third-nerve nucleus, but close to the former one.

3. Supranuclear medialis paralysis or superior intranuclear gaze palsy. Adduction of the right eye in attempted lateral gaze is abolished. But in attempted convergence, normal abduction of the left eye is normal. This lesion is also localized in the left posterior longitudinal bundle, but higher up than in the previous form.

In a case of supranuclear medialis palsy, a paradoxical phenomenon was seen. In binocular vision, the left eye could not look at any object on the right side, but when the right eye was closed, the left eye could turn toward the object. This movement was achieved by a convergence impulse, because the covered right eye was found to stand in adduction and the pupils were narrowed. Hence there was a substitution of a convergence movement for a lateral movement. Of course, this could be shown only when the right eye was covered so that no diplopia occurred.

4. Bilateral intranuclear gaze palsy. In this case both medial recti do not work in lateral gaze but do in convergence. This syndrome is significant for a median lesion involving both posterior longitudinal bundles between the third-nerve nucleus and the sixth-nerve nucleus.

Dr. Kestenbaum summed up by saying that all these forms of incongruous gaze palsy involve all the main forms of gaze movements to the same degree.

Bernard Kronenberg,
Recording Secretary.

OPHTHALMOLOGICAL SOCIETY OF MADRID

March 12, 1948

HYSTERICAL BLINDNESS

DR. MARIN AMAT AND DR. MARIN ENCISO discussed a recent case which showed the importance of careful and conservative diagnosis and treatment in this condition. A young woman, aged 23 years, suffered complete loss of vision in both eyes after a quarrel with her fiancé. The eyes and adnexa appeared to be completely normal.

As her vision began to return, it was possible to map the very reduced central visual field, the inversion of the red and blue fields, the classical field curves of Foerster, fatigue curves of Vilbrand, and so forth.

Psychiatric treatment together with vitamin therapy restored her vision and general equilibrium.

Discussion. Dr. D. Sinforiano Garcia Mansilla said that the case was interesting since it began as an amaurosis and then developed into amblyopia, permitting visual field tests for white and colors.

Many years ago he had published a case of hysterical blindness in a man who presented the following history. He was a student of timid nature who, in the evening before taking a final examination at the academy, suddenly became completely blind.

Eye examination, in which three colleagues assisted, established the presence of complete blindness, the absence of any lesion, and the retention of pupillary motility. These three symptoms pointed to hysterical blindness.

Previous nervous manifestations of the patient were that during the previous year, while explaining an equation on the blackboard at an examination, his vision suddenly became bad, the blackboard appearing red and the chalk green, and he had had to ask the proctor to permit him to rest. After a little rest, he recovered, saw the blackboard and chalk in their natural colors, and proceeded with the examination.

This history made the diagnosis plain. The patient was given a placebo and suggestive treatment. One week later, after a quiet sleep, his sight returned completely.

This is a typical case of hysterical amaurosis with the classical triad of symptoms: sudden blindness, normal fundus, and persistence of pupillary reaction. To these three may be added a fourth symptom—sudden and total recovery.

Dr. Munoz Pato: Given the psychic disturbances that characterize hysteria, one should be prudent both in diagnosis and treatment. Although mild cases can be quickly cured in one session (by instillation of drops, utilization of some complicated instruments, and so forth), other cases are more complex and serious. In these, simple methods will fail and the longer procedure of Dr. Marin Amat and Dr. Marin Enciso must be resorted to.

Dr. Marin Amat said that he does not use the word "hysteria" with either men or women but prefers the term proposed by Babinski, "pithiatism," which implies that the condition is curable by persuasion.

To be sure, the triad of symptoms, sudden blindness, normal fundus, and retention of pupillary reflexes, indicate hysterical amaurosis. There are some conditions, however, that exhibit these symptoms and are not of hysterical nature. Such a one, for example, is uremic amaurosis from lead poisoning. In this instance, the changes are in the visual cortex. The optic fibers that pass to the anterior colliculus and from there to the nucleus of the third nerve and that subserve the pupillary reflexes are not affected. According to Charcot, we find in hysteria a narrowing of the field of consciousness, a narrowing of the field of vision, and an unfolding of the personality.

Dr. Martin Amat agreed with Dr. Munoz Pato that there are always certain phases of a neurosis in hysterical amaurosis. Application of psychiatry should, however, be reserved for special cases. In the ordinary cases, the ophthalmologist should have enough general and psychiatric knowledge to treat the condition.

ERB-GOLDFLAM DISEASE

DR. BARTOLOZZI presented two patients, a mother and daughter, with the typical picture of pseudoparalytic myasthenia or Erb-Goldflam disease. The girl showed marked bilateral ptosis and almost total paralysis of the extrinsic musculature of both eyes, with perfect preservation of the power of the intrinsic eye muscles.

The mother showed pseudoparalysis of the muscles of the lips, tongue, and larynx. Electrical exploration disclosed the nuclear origin of both processes. The myasthenic reaction was negative, but the clinical picture, the improvement of the condition by rest, its aggravation during the day, as well as the amount of creatine in the urine, all testified that it was a case of myasthenia, although different clinical pictures were present in mother and daughter.

NEVUS PIGMENTOSUS IN A PYTERYGIUM

DR. MARIN AMAT AND DR. MARIN ENCISO demonstrated the case of a 48-year-old peasant who for 30 years had had a little black spot on the conjunctiva of the left eye near the sclerocorneal margin at about the 9:30-o'clock position.

This spot did not give him any trouble but when he developed a pterygium in this eye several years ago, the spot seemed to increase in size. The pigment spot was removed during the operation on the pterygium. The laboratory diagnosed it as nevus pigmentosus.

Joseph I. Pascal,
Translator.

AMERICAN JOURNAL OF OPHTHALMOLOGY

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INTERNATIONAL CONGRESSES

For the physician tourist an international congress combines the stimulation and recreational delights of travel with the deepened sense of fellowship between professional colleagues. There are the teachers and thinkers whom we have perhaps known only through the printed page or by the medium of casual correspondence. Sometimes, it is true, these may disappoint us and take on less significant stature, physically or intellectually, than they had carried in our imaginations before the personal encounter. On the other hand we now and then enjoy the pleasurable stimulus of becoming acquainted with brilliant personalities never revealed to us through medical journals; for there are many such among our great profession in general and our specialty in particular. It is unfortunate that some of the friendships thus created suffer too easily the attrition due to time and space.

The First International Congress of Ophthalmology, held in Brussels in 1857, must have displayed the wonderful freshness of knowledge, discovery, and enthusiasm associated with a decade of study in the revelations of ophthalmoscopy. At that time

this technique of examination was still sufficiently youthful to have acknowledged a period during which the master Graefe had regarded glaucomatous excavation as a protrusion of the optic disc (an impression which he soon revised). There followed the Paris Congress of 1862, the first Amsterdam Congress of 1867, London in 1872, New York in 1876 (Herman Knapp as a shining light), Milan in 1880, Heidelberg in 1888, Edinburgh 1894, then Utrecht (Holland) 1899, Lucerne 1904, Naples 1909.

War of course interfered with the regular succession and sometimes with place of meeting. There had been the Franco-Prussian conflict. World War I clashed with the arrangements for the twelfth Congress, planned for St. Petersburg (now Leningrad) in 1914. The very successful second Amsterdam Congress fell about midway between World Wars I and II, in 1929. The fourteenth Congress, in Madrid, 1933, was a few years ahead of the Franco revolt in Spain. The Cairo Congress of 1937 was held while Spain was still in the throes of fratricidal warfare.

Very successful gatherings occurred respectively in Washington in 1922 and in London in 1925. The former could not be completely international in its scope, because officially the United States was not yet at peace with Germany and Austria. It is not, however, accurate to state (as was done quite recently) that the Washington Congress was limited to English-speaking ophthalmologists. German could not be recognized, but the official languages of the Congress were English, French, and Spanish, and papers were read in all three. The Congress at London in 1925 was definitely a Congress of English-speaking ophthalmologists, and was very well attended.

After a good deal of discussion between the official representatives of different countries, it appears now that the sixteenth International Congress of Ophthalmology will be held in London, England, July 17 to 21, 1950. Apart from any startling complications in the international political situation, that Congress is likely to be attended by a large number of colleagues from the United States, and the making of necessary reservations will soon be proper matter for consideration.

During World War II, the impossibility of holding such Congresses in Europe led an energetic group of American ophthalmologists, north and south of the Equator, to plan for the organization of a Pan-American Congress of Ophthalmology. As a beginning, this was held after the conclusion of the meeting of the American Academy of Ophthalmology and Otolaryngology at Cleveland in 1940, the languages officially used in the program being Spanish, Portuguese, and English.

A second Pan-American Congress of Ophthalmology was planned for November, 1943, in Montevideo, Uruguay, but the travel difficulties arising from the War caused repeated postponements of this gathering, which was finally held in November, 1945. A third Pan-American Congress was very successfully staged in Havana in January, 1948, with a large attendance by ophthalmologists (and their families) from North, South, and Central America. The next, fourth, Pan-American Congress will be held in Mexico City in 1952.

Undoubtedly, under peaceful conditions, many ophthalmologists of the United States will attend both the London International Congress in 1950 and the Mexico Pan-American Congress in 1952, and both events should be kept in mind in making travel plans for the coming four years.

W. H. Crisp.

BASIC SCIENCE RESEARCH
IN OPHTHALMOLOGY

One of the encouraging features of postwar ophthalmology in the United States is the number and quality of basic science studies dealing with eye problems that have

been reported. A substantial proportion of these studies has been made by ophthalmologists but more have been made by nonophthalmologists working in university eye departments or institutes or in the basic science departments of the medical schools and universities.

The Association for Research in Ophthalmology, which is the only national ophthalmological society dealing primarily with experimental ophthalmology and offering membership on an equal basis to both ophthalmologists and nonophthalmological basic science workers, has recognized the importance of providing a common meeting ground for the ophthalmologist and the nonclinical investigator. At the 1948 meeting of the association, its constitution was amended to permit the formation of regional sections similar to those established by such other organizations as the Society of American Bacteriologists. Section secretaries have already been named and two sections—the Western Section whose secretary is Dr. Michael J. Hogan of San Francisco; the Eastern Section whose secretary is Dr. Alson E. Braley of New York—have already held section meetings.

The Western Section meeting was held on March 27, 1948, in San Francisco and was attended by about 75 ophthalmologists and nonophthalmological investigators from the various basic science departments of the western universities. The program included the presentation of five experimental studies, followed by a banquet and an address by Frank W. Weymouth, Ph.D., professor of physiology at Stanford University, entitled, "Recent measurements of the living eye and their relation to the development of myopia." A second meeting is to be held in San Francisco this month, immediately following the examinations of the American Board of Ophthalmology.

The first meeting of the Eastern Section was held in New York City on November 13, 1948. Four papers were presented, one by an ophthalmologist and the other three by basic science workers from Harvard University and Columbia University. About 100 persons attended the meeting.

The section meetings, as judged from these first two, will not be in competition with the annual meeting of the national association but on the contrary will, in the main, provide a forum for the presentation of preliminary reports, the more important of which may subsequently be developed for presentation at the national meeting. Perhaps the most important function of the sections will be to bring together on a regional basis all the clinical and nonclinical investigators interested in ophthalmic research. In this age of coöperative research it is only by a constant interchange of ideas, facilitated by personal contacts between workers, that we can hope to see the full development of basic science investigation.

Phillips Thygeson.

THE FOURTH ARGENTINE CONGRESS OF OPHTHALMOLOGY

The Argentine Congress of Ophthalmology, which is held every four years, had its fourth assembly December 13 through 18, 1948, at Mar Del Plata, Argentina. The officers this year were: President, Dr. Diego M. Argüello; vice-president, Dr. Roberto F. Pereira; secretary, Dr. Juan L. Giambruni; treasurer, Dr. Bruno Tosi.

Mar Del Plata, Argentina's most famous and fashionable summer resort, is located on the coast 250 miles south of Buenos Aires. The meeting was held in the modern, air-conditioned auditorium of the Casino, or Kursaal, and most of those attending the congress lived at the beautiful Hermitage Hotel just across the street from the Casino.

The entire week was devoted to the meeting. On Monday morning the formal inaugural ceremonies were held at which time a cordial welcome was extended by the president of the congress, by federal and municipal officers, and by the titular professors of ophthalmology at the various uni-

versities. Greetings were received from the official visitors. A scientific session was held each morning from 9 to 12 o'clock, and this was followed by a 4-hour interlude for lunch, siesta, and recreation. The afternoon sessions began at 4 o'clock and lasted until 7; the evenings were free for social gatherings.

The scientific program was arranged along the lines usually employed in Europe. Certain subjects were selected for discussion, and this congress was devoted primarily to "Tumors of the eye and adnexa." Two other official themes were "Surgery of the extraocular muscles" and "Prevention of blindness." In addition to these subjects there were miscellaneous papers and moving pictures on aspects running almost the entire gamut of ophthalmology. Fourteen instruction courses were given. These were excellently arranged and presented and were most enthusiastically received.

In the spacious anterooms adjoining the auditorium there were scientific and commercial exhibits. The scientific exhibits were particularly meritorious. These were sponsored by the various universities instead of by individuals. There were exhibits from the Universities of Buenos Aires, La Plata, Cordoba, and Litoral. In addition, the government agencies, such as the Secretary of Public Health and the Secretary of Education, had comprehensive exhibits demonstrating the efforts they are making along lines related to ophthalmology and projecting their plans for the future.

There were the usual commercial exhibits, not only of Argentine firms, but also those of various foreign nations. Of particular interest was the wide variety of publications on display: the latest ophthalmological books of English, French, Swiss, German, Italian, and American authors were exhibited. Argentine manufacturers had on display their own model of a slitlamp, ophthalmometer, refractometer, ophthalmoscope, and so forth, as well as various surgical instruments.

The meeting had a strong international flavor due to the presence of many foreigners, including leading ophthalmologists of Europe and the other South American countries. Eminent visitors from Europe were Franceschetti of Switzerland, Arruga of Spain, Barraquer of Spain, and Velter of France. Alvaro was the official delegate from Brazil and the United States. Castroviejo and Hanson from the United States attended and participated in the program.

Argentine ophthalmologists are very versatile. In their number they include an international playwright, Dr. Carlos S. Damel, and an olympic fencer, Dr. Jorge Balza. They are all surprisingly good linguists. Most of them speak English, but all seem to have a knowledge of at least one language other than Spanish. They are amazingly indulgent of a foreigner's efforts to speak their language.

It was early summer in the Argentine, when the Congress was held, and the weather lent itself to recreation and social activities which were a delightful feature of the meeting. The beach was readily accessible to the hotel and, in addition, golf and other sports were available. The Casino, a tremendous recreational center operated by the government, has the largest gambling facilities in the world.

The impromptu gatherings for lunch and dinner were diverting and stimulating. Since on Wednesday afternoon there was no scientific session, a barbecue was held at a large private estancia in the pampas. After lunch some Argentine cowboys, or gauchos, demonstrated their horsemanship. Later in the afternoon a visit was made to another ranch where race horses and polo ponies are bred. A number of former Derby winners were exhibited.

The congress was concluded on Saturday evening by a most delightful banquet at which there were after-dinner speeches by the representatives of the various countries.

To me it was a great privilege and pleasure to attend this meeting. The scientific program was excellent; the subjects for dis-

cussion were many and varied; the presentations were well done; discussions were spirited but always tolerant. The Argentine people are extremely hospitable and friendly, and have the happy faculty of combining their serious scientific endeavors with the light touch of pleasure and conviviality.

I departed with a great affection for the Argentine ophthalmologists and a great respect for their ophthalmology.

Algernon B. Reese.

BOOK REVIEWS

DETAILED ATLAS OF THE HEAD AND NECK. By R. C. Truex and C. E. Kellner. New York, Oxford University Press, 1948. 135 pages, 136 colored plates, index. Price, $15.00.

We have waited a long time for an atlas like this. It vividly recalls the famous anatomic atlas of Johannes Sabotta and J. Playfair McMurrich, long out of print and a collector's item. Dr. Truex, associate professor of anatomy, and Mr. Kellner, artist, Department of Anatomy, College of Physicians and Surgeons, Columbia University, have worked, in the words of Professor Detwiler in his foreword, "diligently and untiringly on this atlas, and in a state of true symbiosis!"

The beauty of the plates and the concise, accurate descriptions that accompany them cannot be improved upon. Figures 1 to 82 detail the regional anatomy; Figures 83 to 104, the skeletal structures; Figures 105-116 are representations of frontal sections; and Figures 117 to 136 are those of transverse sections.

The anatomy of the globe, the orbit, and the adjacent structures are clearly displayed, better perhaps than if the actual injected specimens were in a tray in front of you. Those who are sensitive to formaldehyde had better take care, for the pictures are so true that an allergic response could result, if our friends the psychosomatic experts are correct.

The publishers deserve enormous credit for their splendid job. Not a single ophthalmologist should be without his own private copy.

Derrick Vail.

THE W. H. ROSS FOUNDATION (SCOTLAND) FOR THE STUDY OF THE PREVENTION OF BLINDNESS. Reprinted Papers. London, University of London Press, Ltd., 1948. Paper binding, 232 pages, appendix with statistical tables. Price, 3 shillings.

The Ross Foundation is an organization of the broadest scope with a full-time research ophthalmologist as director. The present volume contains the history of this great undertaking and a report on the research sponsored to date. All the technical papers have been published in various professional journals as selected by the individual investigator. The AMERICAN JOURNAL OF OPHTHALMOLOGY was the choice for the significant paper on ocular siderosis by Loewenstein and Foster.

William Henry Ross, a self-made man of great wealth, established the Foundation in 1935 after becoming sightless. He lived until 1944 and was impressed by the continuous achievements of his philanthropy. The Foundation popularized sodium sulfacetamide, first for counteracting infections of the eye following mustard gas, next for the better control of corneal ulcers. The treatment recommended was direct application of the powder to the ulcer followed by after-instillations of sulfacetamide solution. The sulfacetamide penetrated readily into the cornea, much more than sodium sulfadiazene, did not produce deleterious irritation, and its local use resulted in a much greater concentration in the ocular tissues than was attainable by systemic sulfonamide therapy. The intravitreal injection of pure penicillin was found highly effective in preventing panophthalmitis experimentally. The drug diffuses so slowly from the vitreous that an adequate concentration is maintained for 2 to 3 days.

The industrial studies showed that fluorescent lighting lost 50 percent of its effectiveness in 18-months' time. In the schools a careful comparison of reading age with mental age revealed dyslexia in some degree in 11.5 percent of boys and 7.4 percent of girls. The Foundation is now assembling records of blindness in one eye for their great value in the study of prevention. Cannot a similar survey be made in this country?

James E. Lebensohn.

ESSENTIALS OF PATHOLOGY. By L. W. Smith and E. S. Gault, with a foreword by the late James Ewing. Philadelphia, The Blakiston Company, 1948, Edition 3. 764 pages, 740 illustrations, a number in color; bibliography, index. Price, $12.00.

The busy ophthalmologist, immersed in the minute aspects of his field of activity, is in constant danger of forgetting that he is primarily a physician. There are times when he longs for the opportunity to renew his student days and to recall his absorption in the basic studies of medicine. Alas, not many of us have the time or energy to read textbooks of general medical subjects, along with our specialized reading.

One of America's great ophthalmologists of an older vintage, when catch-as-catch-can training was all that was available, had for his personal program of self-instruction a schedule of reading every night for five nights a week, divided into three one-hour periods. The first was given to ophthalmology, the second to general medicine, and the third to the world's great English literature. He faithfully pursued this schedule throughout his happy life. He was an educated man.

Ophthalmologists who wish to recapture their medical soul will take pleasure in owning and reading Smith and Gault's well-known Essentials of Pathology, particularly in this beautiful new and completely revised edition. They will find, on nearly every page, information that is pertinent to ophthalmology and of use to them in their daily work.

For example, to pick some chapters at random, there is a splendid discussion of retrograde processes, another on disturbances of circulation, an excellent description of the avitaminoses, another of inflammation, and, particularly important in these days of a wide-open world, new information on animal parasites. These authors have taken great pains to illustrate their text liberally and most satisfactorily.

Apparently every system of the body is well covered, except the eye. This is deplorable, because general physicians and pathologists are entirely ignorant of ocular pathology. A chapter on this subject would complete a fine piece of work.

Derrick Vail.

TRANSACTIONS OF THE OPHTHALMOLOGICAL SOCIETY OF PARIS (and of the Ophthalmological Societies of the East, of Lyon, and of the West). Meeting of March, 1948, pp. 83-102.

Deschamps presents a man, aged 58 years, with all the signs and symptoms of an orbital neoplasm. Exact diagnosis of a mucocele of the frontal sinus was made only after orbitotomy. Recovery was uneventful, motility improved slowly, and the exophthalmos disappeared. Vision was restored. There was only a mild disturbance in the function of the superior oblique muscle. The disc remained pale with some blurring of its margin.

In a study of corneal nerves, Offret found that the staining methods of Cajal were unsatisfactory but that modification of Ranvier's technique was effective. Flat sections and radial incisions gave good exposure. A few Schwann's elements were easily seen.

Guillaumat and Lemaitre observed myopia gravis, retinitis pigmentosa, and congenital luxation of the lenses in a young woman whose parents were first cousins. The patient's general health was good. She

had four normal children, but each pregnancy had caused an increased loss of vision. Although the authors believe that the disease is essentially hereditary, they also suspect that the influence of hormonal factors may have caused the visual impairment after each delivery.

Sédan and Sédan-Bauby discuss micropuncture as a means of testing the resistance of the lens capsule. They comment on the older experiments of Czillag which had only recently become known to them. The authors, themselves, use a needle puncture of the lens capsule in vivo.

Larmande describes calcified and ossified angiomas of the choroid. Choroidal angiomatosis can cause calcium precipitation in the vessel walls of the lesion and its immediate neighborhood, even in the retina. These pathologic processes might be seen combined in a symptom complex which the author calls encephalofacial neurangiomatosis.

Hartmann describes an atypical case of suprasellar meningioma with unilateral dilatation of the optic canal. A woman, aged 49 years, had temporal hemianopia in the right eye with temporal pallor of the disc. The left eye was normal. Exact diagnosis was made only during surgery.

Alice R. Deutsch.

SOME ASPECTS OF OCULO-REFRACTIVE TECHNIQUE. By Malcolm Cholerton. London, Hammond, Hammond, & Co., Ltd., 1948. Clothbound, 147 pages, 23 figures, index and bibliography. Price, 21 shillings.

The author, a British ophthalmic optician (equivalent to the American optometrist), is concerned with the professional preparation of his colleagues, and this book aims to broaden their acquaintance with visual functions. His very readable digest is based on the works of Duke-Elder, Parsons, Traquair, Chavasse, and Luckiesh, supplemented by selected articles from the journals of ophthalmology, all of which are duly credited. Mr. Cholerton, who worked in the war with British and American ophthalmologists, maintains throughout a correct professional attitude. Scorning practitioners who prescribe base-in prisms for migraine, he states, "In view of the incidence, not infrequently, of migraine associated with pathological disturbances such as cerebral aneurysm or tumor, the patient should be referred for ophthalmological and neurological investigation."

His discussion on dynamic retinoscopy opens with this opinion: "In its present state of development as a technique it is based upon certain assumptions, the validity of which are still questionable." As regards tinted lenses, "The aim should be to remove or diminish the patient's conviction that a tint must be incorporated as a necessary part for the solution of his ocular disability."

The optical data submitted is at times insufficiently explicit. He suggests the use of a trial-case telescope, made by placing plus 20D. and minus 20D. lenses in the front and back cells respectively, but does not mention that this combination only functions at a distance of 10 inches. This slim volume no doubt will be of value to the group for whom it was written.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension

10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

v. Bahr, Gunnar. **Measurements of the thickness of the cornea.** Acta ophth. 26: 247-266, 1948.

The literature on this subject is reviewed and a new instrument for this purpose used in conjunction with the Gullstrand slitlamp is described in detail. The mathematical formula used to calculate the corneal thickness is explained. Normal eyes of 125 persons of both sexes and different ages were examined. The effect of hypertonic and hypotonic solutions on the corneal thickness was tested on rabbit and human eyes. The average thickness of the cornea is 0.565 mm. and varies between 0.46 and 0.67 mm. The cornea in eyes with myopia over four diopters was thinner. Changes in the corneal thickness of rabbits were produced experimentally by baths in solutions of unphysiological osmotic pressure. The thickness is increased by baths of 0.5-percent sodium chloride, and decreased by baths of a 2-percent solution.

Ray K. Daily.

Fornes Peris, Enrique. **The comparative morphology of the corneal fibrocytes.** Arch. Soc. oftal. hispano-am. 8:821-826, Aug., 1948.

This is a detailed report on an investigation of the cornea of man, the rabbit, pig, bull, chicken, lamb, frog, cat, snake, and mullet with the Llombart silver stain method. All the corneal cells are fibrocytes. No histiocytes or leucocytes were encountered. Fibrocytes are irregular elements which under normal conditions are fixed or but slightly movable. They have an abundant cytoplasm which adapts itself to the form of the cell, and flattened anastomizing prolongations. The cells have two predominant forms, membranous as in man, and corpuscular as in the chicken. The cellular elements are abundant in all the corneas investigated; they have numerous prolongations, short in some cells, thin in others, and some cells have both types. The union of these processes forms a true syncitium, best demonstrated in the cornea of man and the hog.

The characteristic form and volume of the cell, the position of its expansions,

the manner of the anastomosis of the fibrocytes varies in different animals. The distribution of the cells in the connective tissue is quite regular in the chicken and complicated in man. The cellular expansions may be filiform, or may originate in a broad base and become narrow at the end; some are smooth and uniform in size throughout their entire extent, while others are bristly with spines, and irregular in size. The cornea of the hog is very similar to that of man and that of the cat less so. The fibrocytes of the hog, and to a lesser extent those of the cat, are similar to those of man in their unequal distribution, in the broad form of their extensions, and in the arrangement in broad layers. Ray K. Daily.

Meves, H. **The structure of the retinal arteries.** Arch. f. Ophth. 148:459-467, 1948.

The tissues of 16 eyes of young persons were embedded in paraffine and stained with Weigert's elastica lithium carmine. Whereas the central artery near the lamina cribrosa shows a single layered internal elastic membrane just beneath the intima, the retinal branches present at least 3 or 4 elastic membranes. The membranes are concentrically arranged and interrupted by numbers of smooth muscle cells. The difference between the retinal arteries and the choroidal vessels of the muscular type is emphasized.
Ernst Schmerl.

Scobee, R. G. **The fascia of the orbit. Its anatomy and clinical significance.** Am. J. Ophth. 31:1539-1552, Dec., 1948. (9 figures, 15 references.)

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Fischer, F. P. **The frequency curves of senile ocular changes.** Ophthalmologica 116:6-9, July, 1948.

In 1941 (Ophthalmologica 106:226) the author reported on the incidence in the various age groups of typical senile changes in man, such as arcus senilis, depigmentation of the iris and acquired cataract. The frequency distribution of these three characteristics of senescence was expressed by S-shaped (Sigmoid) curves (plotting incidence on the ordinate and age on the abscissa). The relationship between the logarithm of the frequency to the logarithm of age was expressed by a straight line except for the extremely high values. In the paper under review Fischer stresses the mathematical difference between growth curves and senescence curves (see the author's contribution on "senescence of the eye in Sorsby's Modern Trends in Ophthalmology, Vol. 2). Peter C. Kronfeld.

Joy, H. H. **Uveopigmentary sensitization.** Am. J. Ophth. 31:1581-1588, Dec., 1948. (54 references.)

Knecht, F. **The influence of climatic conditions upon the non-acute glaucomas.** Ophthalmologica 116:21-37, July, 1948.

This study was made in the department of ophthalmology of the University of Basle (Switzerland) which is suitably located for investigations of the influence of meteorological factors upon the development and course of diseases. In that locality A. Brueckner demonstrated a relationship between the weather and the onset of acute glaucomas. (See Archives of Ophthalmology 20:950, 1938.)

In the paper under review the non-acute glaucomas were classified as simple, chronic (characterized by recurrent mild attacks), secondary, absolute or hemorrhagic forms. More cases of non-acute glaucoma registered as new patients during the winter than during the summer of the years from 1936 to 1945. January and March represented the

maxima and August the minimum of the seasonal distribution curve. Close observation of the diurnal variations of ocular tension revealed a surprisingly high incidence of elevations that could be correlated with cold waves, heat waves or other sudden meteorologic disturbances.

Peter C. Kronfeld.

Rapisarda, Dante. **Conjunctival tuberculous hetero-allergy. Part II: histologic study.** Ann. di ottal. e clin. ocul. 73:344-371, June, 1947.

Part I of this study was reported during the 36th Congress of the Italian Ophthalmological Society. Rabbits and guinea pigs were sensitized by injections of vaccines and of live bacilli of low virulence, and subsequently tests were made to determine the reactivity of the conjunctiva to instillation and subconjunctival injection of tuberculin and nonspecific stimuli (milk and gonococcus vaccine). In all cases the conjunctival reaction was more marked in the sensitized animals than in the controls, and nonspecific stimuli incapable of producing any reaction in normal animals produced intense and lasting reactions in the sensitized animals. This augmented reactivity (hetero-allergy) of tuberculin-sensitized animals to nonspecific stimuli may give a clue to the treatment of certain recurrent and intractable forms of conjunctivitis, and Rapisarda is carrying on further studies. The reactive process was studied histologically in its several phases. Three stages were distinguished, an exudative, a granulomatous, and a sclerotic. (8 figures, references.)

Harry K. Messenger.

Redi, Francesco. **Localized amyloidosis, with particular attention to conjunctival amyloidosis, in the picture of paraamyloidosis and their etiologic relationships.** Giorn. ital. di oftal. 1:227-264, May-June, 1948.

Paramyloidosis, in its localized and circumscribed form, must be considered separately from amyloidosis, differentiated by the history, histologic aspects, and finally by the microchemical reaction. The differentiation is illustrated by a case of paramyloidosis of the myocardium, and one case of paramyloidosis of the conjunctiva. Experimental amyloidosis in the white mouse has all the characteristics of human generalized amyloidosis and not of paramyloidosis. In the course of chronic cavitating tuberculosis degenerative histologic changes are not found in the lids or conjunctiva nor are the infiltrative changes usually thought to be preamyloidosis changes. In the course of trachoma one does not find amyloid changes of the lids or even of the conjunctiva. Mechanical stimuli repeated many times have not given rise to degenerative substances in normal animals nor in animals treated with sodium caseinate. Trementine injected into the area of the lids of guinea pigs causes the amyloid substance to disappear in normal animals and in those treated with sodium caseinate. The experiments indicated that disturbances in metabolism have not influenced the pathogenic mechanism of localized amyloidosis, rather that local conditions are responsible factors.

Francis P. Guida.

Spyratos, S. P. **Promelanine.** Ann. d'ocul. 181:556-565, Sept., 1948.

This nucleoprotein is an inductor for undifferentiated embryonic cells. In the secondary optic vesicle promelanine aids in the formation and differentiation of retinal and choroidal pigmentation. It transforms some cells of the periocular mesenchyme into melanoblasts. Melanophores of the eye and skin are apparently related. After birth, under some environmental conditions largely unknown, promelanine granules may transmit the tendency to specific types of inflamma-

tory reactions to other mesoblastic tissues. Sympathetic ophthalmia is thought to be a reaction of this type which involves primarily mesoblastic pigmentation in the uvea of both eyes.   Chas. A. Bahn.

3
VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Albright, A. A., and Seretan, E. L. Sulfathiazole sensitivity: with a review of the literature. Am. J. Ophth. 31:1603-1606, Dec., 1948. (18 references.)

Bárány, E. H. The influence of gum arabic and dextran on the blood-aqueous barrier and intraocular pressure. Ophthalmologica 116:65-79, Aug. 1948.

Dieter and Duke-Elder reported marked lowering of the ocular tension after intravenous injections of concentrated solutions of gum arabic into rabbits. Both authors interpreted these lowerings as manifestations of the great influence of the colloid-osmotic pressure of the blood on the ocular tension. Closer analysis of these experiments reveals a striking absence of parallelism between the rise in the colloid-osmotic pressure of the blood on the one hand and the drop of ocular tension on the other hand. Bárány repeated these experiments with gum arabic solutions of varying concentration and confirmed the findings of Dieter and Duke-Elder. Following the injections he measured the ocular tension and, by means of the colloidometer of Roenne, the intensity of the aqueous flare. A striking parallelism between the colloid content of the aqueous and the drop in ocular tension became apparent. Both phenomena were also found to occur after the intravenous injection of gum arabic solutions of lower osmotic concentration than plasma. The same effects could be obtained with dilute solution of

dextran which is a polysaccharide used in Sweden as a plasma substitute. In its natural form dextran has a molecular weight of many millions. By hydrolysis the molecule can be broken down to particles of a molecular weight of less than 200,000. The natural substance in dilute solution produced a drop in ocular tension with marked aqueous flare, while equivalent amounts of the hydrolysate were ineffective. These observations show that the hypotony after the intravenous injection of high-molecular colloids is not caused directly by osmotic factors. "When hypotony occurs it is always associated with colloid increase in the aqueous, signalling a breakdown of the blood-aqueous barrier. Injury to the barrier is probably a causal factor in the production of hypotony by these substances (gum arabic and dextran)."

Peter C. Kronfeld.

Boros, B., and Vönöczky, J. Penetration of sulfonamides into the eye. Ophthalmologica 116:177-186, Sept., 1948.

The penetration into the eye of systematically applied sulfonamides was studied in cats. Topically applied pilocarpine, atropine or adrenaline did not significantly alter the rate of sulfonamide penetration. Gynergen and bacterial inflammation raised the intraocular sulfonamide concentration significantly. After single intravenous doses of 3 to 4 grams of sulfonamides adequate sulfonamide levels were found in the vitreous of a few human eyes which had to be enucleated because of endophthalmitis or absolute glaucoma. The ineffectiveness of sulfonamides in many types of intraocular infection should not be attributed to low intraocular sulfonamide levels.

Peter C. Kronfeld.

De Vincentiis, M. The oxidation activity of the human cataract in the pres-

ence of amino acids. Rassegna ital. d'ottal. 17:247-253, July-Aug., 1948.

The author studied the respiratory behavior of the cataractous human lens in the presence of amino acids. He established the fact that cystine, asparagine and tyrosine were increased and that glycocol, leucine and histidine were diminished in amount. He also observed a diminution of alanine and tryptophane. The changes established the fact that all respiratory activity of the lens disappears from the opaque lens fibers.

Eugene M. Blake.

Duke-Elder, S., and Davson, H. The present position of the problem of the intra-ocular fluid and pressure. Brit. J. Ophth. 32:555-569, Sept., 1948.

For many years it has been accepted as fact that the aqueous is an ultrafiltrate of the plasma, a dialysate which moves directly through the capillaries of the ciliary body into the anterior chamber by simple osmosis. If this were true this dialysate should be in dynamic equilibrium with the plasma. This theory fails to explain some of the data. The concentration of the electrolytes sodium and chloride in the aqueous is consistently higher than in the blood stream. It has been suggested that these substances were involved in metabolism of the lens, but since the same imbalance holds in the aphakic eye there must be some other explanation. The concentrations of carbohydrates in the aqueous of the normal and aphakic eye are much lower than in the blood and that complicates the problem further.

Nitrogenous substances, especially urea, are also present in lower concentration in the aqueous. Factors other than those of simple osmosis must be at work. As an alternative theory, the authors suggest that aqueous is actually elaborated entirely within the cells of the ciliary body and is drained away too quickly to be altered by osmosis with the plasma.   Morris Kaplan.

Ferguson, W. T. W. Ocular disturbances associated with malnutrition. Tr. Ophth. Soc. U. Kingdom 66:108-109, 1946.

The author reports on the ocular manifestations of volunteers whose diet was deprived of vitamin A in one experiment, and of vitamin C in another, conducted for the Medical Research Council in Sheffield. The two best criteria for assessing the course of the depletion of vitamin A were the vitamin A and carotenoid content of the blood plasma, and the capacity for dark adaptation.

There was a rapid drop in the carotenoid content of the blood in three months. The average value fell from an initial 150 i.u. per 100 ml. of plasma to 12 or 40. There was a distinct correlation between the vitamin A level in the blood plasma and the capacity for dark adaptation. The latter was normal if this level was about 50 i.u. per 100 ml. In only three subjects was this level reached after a period of 25 months. No changes were found in the degree of opacity in the conjunctiva that were not found also in the controls and a few small aneurysmal dilatations of the limbal vessels were also noted in the controls.

The depletion of the diet in vitamin C caused no change in the capacity for dark adaptation and no changes were visible with the corneal microscope.

Beulah Cushman.

Gandolfi, C. The action of Priscol on the retinal arterial pressure. Ann. di ottal. e clin. ocul. 73:336-343, June, 1947.

Priscol "Ciba" is 2-benzylimidazoline hydrochloride, a new peripherally acting vasodilator. Conjunctival instillation of Priscol in man had no effect on the

retinal arterial pressure as measured with Baillart's ophthalmodynamometer. The intramuscular injection of 1 cc. of a 1-percent solution caused only a slight and inconstant reduction, but a retrobulbar injection of the same quantity caused a rapid, definite, and prolonged reduction of the retinal arterial pressure. The injection did not affect the systemic blood pressure and made no significant alterations in the intraocular pressure.

Harry K. Messenger.

Gandolfi, C. **A new drug for surface anesthesia in ophthalmology.** Ann. di ottal. e clin. ocul. 73:439-441, July, 1947.

A ½-percent solution of Butococaine, a butyn-like product of the Zambelletti laboratories, was found on clinical trial to meet all the requirements for satisfactory surface anesthesia. An instillation of a single drop produced in one minute complete corneal anesthesia which lasted ten minutes. There was no mydriasis or desquamation of the corneal epithelium, and the pupillary reactions and the ocular tension were not altered. No intolerance was noted in several hundred patients. Solutions may be sterilized by boiling. The slight hyperemia which follows the instillation may be prevented by the addition of epinephrine solution.

Harry K. Messenger.

Jones, I. H., Muckleston, H. S., Lewis, E. R., and Owens, G. R. **Nutrition in ophthalmology and otolaryngology.** Ann. West. Med. and Surg. 2:491-499, Nov., 1948.

The authors emphasize the embryological view of nutrition in that the germ layers have specific vitamin requirements. Rats on controlled diets were perfused and the microscopic tissue studies are reported. In dietary deficiencies the cells were found to be shrunken, many absent. When the animals were given complete diets the tissues rapidly returned to normal. Orwyn H. Ellis.

Kapuscinski, W. **On symptoms of the pulse in the central retinal artery.** Brit. J. Ophth. 32:881-885, Dec., 1948.

Direct examination of the fundus shows two kinds of pulse, one spontaneous and the other artificial, from pressure on the eyeball. The author has observed that when pressure is made on the eyeball the first movement is a sagging of the walls of the artery which is synchronous with the cardiac systole. If the pressure on the eyeball is increased then the rhythm of the arterial pulse becomes alternate. There is then a dilatation in the retinal artery simultaneously with the cardiac systole, and a contraction of that artery with diastole. The latter is the phenomenon which should be interpreted according to Graefe's theory.

Orwyn H. Ellis.

Knape, Birgitta. **Studies on the effect of certain stimulants on the accommodation of the eye and of the threshold value for the effect of vitamin B₁ on the accommodation.** Acta ophth. 26:35-40, 1948.

Accommodation was tested by the Vannas method for each eye separately immediately before the administration of the stimulant, directly after, and at intervals of varying length. The effect of the oral administration of pervitin was tested in 20 persons, of intramuscular injections of coramin in 6, of caffein in 10, and of intravenous injections of vitamin B_1 in 64. The charted data show that the maximum effect, a 5-percent increase in accommodation for pervitin, occurs after 1½ to 2 hours, and accommodation falls below the initial strength after 2½ hours. The maximum effect, a 5-percent increase in accommodation, occurs almost immediately after the injection of coramin, and there is no subsequent depres-

sion. The tests for vitamin B_1 were controlled with injections of physiologic saline solution, which had no effect on accommodation. The threshold value for the effect of vitamin B_1, to which accommodation appears to be very sensitive, is between 2 and 5 mg. Half an hour after the intravenous injection of 5 mg. of vitamin B_1 accommodation is increased 6.1 percent, and the effect lasts about 24 hours; the effect of smaller doses is less marked and of shorter duration.

Ray K. Daily.

Macaskill, J., and Weatherall, M. Observations on experimental pneumococcal infection of the rabbit's cornea and on their treatment with penicillin. Brit. J. Ophth. 32:892-899, Dec., 1948.

The authors used a strain of pneumococcus that produced constant lesions when injected intracorneally. Subcutaneous administration of penicillin was found to be much less effective than the subconjunctival injection of 1,000 units per kg. body weight at 12-hour intervals which completely arrested these infections. Orwyn H. Ellis.

Mann, Ida. Tissue cultures of mouse lens epithelium. Brit. J. Ophth. 32:591-596, Sept., 1948.

Attempts to grow mouse lens epithelium in tissue culture are described. Lenses of embryo mice in late stages of development were used. No culture survived more than 12 days. If the capsule was left intact no changes in the tissue occurred. If the capsule was ruptured at the moment of planting the subcapsular epithelium proliferated and grew all around the capsule in a flat sheet of large, globular, clear cells. These cells did not survive beyond ten days. (8 figures.)

Morris Kaplan.

Neujean, G., Weyts, E., and Bacq, Z. M. Action of B.A.L. on ophthalmologic accidents resulting from treatment with tryparsamide. Bull. Acad. roy. de méd. de Belgique 13:341-350, 1948.

Eye complications during treatment of trypanosomiasis with tryparsamide are frequent. Observations made on negroes at the Institure for Tropical Medicine at Léopoldville, in whom the trypanosomiasis had attacked the central nervous system and who had been treated with tryparsamide, showed the efficacy of B.A.L. in combating visual complications. This action, though never spectacular, is often, but not invariably, favorable, even when the trouble has been of long standing, and when no improvement can be seen ophthalmoscopically in the lesions of the optic nerve. B.A.L. hinders the therapeutic value of the tryparsamide. The authors demonstrate this action by means of a chemical equation. Nine detailed case histories are given. (6 references.) B. T. Haessler.

Palm, Erik. The phosphate exchange between the blood and the eye. Acta ophth. Suppl. 32, pp. 1-114, 1948.

The objective of the present investigation was to follow the passage of the radioactive isotope of phosphorus, 32 P in its transit from the blood through the anterior uvea and aqueous to the lens; it was hoped that the findings might throw some light on some of the as yet unknown processes of the eye, such as the formation of aqueous and the metabolism of the lens. The use of an isotope of a substance which normally occurs in the body, in the study of vital processes, permits the making of investigations under undisturbed physiologic conditions; the data of former investigations are vitiated by the error in the results caused by an interference in these processes by the introduction of substances foreign to the organism, such as dyes, or by a disturbance in the osmotic balance through the use of abnormally high concentrations of substances nor-

mally occurring in the body. The chemistry of the phosphorus compounds that take part in the metabolism of the eye is reviewed, the experimental arrangement for the present investigation described in detail, and the results are tabulated and presented graphically. The experiments were done on living rabbits and on isolated lenses in vitro. Labeled phosphate in negligible amounts was injected intraperitoneally in rabbits, and its concentration in the blood determined at various intervals. At different times the animals were killed, their eyes extirpated, and the aqueous humor, vitreous body, anterior uvea, lens and cornea removed for chemical analysis, which revealed to what extent the phosphate in the various fractions had been replaced by the newly administered phosphate. The experiments on isolated lenses were performed by placing the lenses in a labeled phosphate bath the composition of which approximated that of aqueous. At different intervals the amount of this phosphate in the lens was determined by radioautographs. The radioactive substance darkens a photographic film and provides a rough picture of the distribution of the newly added phosphate in the lens. At the conclusion of the experiment the phosphate content was determined by trichloracetic acid extracts. The anterior and posterior lens surfaces were tested separately to determine the difference in the metabolism The data show that a short time after the intraperitoneal injection the newly introduced molecules are found inside the lens and are distributed along the path of transport to it. The slowest exchange takes place between the blood and the anterior uvea. Apparently there is a barrier to the permeability in that area. Determinations of the organic phosphate in the uvea reveal that approximately all phosphate passing through the uvea undergoes a transitory organic phase; this metabolism in the uvea lends support

to the secretory theory of the formation of aqueous. The concentration of the labeled substance is almost the same in the uvea, the aqueous, and in parts of the organic and inorganic phosphate of the lens. The variations in the phosphate content of the anterior uvea and the aqueous follow one another closely, indicating a rapid exchange between the anterior uvea and the aqueous. The author suggests that this agreement indicates that the phosphate has a similar function in these tissues, perhaps as a carrier for a flow of carbohydrates from the blood to the lens. In the lens the newly introduced phosphate is rapidly converted into an organic form. Experiments on isolated lenses indicate that the metabolisms are different in the epithelium and in the substance of the lens. The material penetrates into the lens from the experimental bath through both the anterior and posterior surfaces with about equal intensity. An esterification of the labeled phosphate takes place at both surfaces, and the newly formed hydrolysable phosphate compounds appear in about the same proportion at both surfaces. The phosphate fraction remaining after hydrolysis for seven minutes is found only at the anterior surface of the lens. Since this fraction, which contains the first compounds of phosphorylation of carbohydrates, is found only at the anterior surface of the lens, it seems probable that such a process is associated with the epithelium of the lens, perhaps in connection with an absorptive activity.

Ray K. Daily.

Remler, O. Examinations in blind people with regard to the 24 hour rhythm. Klin. Monatsbl. f. Augenh. 113: 116-137, 1948.

Th vegetative functions of the body which include temperature, ocular tension, metabolism, digestion, and the activities of the renal, the cardiovascular

and the central nervous system are subject to a 24-hour rhythm. Excretion of urine, for instance, normally has its peak in the morning, the temperature in the late afternoon. The author examined 75 blind persons, eight of whom had been blind since early childhood, in regard to the behavior of the rhythm of their vegetative functions. There was relative similarity in behavior of temperature curve, pulse, blood pressure and urine excretion. Whenever the temperature curve was normokymatic, the others were normokymatic, too. Whenever the temperature curve was inverse, the other functions usually behaved in an inverse manner. One half of the persons who became blind later in life, as well the eight who were blind early had a normal pattern of 24-hour rhythm. This group comprised mostly people who were psychologically of the cyclothymic type and were mentally well adjusted. The greater number of the other half exhibited an inverse type of rhythm. A few showed a dyskymatic curve without any special characteristic feature. Most of the men in this latter group were psychologically of the schizothymic type, which comprises the introverts, the neurotics and those living under tension. Remler points to the normal behavior of rhythm in those who became blind early as proof that the day and night change has no influence on the establishment of such rhythm, and that rhythm is of endogenous origin. He believes that the inverted rhythm in the schizothymic types is a reaction to the new sightless environment and is influenced by the mental attitude. (References.) Max Hirschfelder.

Røe, Oluf. The ganglion cells of the retina in cases of methanol poisoning in human beings and experimental animals. Acta ophth. 26:169-182, 1948.

In a clinical study reported by the author in 1946, he showed that severe acidosis is necessary for the development of amblyopia and amaurosis. Experimental work on rats failed to find any acidosis in poisoned animals. He now reports the histologic examination of 12 eyes enucleated from patients who had died of methanol poisoning and of 21 rats and rabbits killed with methanol. The human retina shows severe degenerative changes in the ganglion cells. These changes did not develop in the experimental animals. A comparison of the clinical and experimental findings thus shows that there is a fundamental difference in the action of methanol on animals and human beings. Because of the failure to verify the significance of acidosis in animals, its importance to human beings was not recognized, and the failure to treat it resulted in unnecessary loss of life and sight. Ray K. Daily.

Sorsby, A., and Ungar, J. Distribution of penicillin in the eye after injections of 1,000,000 units by the subconjunctival, retrobulbar and intramuscular routes. Brit. J. Ophth. 32:864-873, Dec., 1948.

The authors review the literature and point out that adequate intraocular therapeutic levels have been obtained with subconjunctival penicillin injections, and that higher levels can be obtained when adrenalin is used as a diluent. In the present experiments adequate therapeutic levels were obtained for 48 hours after one injection. The levels obtained with retrobulbar injection, although considerable, are distinctly lower than those obtained by subconjunctival, and the levels from intramuscular injection are lower still. Massive systemic doses showed adequate therapeutic levels intraocularly. Orwyn H. Ellis.

Vannini, A. The influence of vitamin B_1 upon corneal anesthesia. Rassegna ital. d'ottal. 17:197-205, May-June, 1948.

Experiments were conducted upon human and rabbit eyes to determine whether vitamin B_1 has any influence upon the induction of anesthesia of the cornea. The vitamin was used in solution, the tonicity of which was less, greater than, or equal to that of the aqueous. No evidence of production of anesthesia could be determined. The use of cocaine upon one cornea and cocaine plus thiamine solution in the other eye resulted in lessened anesthesia from the latter. The same was true of novocaine and other local anesthetics. Experiments upon rabbits seemed to suggest that the vitamins aid in the process of regeneration of nerve fibers.

Eugene M. Blake.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Bailliart, P. Reflections on the theories of vision. Ann. d'ocul. 181:514-534, Sept., 1948.

This contribution deals with a series of subjects which are suggested in a program for ophthalmic investigation. The first includes the specific photochemical and electrical reactions which transform light into sight, especially in the retina. Little is known of the details involved in the chemical composition or action of rhodopsin and its allied substances, the functions of the rods and cones, and the intercommunicating fibers of the retina. The relative differences in the perceptive powers of the nasal and temporal retina as well as their respective involvement in diseases such as glaucoma are also fruitful fields for investigation. The same is true of the shadows formed on the neuroepithelium by the retinal and choroidal vessels, and the complex subject of color vision. For those interested in ophthalmic problems this contribution has much of interest.

Chas. A. Bahn.

Beach, S. J. Verified refraction. J.A.M.A. 138:952-954, Nov. 27, 1948.

A refraction routine is described in which several methods of testing are used so that the results of one verify those of another. It is as simple as is possible without a sacrifice of accuracy. The history and visual acuity are taken first. A pinhole disc is next used. A preliminary noncycloplegic retinoscopy is performed and with the lenses in place, the fogging method of noncycloplegic examination is done. The use of the astigmatic dials is discussed here. The cross cylinders are then used. The vision is then corrected binocularly by the use of "cyclodamia" in which both eyes are unfogged gradually and equally. (When binocular vision is 6/60 the eyes are fogged by approximately +1.50 diopters, when the vision is 6/12 by about +0.50, and when the +0.50 D-lens is removed the 6/6 line should be read.) The near point of accommodation is then measured. Cycloplegia should be used routinely in young persons with active accommodation. The postcycloplegic examination follows the precycloplegic routine. The author recommends that the ophthalmologists learn to use these methods of refraction.

H. C. Weinberg.

Berger, A., and Monjé, M. The influence of aniseikonia upon depth-perception. Arch. f. Ophth. 148:515-528, 1948.

The authors place aniseikonic lenses in front of their eyes and study their own depth-perception with the help of the stereoeidometer. This instrument and its use have been described in a former article. When aniseikonic lenses were used which produced differences in size of the retinal images up to 17 percent, just a slight deterioration of the depth perception became noticeable. In another experiment adaptation to an artificially produced aniseikonia of 3.2 percent took place within an hour. Ernst Schmerl.

Bornschein, H. The avoidance of line voltage variations in adaptometry. Ophthalmologica 116:187-191, Sept., 1948.

The author who is engaged in exact adaptometry states his experiences with automatic devices intended to compensate for the usual and practically unavoidable line voltage variations.

Peter C. Kronfeld.

Boshoff, F. H., and Jockl, E. Errors of refraction and visual efficiency. Acta Med. Orient. 6:384-385, Dec., 1947.

Three cases of moderately high degree of myopia, one of them due to keratoconus are cited. All three patients were very proficient athletes, although they did not wear corrections for their refractive errors. One patient competed in the 1928 Olympic Games as a cricket player and was also an above average tennis player. The patient with the keratoconus was also an outstanding tennis player, and the third was an unusually good cricket player.

The authors believe the observations are worthy of record. They show that in the presence even of high degrees of uncorrected refractive errors precision performances, involving the handling of small fast-moving objects, can be carried out with a measure of efficiency exceeding that of fit healthy persons with normal refraction. Sharp definition of the retinal image can be only one of the factors which determine visual efficiency. The observations direct attention to the scope of effectiveness of the optical reception and interpretation fields in the brain and they demonstrate that athletic performances have a "total character," in which the visual functions involved become embedded in a comprehensive action pattern of the entire organism. Physical education can play an important part in ophthalmologic therapy, and the value of special eye exercises may be en-hanced by the systematic use of sport and general training.

Donald T. Hughson.

Broendstrup, Poul. The functional and anatomical differences between the nasal and temporal portions of the retina. Acta ophth. 26:351-362, 1948.

The difference between the nasal and temporal portions of the retina are reviewed and the author's own investigations to outline the anterior limits of the visual field by means of pressure phosphenes is reported. It was sought to determine whether the limits outlined by the phosphenes are identical with those charted perimetrically and campimetrically. The method consisted in making very slight pressure with a Bowman probe on the anesthetized eye. The pressure was made systematically, proceeding from the limbus backward in the horizontal, vertical, and two oblique meridians. The response to the pressure is a dark spot with a lighter center and a light halo. The distance between the limbus and the point of the most anteriorly possible phosphene was measured with a compass. Twelve persons, 8 of whom were emmetropic, were each examined twice. A visual phosphene field was constructed on the basis of the data thus obtained. Upward and downward the composite, constructed field practically coincides with the perimetrically measured visual field. Temporally, the field on the perimeter is more extensive, and on the nasal side the phosphene field. It is possible to release pressure phosphenes in a part of the peripheral field which is insensitive to light stimuli. Nasally the retina functions to the ora serrata; temporally, although the ora serrata lies 7 mm. behind the limbus the temporal phosphene boundary is 10 mm. behind the limbus, and the limit of light perception 12 mm. The determination of the anterior phosphene boundaries thus confirms the physio-

logical difference between the temporal and nasal parts of the retina. (2 figures.)
Ray K. Daily.

Cibis, P., and Mueller, H. **Studies in local adaptation with Maggiore's projection-perimeter.** Arch. f. Ophth. 148:468-489, 1948.

According to Hering local adaptation is described in the following way. When a person continues to fixate a definite point, a colored stimulus in his peripheral field slowly looses its color and finally disappears completely. The time from the beginning of the stimulation to the disappearance of the colored impression is called the specific time of local adaptation, the time from the beginning up to the disappearance of any impression is called the general time of local adaptation. The authors use Maggiore's projection-perimeter and study the local adaptation of their own visual fields. The results are presented by curves similar to Wertheim's curves for peripheral visual acuity. The authors state that with weak stimuli and for a visual field of 15 degrees, points on different meridians but of the same distance from the retinal point of fixation are functionally equivalent. With stronger stimuli the corresponding points of the various meridians show pronounced differences with respect to functional value.
Ernst Schmerl.

Fabre, P. **Exact determination of axes of astigmatism by alignment of focal lines.** Arch. d'ophth. 8:495-505, 1948.

The author describes a subjective method for the determination of the axes of astigmatism. He notes that the principal meridians in an astigmatic eye are perpendicular to the corresponding focal lines. Certain subjects are ametropic for one of the foci. For example, they see, without accommodating, a star in the form of a straight line. The author's method gives to the subject a method of describing a focal line which he perceives and allows him to indicate exactly the azimuths of the principal meridians of his eye. For the test two types of apparatus are necessary. The first consists of a testing lens of variable power and the second of an apparatus containing a central luminous point around which can revolve a second luminous point. This second luminous point gives a focal line parallel to the first in the field of the test lenses. The subject must be able to move the apparatus in such a way that the two focal lines lie end to end. The alignment of these two images coincides with the direction of the focal lines and the axis of astigmatism. The method by which the apparatus works is described in full detail and is illustrated with drawings. The author claims that this is a precise means of determining the axes of astigmatism and that it also gives information as to the presence or absence of aberration.
Phillips Thygeson.

Granit, R. **The off/on-ratio of the on-off-elements in the mammalian eye.** Brit. J. Ophth. 32:550-554, Sept., 1948.

Some aspects of the micro-electrode work done with the retina of the dark adapted decerebrate cat are reported. The retinal elements are on-elements, off-elements and on-off-elements. The on-elements respond to light with a stream of impulses, the off-elements with a discharge at the cessation of illumination and the on-off-elements combine these two properties. For the discrimination of light and colors the on-off-elements predominate, and were here found to be fully 80 percent of all the elements. There was a tremendous variation in the ratio of the on and off components of the on-off-element (from 1,000 to 0.001) but the purpose of such variation is not known. In general, it is believed that it improves discrimination. It is highly probable that the slow electrical changes induced by light de-

termine the off-on ratio because electrical stimulation strongly affects this relationship. Anatomical organization is probably not fixed and unchangeable; instead the "boutons" at the synapses expand or contract so as to alter the contact surface and thus alter the function.

Morris Kaplan.

Guenther, G. An instrument for the objective determination of the visual acuity. Arch. f. Ophth. 148:430-442, 1948.

Optokinetic nystagmus serves as a basis for the objective determination of the visual acuity. A frame 15 by 15 cm. is placed in front of the examined person at variable distances of one to four meters. Behind the frame a moving strip of paper presents checkerboard designs with squares 2, 5 and 10 mm. in diameter. With varying distances and varying sizes of the designs a variable visual stimulus is offered. When the stimulus passes the threshold and the moving squares can be discriminated as such, optokinetic nystagmus occurs. The normal minimum separabile determined in this way was found to equal two minutes. Ernst Schmerl.

Györffy, A., and Kahán, A. Tolerance of contact lenses. Ophthalmologica 116: 1-6, July, 1948.

The wearing time of contact lenses was significantly lengthened in nine out of fifteen patients by the instillation of a mixture of 0.5-percent antistine and 0.025-percent privine before the insertion of the lenses. The history and theory of the histamine antagonists is reviewed.

Peter C. Kronfeld.

Hartridge, H., and Thomson, L. C. Methods of investigating eye movements. Brit. J. Ophth. 32:581-591, Sept., 1948.

There is controversy concerning the normal existence of rapid oscillations of the eye during fixation. The precision of measurement of the movement must be

within 6 seconds of arc, which corresponds to a cone unit of size. In this article a method is described in which a point of light reflected from the cornea is photographed by means of a camera mounted on a small bench which is held in the mouth of the subject. The movie film used is examined, a single frame at a time, under a microscope. (5 figures.)

Morris Kaplan.

Hecht, S., Hendley, C. D., Ross, S., and Richmond, P. N. The effect of exposure to sunlight on night vision. Am. J. Ophth. 31:1573-1580, Dec., 1948. (3 tables, 4 figures, 10 references.)

Katz, J. Supplementary observations concerning night myopia. Klin. Monatsbl. f. Augenh. 113:170-172, 1948.

In this short article the possible practical implications of the fact that the sensitivity of the human eye varies for various wave length are discussed. There is a difference of 0.4 diopters between the maxima of the sensitivity curves during day vision and those during night vision. This would mean that an emmetropic or fully corrected eye becomes myopic (0.4 diopter) during twilight vision. Experiments in this field are suggested, especially as the correction of optical instruments and of spectacles for night use would be of practical interest. (References.) Max Hirschfelder.

Langer, F. My experience with the Cobalt lamp of Roessler. Klin. Monatsbl. f. Augenh. 110:26-32, Jan.-Feb., 1944.

The use of the Cobalt lamp of Roessler is recommended for subjective refraction. The test is simple, easy for the patient, fast and quite reliable. The patient is seated 175 cm. from the lamp. A blue disc with red margin indicates hyperopia, a red disc with blue margin myopia. Spherical lenses are put in front of the eye until the color arrangement is reversed. Mixed

astigmatism is characterized by a blue line crossed by a red line. The blue line corresponds to the myopic meridian, the red line to the hyperopic. Plus cylinders are given until the astigmatism is corrected and the eye presents a simple myopia. The same cross appears when in myopic or hyperopic astigmatism one meridian is corrected by spherical plus or minus lenses until the interfocal space is reached. By changing the distance between lamp and patient from 175 cm. to 39 cm. the amount of accommodation is tested. Patients with asthenopia exhibit an excess of accommodation. The refraction is completed by having the patient read the Snellen chart. George Brown.

Lebensohn, J. E. **Practical problems pertaining to presbyopia.** Am. J. Ophth. 32:22-30, Jan., 1949. (3 figures, 3 tables.)

Letchworth, T. W. **Stereoscopic vision in monocular aphakia.** Tr. Ophth. Soc. U. Kingdom 66:261-262, 1946.

The author describes his own experience with monocular aphakia. His right eye had 6/12 vision with −1.00 cylinder and the left 6/6 with a +6 sphere combined with +4.00 cylinder at 160°. He was able to get stereoscopic vision through the optical center of the cataract glass only if the head was not moved. The area was gradually increased by sitting before a tangent scale and moving the eyes up, down and laterally. A prism controlled bifocal was not quite so comfortable and he advises the Franklin type. He suggests occluding the periphery of one lens by an opaque material or ground glass and leaving only the central portions free for binocular vision. Beulah Cushman.

Lorenz, R. **Aniseikonia. A simple method for measuring it.** Klin. Monatsbl. f. Augenh. 110:16-25, Jan.-Feb., 1944.

Two pictures, one green and the other red, are displayed on a stereoscope. In aniseikonia the binocular picture is slanted. The percentage of aniseikonia is figured from the angle of slanting.

One hundred fifty-four persons were tested. None of the emmetropic patients had aniseikonia. Therefore, the author questions the existence of a functional aniseikonia. In the myopic group aniseikonia was found only when there was a difference in the refraction. The aniseikonia disappeared when normal binocular vision was obtained with full correction, but persisted when full correction was impossible. In hyperopia aniseikonia was the more frequent and the more marked the greater the difference between the two eyes and the poorer the vision. However, there is no direct proportion between the amount of aniseikonia and the error of refraction. In practice aniseikonia is not too important. It is most frequent and most marked in patients who have poor stereoscopic vision and who, therefore, are not greatly bothered by the aniseikonia. In persons with well developed stereoscopic vision aniseikonia is comparatively infrequent or small. When there is considerable difference between the eyes the patient usually uses one eye only. Such patients, when fully corrected and with good vision of both eyes, complain about dizziness and slanting due to the now apparent aniseikonia. In hyperopia poor vision of one eye or poor stereoscopic vision often prevent the appearance of aniseikonia. There may be complete suppression of one eye in order to avoid aniseikonia. George Brown.

Marchesani, O., and Schober, H. **The action of lactoflavine upon the color vision.** Arch. f. Ophth. 148:420-429, 1948.

After intravenous or intramuscular injections of 10 mg. of lactoflavine the authors found a significant enlargement

of the visual fields for red in 47 persons.
Ernst Schmerl.

Melanowski, W. H. **The simple method of calculation of the optic system in high anisometropia.** Tr. Ophth. Soc. U. Kingdom 66:263-264, 1946.

Formulas are given for the calculation of the change in size of image made by telescopic spectacles for distance and near. Beulah Cushman.

Miles, P. W. **Refractive treatment of asthenopia.** Am. J. Ophth. 32:111-121, Jan., 1949.

Pacalin, G. **Physiologic diplopia.** Ann. d'ocul. 181:604-612, Oct., 1948.

Diplopia begins with the stimulation of noncorresponding retinal areas. Binocular integration as well as projection, or fusion, are largely accomplished in the peri- and para-striate areas that Brodman has numbered 18 and 19. The subsequent course of binocular visuomotor impulses is not accurately known. Memory impressions, however, largely determine our interpretations of size, form and distance. The well-known steps of Schroeder demonstrate that visual interpretation is not technically correct. Chas. A. Bahn.

Papagno, M. **Acetylcholine effective in a case of spasm of accommodation.** Boll. d'ocul. 27:464-470, July, 1948.

A 17-year-old girl with dysmenorrhea associated with headache, abdominal pain, cardiac palpitations, vomiting, vertigo, and diarrhoea since she was 14, noticed a blurred vision for distance during her two last menstrual periods. Examination revealed normal eyes and retinoscopic refraction of three diopters of miopia. With a −3.00 D. lens, she could read 10/10. Intramuscular acetylcholin injection immediately reduced the spasm from three diopters to one and soon after

to emmetropia. The next menstrual period was accompanied by a slightly milder spasm of accommodation and again relieved by intramuscular acetylcholin.
K. W. Ascher.

Sauter, H. **Origin and observation of the shadows seen in sciascopy.** Arch. f. Ophth. 148:529-543, 1948.

This is a presentation for the practitioner and the teacher of what is known about the phenomena of sciascopy.
Ernst Schmerl.

Siebeck, R. **The form-threshold problem of optical stimuli.** Arch. f. Ophth. 148:443-458, 1948.

If two figures, say a circle and an equilateral triangle of the same area and color, are compared with each other, the triangle appears to be larger than the circle, whereas the color of the circle appears to be more saturated than that of the triangle. Starting from these observations, the author studied the form-threshold problem. He finds a definite relationship between shape and threshold values of the offered stimuli. The field which surrounds stimuli of varying sizes but similar shapes becomes more important the smaller the objects are. This is probably due to the increasing ratio of circumference to area. Unavoidable ocular movements cause differences in local retinal adaptation with different stimuli of the same area but of different shapes. Because of this factor a quantitative correlation between form and threshold cannot be satisfactorily presented. However, it is safe to say the shape of a visual stimulus affects the threshold sensitivity, although the size of the object is of much greater importance. Ernst Schmerl.

Sinclair, A. H. H. **Developmental aphasia.** Brit. J. Ophth. 32:522-531, Sept., 1948.

Developmental aphasia is a failure of visual comprehension probably caused by delayed development of unilateral hemispherical dominance. Letters and words are seen but are not recognised but aural perception remains unaffected and is of great use to the affected children. The condition may be mild and transitory or severe and difficult to overcome. There is a natural tendency to recover which increases progressively with the child's development and education.

The important diagnostic criterion is the brightness of the child in other processes of learning. He can easily read numbers, music or pictures and learns easily by ear but cannot appreciate the printed word. There is most probably an absence or a delay in the myelinization of the neurons going to the exteroceptive centers in the cerebral cortex. Treatment consists of meticulous training by parents and teachers and almost always brings good results.

In the Edinburgh Primary Schools about 10 percent of the children had developmental aphasia, of whom half recovered in the ordinary course of education and half required special treatment.   Morris Kaplan.

Starke, H. **Changes of corneal astigmatism following instillations of eye drops.** Arch. f. Ophth. 148:544-554, 1948.

The author used Hartinger's ophthalmometer as manufactured by Zeiss to measure the radii of corneal curvature in about 40 persons. The instrument permits a determination of the radius with an error of not more than ±0.01 mm. The radii of normal corneas of younger people show changes of several hundredths of a millimeter caused by variation of the ocular tension and the pressure of the eyelids. With instillations of atropine corneal astigmatism usually decreases, with pilocarpine it increases.   Ernst Schmerl.

Tschermak-Seysenegg, A. **One hundred years of "Haidinger brushes."** Klin. Monastbl. f. Augenh. 113:167-169, 1948.

One hundred years ago the mineralogist Haidinger discovered the appearance of a figure like a double-sheaf in polarized light, afterward called "Haidinger's bundles or brushes." The cause for this phenomenon which appears only in light of short wave length is the presence of doubly refracting fiber elements in the macular region of the human retina. The phenomenon serves also as proof for the polarization of the light of the sky which is vertical to the apparent course of the sun. Using doubly refracting prisms before each eye one can use the phenomenon of these brushes for tests of binocular vision. (References.)
                    Max Hirschfelder.

Weston, H. C. **The effect of age and illumination upon visual performance with close sights.** Brit. J. Ophth. 32:645-653, Sept., 1948.

Twelve patients of different ages were studied while performing a series of special visual tasks that involved the perception of fairly small detail. Each task was repeated with different degrees of illumination. Each subject had previously been refracted and fitted with necessary glasses and all read fine print with their glasses. They were arranged in five age groups, from 24 to 48 years. The task consisted in finding all the similarly placed gaps in a series of Landolt rings and results were recorded as time per correct ring. Although age had no effect on visual acuity, there was definite and regular effect of age on visual efficiency. The rate of decline is fairly consistent and amounts to about five percent per annum. The effect of illumination changed greatly with age; a change from the lowest to the highest illumination tried increased the performance of the

youngest subjects only 18 percent but it increased the performance of the oldest subjects 400 percent. In addition, it was noted that with the lowest illumination and the finest visual task, the performance of the 24-year-olds was as good as that of subjects of 47 years with the easiest visual task and the highest illumination. Morris Kaplan.

5

DIAGNOSIS AND THERAPY

Albright, A. A. An economical screen. Am. J. Ophth. 32:126, Jan., 1949. (1 figure.)

Anthony, D. H., and Fisher, D. F. Evaluation of X-ray diagnosis in ophthalmology, rhinology and otolaryngology. Mississippi Doctor 26:79-89, Sept., 1948.

The authors indicate the conditions in which X-ray diagnosis is helpful and make it clear that the ophthalmologist is for the most part quite unaware of the not inconsiderable help that the X-ray can give him. F. H. Haessler.

Atkinson, W. S. Local anesthesia in ophthalmology. Am. J. Ophth. 31:1607-1618, Dec., 1948. (17 figures, 13 references.)

Berens, Conrad. Lens loop with serrations, longitudinal wires and flexible shaft. Am. J. Ophth. 32:122-123, Jan., 1949. (3 figures.)

Carlevaro, Gianfranco. A clinical form for the functional examination of the eye. Ann. di ottal e clin. ocul. 73:442-446, July, 1947.

A four-page blank form is described and recommended for use in making a detailed systematic examination of the ocular functions. The various tests are outlined. (35 references.)

Harry K. Messenger.

Durham, D. G. The new ocular implants. Am. J. Ophth. 32:79-89, Jan., 1949. (12 figures.)

Engel, Sam. A new model contact lens. For observation of the eyeground and of the posterior part of the vitreous with the slitlamp. Am. J. Ophth. 32:123-125, Jan., 1949. (2 figures.)

Filatov, V. P. Some considerations on therapy with tissues. Arq. brasil de oftal. 11:103-121, 1948.

This is a Portuguese translation from the author's paper in the Russian Vrachnoe Delo, 1945, dealing with the author's experiments in subconjunctival insertion of fragments of tissue from other parts of the body, for the purpose of producing a beneficial reaction in cases of uveitis and other conditions. W. H. Crisp.

Foddis, Antonio. A simple device for adapting the Zeiss stereoscopic camera (for photography of the anterior segment) to photokeratoscopy. Ann. di ottal. e clin. ocul. 73:332-335, June, 1947.

A device embodying a Placido's keratoscopic disk is described. For ordinary keratoscopy Foddis uses a Placido's disk that has two openings in place of the usual central one so that he can study the keratoscopic reflex binocularly. (3 figures.) Harry K. Messenger.

Fried, Carl. Roentgen and radium therapy in ophthalmology. Ophth. ibero am. 9:323-344 (Portuguese), 345-366 (English), 1948.

The results briefly described by the author relate to 28 cases of inflammation of bacterial and 49 of nonbacterial origin, and to 23 of malignant and 5 of benign neoplasms. All patients were treated in the São Francisco de Assis Institute (Brazil). Rather diffuse claims are made for benefit in the inflammatory diseases

and in painful blind glaucomatous eyes. Brief comments are made as to papers published by other authors.

W. H. Crisp.

Gut, A. Indirect illumination in direct ophthalmoscopy. Ophthalmologica 116: 79-85, Aug., 1948.

The conventional method of direct ophthalmoscopy utilizes diffusely reflected light. Indirect illumination is obtained if, by means of an adjustable condenser, the borders of the directly illuminated portion of the retina are sharply focused. The portion of the fundus adjacent to the directly illuminated area can now be examined in indirect light. The method is especially revealing in diseases of the macula. In such cases the light source or its equivalent (the diaphragm of the ophthalmoscope) is brought to a sharp focus below or temporally to the macula while the latter is studied for minute pathologic changes. Six instructive cases are described and depicted. An ophthalmoscope with variable angle between the axes of the illuminating and the observation system is especially suitable for examination in indirect light. The author's main point is that this simple and widely known method is not used as much as it deserves.

Peter C. Kronfeld.

Landers, P. H. Simplified external eye photography. Am. J. Ophth. 31:1624-1625, Dec., 1948. (3 figures, 5 references.)

Lijó Pavía, J. Papillary edema; comparative study with sodium light. Rev. oto-neuro-oftal. 23:45-51, July-Sept., 1948.

Two cases of papillary edema are presented, one due to malignant arterial hypertension and the other a sequel of hypophyseal tumor. The fundus was studied in ordinary white light, red-free light, and sodium light. With yellow light,

in the case of malignant neuroretinitis, the vessels were well demarcated, superficial precapillaries and peripapillary lipoidal deposits were visible and the macula was more precise, though the fovea could not be delimited. In the second case, too, sodium light ophthalmoscopy resulted in finer visualization of the vascular system and the exudative deposits. (5 figures.)

Edward Saskin.

Morgan, O. G. The value of vitamins in ophthalmology. Medical Press 220:385-389, Nov. 10, 1948.

Many serious diseases of the eyes are associated with poor general health. It is usually worth while to supplement local treatment with vitamins B and C. The outstanding effect of vitamin A deficiency is xerosis and night blindness. Retrobulbar neuritis and increased corneal vascularization may be due to thiamine deficiency. Rosacea keratitis responds to riboflavin therapy. Ascorbic acid has been used in corneal ulcer and keratitis of various types with satisfactory results. Vitamin D regulates calcium and phosphorus metabolism. Vitamin D has been suggested in myopia in the child. Rutin or vitamin D decreases capillary fragility. It neutralizes the effect of potassium thiocyanate in hypertension. I. E. Gaynon.

Pérez Toril, Francisco. Penicillin in ocular diseases. Arch. Soc. oftal. hispanoam. 8:833-838, Aug., 1948.

From his experience with the use of penicillin in 87 cases of ocular disease, Pérez concludes that penicillin is of great value in ophthalmology. Its employment is not necessary in diseases easily amenable to other forms of therapy but should be used promptly when irreparable damage seems immanent. Intramuscular and intravenous administration is adequate for extraocular lesions but intraocular lesions require subconjunctival, intra-

vitreal, and intracameral administration in addition to the use of collyria, ointments and baths. Agents for local application should contain not less than 500 units and not more than 10,000 units per cc. of solution. The early use of penicillin has modified the grave prognosis formerly associated with such diseases as gonorrheal ophthalmia and serpigenous ulcer.

Ray K. Daily.

Ploman, K. G. Examination of the media of the eye with a plane mirror combined with a loupe, in severe myopia. An improvement in the method. Acta ophth. 26:213-214, 1948.

Ploman found that improved visibility is obtained by correcting the myopia with a minus lens held in front of the eye.

Ray K. Daily.

Rosengren, Bengt. A method of sciascopy with the electric ophthalmoscope. Acta ophth. 26:215-221, 1948.

The technique of sciascopy with the electric ophthalmoscope is described in detail. The advantages are the possibility of sciascopy with an undilated or constricted pupil, and the rapidity of the procedure. (2 figures.) Ray K. Daily.

Saint-Martin, R. Tissue therapy in complicated myopia. Ann. d'ocul. 181: 578-587, Oct., 1948.

Filatov's technique for placental subconjunctival implants and intramuscular infiltrate injections was closely followed. In the use of the former, 5 inclusions at 8 to 15-day intervals were made, of the latter 30 injections at 2-day intervals were made. In a series of 30 patients, all received both types of treatment. There was definite subjective improvement in 8, appreciable improvement in 14, doubtful improvement in 6, and failures in 2. The author suggests that this treatment

be tried experimentally more extensively.

Chas. A. Bahn.

Siboni, B. The virtues of sulfanilamide powder in ophthalmology. Ann. d'ocul. 181:629-644, Oct., 1948.

In North Africa sulfanilamide powder has numerous advantages over solutions or ointments in a wide range of ophthalmic conditions such as exogenous infectious and traumatic diseases of the lid, conjunctiva, sclera and iris, and bacterial, viral, and rickettsial infections, such as trachoma. Chas. A. Bahn.

Sykowski, P., and Lawrence, W. Streptomycin in ophthalmomiliary tuberculosis. Am. J. Ophth. 31:1629, Dec., 1948.

Vannas, Mauno. The diagnosis of intraocular tumors and foreign bodies by means of anterior pupillary transillumination. Acta ophth. 26:125-134, 1948.

The limitations of posterior bloodless diascleral transillumination and of posterior transillumination with the transilluminator introduced far back through a conjunctival incision are discussed. The main source of error is the uncertainty of the position of the transilluminator in relation to the tumor. In addition, in diascleral transillumination the pupil becomes illuminated only if the eye of the examiner is within the light cone whose point is formed by the point of the lamp and whose aperture is the pupil. If the examiner moves his head, or the patient his eye the iris comes between the lamp and the eye of the examiner, and the pupillary reflex is complicated by two shadows, that of the tumor, and that of the iris. Transillumination through the pupil with the transilluminator applied directly to the cornea is superior. Also, with this method, experiments in transillumination on enucleated eyeballs demonstrated that shifting the point of light

from the center of the cornea over the iris greatly reduces the transillumination of the sclera. Pupillary transillumination is of value also for localizing purposes in cases of foreign bodies in the wall of the eyeball or its vicinity. Foreign bodies in the wall of the eyeball or in contact with the inner surface of the retina are recognized by distinct shadows; when the experimental object is transferred inward into the virtreous its shadow becomes less distinct. Clinical case reports illustrate the superiority of pupillary over diascleral transillumination.   Ray K. Daily.

Velhagen, K. **Technical arrangement for the dark adaptation test.** Klin. Monatsbl. f. Augenh. 113:170, 1948.

The author recommends a lightproof cabinet which can be arranged in the corner of any room. The patient sits within the cabinet and observes the adaptometer, which is built within the side of the cabinet and can be regulated from the outside. Such an arrangement leaves the examiner free for other duties during the time-consuming test.

           Max Hirschfelder.

6

OCULAR MOTILITY

Abraham, S. V. **A new classification of nonparalytic strabismus** Am. J. Ophth. 32:93-98, Jan., 1949. (1 table, 19 references.)

Anderson, J. R. **Sidelights on the inferior oblique muscle.** Brit. J. Ophth. 32: 653-667, Sept., 1948.   -

This detailed discussion of the inferior oblique muscle emphasizes the need of a knowledge of its anatomy and physiology in adequate diagnosis and selection of treatment of its disorders. Its insertion into the sclera is oblique and about 10 mm. in length which lies in and below the horizontal meridian. It is under the external rectus, its anterior end being 2 mm. above the lower level and almost 10 mm. behind the insertion of the external rectus. Its insertion extends to a point 4 mm. from the fovea. Its function is considered to be 56.1-percent extorsion and 42.9-percent elevation. The very early anatomists called the inferior obliques the amatorii or lovers' muscles since rolling of the eyes were signs of affection.

Often in diagnosis the malfunction of a muscle is ascribed to overaction, underaction or palsy of the inferior oblique when actually the contralateral or homolateral antagonist or yoke muscle is defective. The surgeon must be very careful to correct large horizontal errors before he deals with most vertical defects, as the latter may then become only negligible sources of disfunction. (38 references.)   Morris Kaplan.

Angius, Tullio. **The treatment of the heterophorias.** Rassegna ital. d'ottal. 17: 190-196, May-June, 1948.

While employing acetylcholine in the treatment of chorioretinitis and accommodative spasm, the writer noted a regression of the concomitant heterophorias. The subjects reported upon in the article were in good health and were emmetropic. The muscle balance was studied by various methods, among them with Maddox rod, stereoscope and prisms. The subjects were divided into five groups according to the medication administered. The first group received daily intramuscular injections of acetylcholine bromide, the second prostigmin intramuscularly, the third intravenous vitamin B_1, the fourth d-phenylisopropylmetilamine chloride, and the fifth group vitamin A, 100,000 units and D 25,000 units by mouth.

It was observed that fatigue, even though not excessive, caused an aggravation of the heterophoria, especially in older subjects. Heterophoria was often associated with spastic conditions else-

where, in the colon, for example. Excellent results were obtained in the patients receiving prostigmin and those getting vitamin B_1, either alone or combined. Esophorias showed a greater tendency to recur than other phorias. The treatment was more effective than orthoptic measures, but in the more severe cases a combination of the two yielded better results.

Eugene M. Blake.

Apin, K. Exercises in strabismus. Klin. Monatsbl. f. Augenh. 110:62-67, Jan.-Feb., 1944.

The first important step is the measurement of refraction after instillation of atropine for three successive days. Full correction with the eyes still under the action of atropine is indicated and permanent occlusion, if amblyopia of one eye is found. Next the strabismus should be eliminated, if necessary by surgery. Exercises are kept up for years in order to reestablish binocular and stereoscopic vision.

George Brown.

Da Pozzo, Ezio. A case of post-traumatic synkinesia oculo-oculare. Giorn. ital. di oftal. 1:265-273, May-June, 1948.

In a girl cranial trauma initiated a synkinesia oculo-oculare (blepharoptosis of one side associated with contraction of the contralateral medial rectus). The author discusses briefly the hypotheses advanced in explanation of congenital and acquired synkinesis with involvement of the levator palpebrae. He concludes that none solves the problem of the pathogenesis of this picture.

Francis P. Guida.

Gasteiger, H. Rare complications after surgery for strabismus. Klin. Monatsbl. f. Augenh. 113:152-157, 1948.

Postoperative complications after surgery for strabismus are rare. Three cases in which severe inflammation and necrosis of the sclera developed in the operative area after tenotomy or advancement are described. In one a deep keratitis also developed but it finally healed with severe loss of vision due to the scar. One of the three eyes had to be enucleated, whereas the other two could be saved through removal of the necrotic conjunctival and scleral tissue and covering of the defect by a flap of conjunctiva and Tenon's capsule. The author believes that these complications are nutritional and due to disturbances of the blood supply. He points out that the anterior ciliary arteries enter the bulbus in this region and that they suffer damage during surgery. The other possibility is infection of the operative field. Lowered resistance in the patients may have contributed to the abnormal course. (References.)

Max Hirschfelder.

Hartmann, E. Physiology of ocular motility, heterophoria and strabismus. Ann. d'ocul. 181:449-462. Aug., 1948.

Ocular motility, normal and abnormal, involves coördinated, binocular, three-dimensional alignment as well as motion. As practically all ocular motility is subconscious, its quantity and quality are governed by numerous reflexes in which the eyes play a more or less dominant part. For example, postural reflexes include both static and dynamic types. The former involves the "righting" and altitudinal reflexes which are primarily located below the cerebral peduncles. Static-kinetic reflexes involve binocular alignment associated with head rotation. They are involved in nystagmus following especially rapid head rotation and are primarily located in the semicircular canals and vestibular nuclei. Retinal reflexes form part of the sensorial reflex mechanism which also includes smell, hearing, touch and taste and which is an important factor in reflex ocular motility. The visual reflexes involved in binocular alignment and motility include the fol-

lowing: "righting," direction, compensating, fixation, retinal orientation and convergence reflexes. The convergence reflex, the most recently acquired, is most frequently involved in strabismus. It is essentially a conditioned reflex and the others are true or unconditioned. The 45-degree deviation of the axes of the orbits from parallelism results in differences of alignment which are compensated in the phorias but not in the tropias. Muscular anomalies alone, as in the Duane syndrome, seldom play a dominant part in strabismus. It usually is a manifestation of imperfectly coördinated reflexes which produce disalignments. All treatment, surgical and other, should be designed primarily to coördinate faulty reflexes rather than increase or decrease the power of a muscle. (13 references.)

Chas. A. Bahn.

Law, F. W. A point for consideration in the use of the stereoscope. Brit. J. Ophth. 32:639-644, Sept., 1948.

Heretofore the answer to the question "what happens to the inclination of the visual axes on moving the stereogram in a stereoscope towards or away from the observer?" has simply been guessed at. From studies involving the interocular distance, the distance of the card from the viewer, the width of the stereogram and the strength of the lenses in the stereoscope, the author found that the instrument could be used for exercise either of convergence or divergence but to be successful the examiner must understand the principles exactly. With this in view, tables are presented to keep the necessary data perspicuous.

Morris Kaplan.

Riise, Per. Surgical treatment of vertical squint. Acta ophth. 26:153-165, 1948.

The field of surgery of the vertical and oblique muscles has widened. Elschnig's book on surgery in 1922 speaks of these

operations as rare. In Thiel's recent book the surgical indication is a squint of more than 5 degrees. The results of surgery for vertical strabismus are shown by case reports illustrated with photographs and diplopia charts. (31 figures.)

Ray K. Daily.

Spaeth, E. B. The vertical element in the causation of so-called horizontal concomitant strabismus. Surgical principles for the vertical corrections. Am. J. Ophth. 31:1553-1566, Dec., 1948. (21 figures.)

Toth, Zoltan. Forceps in resection of a muscle. Klin. Monatsbl. f. Augenh. 110: 67-68, Jan.-Feb., 1944.

The use of a forceps in advancement or resection of a muscle has many disadvantages. The instrument is too big for the small field and the trauma to the muscle is considerable. A simple bridle suture through the muscle before the insertion is cut serves the same purpose and is technically preferable.

George Brown.

Weekers, L., and Weekers, R. A monocular operation for severe divergent strabismus. Ann. d'ocul. 181:493-499, Aug., 1948.

A provisional attachment is made of the internal rectus tendon across the cornea to the external rectus tendon. In very high degrees of strabismus tenotomy of the external rectus is also performed. In strongly amblyopic divergent eyes, this operation is recommended from a cosmetic point of view as simple and safe. Anesthesia includes local instillation and retrobulbar injection, without conjunctival infiltration. The external rectus muscle is raised with a forceps and a double thread is passed between the sclera and the muscle immediately behind the tendon, forming a strong support for traction. The conjunctiva over the internal rectus is then dissected, sutured,

and sectioned. The conjunctiva and tendon are placed across the cornea and are sutured to the tendon of the external rectus. Both sutures are now united. The conjunctiva and advanced internal rectus tendon cover the cornea. After seven days the sutures and the tongue of conjunctiva are removed.

The advantages of this procedure are its simplicity and safety in all types of divergent strabismus of 25 to 35 degrees or more. (9 references.) Chas. A. Bahn.

Wilhelm, G. **Treatment of amblyopia.** Klin. Monatsbl. f. Augenh. 110:56-62, Jan.-Feb., 1944.

In 11 children, 2 to 10 years old, with strabismus and amblyopia of one eye, improvement followed permanent occlusion in 90 percent in two to four weeks. Normal vision was achieved in 11 percent of those whose initial vision was 5/10, in 70 percent with vision of 5/25 and in 34 percent with less than 5/50. The necessary time of occlusion was independent of the age, but longer with lower initial vision. Treatment of amblyopia should be started before the sixth year, but is possible after this age. In 42 percent the amblyopia recurred, especially in children of two to four years. After repeated occlusion, lasting results were eventually attained in 85 percent of patients. Subsequent amblyopia of the occluded eye occurred in 46 percent of the two to four year old children, never after the sixth year. In 46 percent the strabismus disappeared after elimination of the amblyopia and prescription of glasses.

George Brown.

7

CONJUNCTIVA, CORNEA, SCLERA

Alvarez Alvarez, Abundio. **The therapy of herpetic ocular diseases.** Arch. Soc. oftal. hispano-am. 8:687-698. July, 1948.

The literature on the numerous thera-

peutic agents used in these conditions is reviewed, and three cases of herpetic keratitis treated with applications of an alcoholic solution of iodine and potassium iodide are reported. One case of herpes zoster ophthalmicus responded to the administration of chromesulfur.

Ray K. Daily.

Anderson, Banks. **Corneal and conjunctival pigmentation among workers engaged in manufacture of hydroquinone.** Arch. of Ophth. 38:812-826, Dec., 1947.

Observations are presented on a group of workers employed in the manufacture of quinone and hydroquinone in whom certain characteristic lesions of the cornea and conjunctiva have developed. These lesions consist of a variable degree of pigmentation of the interpalpebral portions of the conjunctiva and cornea, proportional to length of employment and to age and corneal changes. These corneal changes consist in pitting and erosion of the corneal surface, thinning of the cornea, development of irregular pigmented or staining areas, wrinkling or modification of Descemet's membrane and, possibly, keratoconus. The changes are apparently reversible up to a certain point in that conjunctival staining may disappear. The corneal stain is more permanent. The lesion could not be produced in albino rabbits. While the chemical is said not to belong to the carcinogenic group, some of the lesions resemble Bowen's disease. The development of a frank malignant growth is not beyond the bounds of probability. John C. Long.

Bakker, A. **A myxo-haemangioma simplex of the conjunctiva bulbi.** Brit. J. Ophth. 32:485-88, Aug., 1948.

A pedunculated hemangioma of the conjunctiva under microscopic examination showed intensive growth with mitotic figures and myxomatous degenera-

tion. There has been no recurrence eight months after simple excision.

Orwyn H. Ellis.

Blodi, F. A case of a horizontal Krukenberg splindle. Acta. ophth. 26:373-378, 1948.

A case of bilateral horizontal Krukenberg spindle is reported in a woman 76 years old. The spindle was demarcated by a glassy line situated in the posterior corneal layers and visible only in indirect light. There was no other abnormality in the eyes. The etiology is believed to be a change in Descemet's membrane, limited by the glassy line. Although the change could not be demonstrated biomicroscopically it is believed that colloidochemical changes in the endothelial cells could account for the deposit of pigment on the posterior corneal surface.

Ray K. Daily.

Bonavolontà, Aldo. Biomicroscopic examination of the limbus as a basis for a new classification of the various stages of trachoma. Giorn. ital. di oftal. 1:207-226, May-June, 1948.

The author studied the corneal manifestations said to be pathognomonic of trachoma. These manifestations may be grouped into quite variable complex pictures. Several groups are of very little interest, namely the sign of the crescent, the kaleidoscopic sign, and the disappearance of the primary sulcus; others are of definite value, namely the accelerated development of the terminal limbal loops, and the superficial neovascularization with the characteristic accompanying infiltration. Of greatest value are the nodules and their residua. He points out the value of biomicroscopic examination of the limbus to reveal and evaluate these manifestations and to establish the diagnosis of trachoma from its incipiency to its end. He noted several cases in stage 1 and 2 with corneal signs and others without. It seems important to him to establish a classification based on the biomicroscopic findings which takes into consideration the conjunctival and corneal picture. He suggests one in which T_a includes T_1 and T_2 of MacCallan, without corneal signs of trachoma, T_b consists of those cases in T_1 and T_2 which show corneal signs, and T_c consists of cases in T_3 and those in T_4 in which examination of the cornea shows active trachoma. The fully evolved trachoma, both corneal and conjunctival is known as T_d.

Francis P. Guida.

Brand, E. A new quick staining procedure of the inclusion bodies of trachoma. Orvosi Hetilap 26:405-406, 1948.

Report on a new, simple and quick procedure lending itself to demonstration of the inclusion bodies of trachoma. A 1-percent solution of toluidine blue stains the inclusion bodies with due contrast in one-half minute.

Gyula Lugossy.

Brand, E. A new quick staining method for trachoma inclusions. Ophthalmologica 116:61-63, July, 1948.

The material is spread on a clean slide, allowed to dry at room temperature, fixed in absolute alcohol for ½ minute, dried again and stained with a 1-percent aqueous solution of toluidine blue for two minutes. The author believes that the trachoma inclusions are actually a part of the Golgi network altered by the trachoma virus.

Peter C. Kronfeld.

Busacca, A. Certain corneal diseases observed under the influence of penicillin therapy. Ophthalmologica 116:43-50, July, 1948.

The author describes his experiences with penicillin applied topically in diseases of the lids, conjunctiva and cornea.

He reports good results with penicillin injections (5,000 units per cc.) into the lid in cases of severe chronic blepharitis. He uses the same technique for hordeola. The course of a large portion of infectious ulcers of the cornea is rapidly and beneficially changed by repeated subconjunctival injections of penicillin. Specifically, he describes two types of keratitis which have responded surprisingly well to subconjunctival penicillin therapy. He proposes the term "keratitis epithelialis desquamativa" for the first type which is characterized by epithelial infiltration and ulceration in the form of small dots arranged in lines or coalescing into larger spots with irregular (geographic) borders. The disease takes a chronic course and may be resistant to all conventional forms of therapy. Busacca has cured two such cases with daily subconjunctival injections of penicillin continued for approximately four weeks. For the other type of keratitis which belongs to the phlyctenular group, Busacca proposes the term "keratitis with polymorphous efflorescenses." The first type has been thought to be of herpetic and the second type of allergic origin. In the light of their favorable response to penicillin Busacca believes that the views concerning their pathogenesis will have to be revised.

Peter C. Kronfeld.

Colditz, Heinz. Keratoconus, operated on according to Sato. Klin. Monatsbl. f. Augenh. 110:233-234, March-April, 1944.

In an eye with rapidly progressing keratoconus in a 25-year-old woman, a discission-knife was introduced and three vertical incisions were made in Descemet's membrane in the area of the conus. The swelling and opacity of the involved area subsided very slowly. Nine months later the curvature of the cornea was almost normal. There was a dense scar at the site of the former apex. The cornea here was much thicker than before the operation. George Brown.

Coverdale, H. Some unusual cases of Sjögren's syndrome. Brit. J. Ophth. 32: 669-673, Sept., 1948.

Sjögren's syndrome (keratitis sicca) is part of a general systemic disturbance of unknown origin. There seems to be no common causative factor. Probably a majority of cases occur in women near the menopause. The case histories of five patients are presented whose eyes had the typical manifestations but whose histories were somewhat unusual. Two occurred in a man and his daughter who had had dry eyes all their lives. The daughter showed signs of pituitary dysfunction. Two others occurred in a woman and her tuberculous daughter, and the fifth in a young woman whose symptoms seemed to originate from a fracture at the base of the skull. Morris Kaplan.

Edström, G., and Österlind, G. A case of nodular rheumatic episcleritis. Acta ophth. 26:1-6, 1948.

In the course of a chronic destructive polyarthritis a patient developed a bilateral nodular episcleritis with a secondary rise in tension. Two nodules were excised from the left eye; one was subjected to histologic examination, and the other was used in a guinea pig test and culture on Loewenstein's medium. The tests for tuberculosis were negative. The nodules were covered with a normal conjunctival epithelium and consisted of granulomatous tissue; collagenous fibrils radiated from the periphery toward the center, which was necrotic. There were collections of large bright, fibroblastoid cells in the periphery and the adjacent fibrous tissue was infiltrated with plasma cells. The disease was fatal and at autopsy in addition to the lesions in the joints

rheumatic granulomas were also found in the myocardium. (2 figures.)

Ray K. Daily.

English, P. B., and White, J. Mc. B. Corneal transplantations. M. J. Australia 1:736-738, June 12, 1948.

The most popular operation is described as a circumscribed penetrating keratoplasty 4 to 6 mm. in diameter. A brief review of the methods used by Castroviejo, Thomas, Filatov, and Weiner and Alvis is given. Corneal transplantation is most likely to succeed when there is no increase in ocular tension, and when the only lesion in the eye is a partial leucoma of the cornea. Aphakia, extensive corneal opacity, increased ocular tension, and corneal vascularization are all unfavorable factors.

An iridectomy should be done if there are synechia which may complicate the surgery. The donor eye should be a young one and if removed from a cadaver should be obtained within 24 hours after death. Eyes doomed to failure become cloudy and vascularized early. Negroid and caucasian corneas may be interchanged. The only case operated in a member of the Australian fighting forces is described. A visual acuity of 6/36 was obtained two months after surgery.

H. C. Weinberg.

Fadda, A., and Zambetti, E. The prophylaxis of ophthalmoblennorrhea by use of penicillin ointment. Rassegna ital. -d'ottal. 17:207-217, May-June, 1948.

The authors at first used an ointment containing 500 units of penicillin per gram of a vaseline base and kept refrigerated. Later a thermolabile ointment was produced which was not subject to hydrolytic influence. These ointments were employed in a large series of newborn infants for a period of a year. The ointment was inserted into the conjunctival sac immediately after birth and its use continued twice a day for five days. In only two instances was there any acute conjunctivitis and these responded to a two-hour use of the ointment. In no case was any irritation noted in the conjunctiva, cornea or lids. The year's experience with the special anhydrous penicillin ointment demonstrated that it was a good substitute for silver nitrate in the prophylaxis of ophthalmia of the new-born.

Eugene M. Blake.

Jirman, J. Treatment of rosacea keratitis. Ann. d'ocul. 181:475-484, Aug., 1948.

The process may be marginal or central or both, and nodular or tongue shaped. There is usually corneal infiltration and progressive or recurrent ulceration, and necrosis and vascularization are variable. The differential diagnosis includes other degenerative, low grade or inflammatory diseases such as scrofula, tuberculous lesions and Mooren's ulcer. Several factors take part in the cause, such as a constitutional predisposition, vasomotor degeneration, exposure to physical or chemical irritants, skin parasites such as the demodex folliculorum and such body catalysts as sex hormones and vitamins, especially riboflavin.

A case of rosacea keratitis in both eyes of a 50-year-old woman is discussed in detail. A conjunctival flap over the diseased area arrested its progress, especially in one eye.   Chas. A. Bahn.

Lee, O. S., Jr., and Lee, A. Keratoplasty. I. A preliminary report on development of instruments. Am. J. Ophth. 32:71-78, Jan., 1949. (9 figures.)

NEWS ITEMS

DEATHS

Dr. Warren Douglas Horner, San Francisco, died October 22, 1948, aged 58 years.

Dr. David L. Tilderquist, Duluth, Minnesota, died September 26, 1948, aged 76 years.

Dr. Edward Andrew Weisser, Pittsburgh, died October 18, 1948, aged 72 years.

ANNOUNCEMENTS

OREGON POSTGRADUATE CONVENTION

The 10th annual spring postgraduate convention in ophthalmology and otolaryngology will be held in Portland, Oregon, June 19 to 24, 1949. Guest speakers who will appear on the fine program, arranged by the Oregon Academy and the University of Oregon Medical School, will be: Dr. Lawrence R. Boies, professor of otolaryngology, University of Minnesota Medical School; Dr. Leland Hunnicutt, associate clinical professor of otolaryngology, University of Southern California; Dr. James H. Allen, professor of ophthalmology, Iowa State University School of Medicine; and Dr. Edmund B. Spaeth, professor of ophthalmology, Graduate School of Medicine, University of Pennsylvania.

In order to make the course more personal and practical, registration will be limited to 125. For preliminary programs and full information, write to: Dr. David D. DeWeese, 1216 West Yamhill Street, Portland 5, Oregon.

KERATOPLASTY SYMPOSIUM

A two-day symposium on keratoplasty will be held in the lecture room of the Manhattan Eye, Ear, and Throat Hospital, 210 East 64th Street, New York City, on April 19th and 20th.

This conference will consist of operative clinics on the morning of April 19th, follow-up clinics on the morning of April 20th, papers by men from the United States and abroad on the afternoon of April 19th, and on the afternoon of April 20th, a round-table discussion.

ORTHOPTIC EXAMINATION

Application for the examinations to be conducted by the American Orthoptic Council during September and October, 1949, will be received by the office of the secretary, Dr. Frank D. Costenbader, 1605 22nd Street, N.W., Washington 8, D.C., and must be accompanied by the examination fee of 25 dollars. Applications will not be accepted after July 1, 1949.

N.S.P.B. MEETING

The National Society for the Prevention of Blindness will hold a 3-day national conference at the Hotel New Yorker, New York City, on March 16th, 17th, and 18th. The theme of the meeting will be "The battle against blindness: The next 40 years," and the following subjects will be discussed: "Eye problems in middle life," "The eyes of children and young adults," "Vision in industry," "Medical advances in sight conservation," and "Glaucoma: A community problem."

MISCELLANEOUS

ORTHOPTIC SCHOOL

A school of orthoptics has been started at the Massachusetts Eye and Ear Infirmary in conjunction with Simmons College in Boston. Students at the college, during the first three years, take courses that will give them an adequate scientific background. Their fourth year is spent at the hospital where practical and didactic work in orthoptics and perimetry is given. This 4-year program leads to the degree of Bachelor of Science and the Diploma in Orthoptics. Miss Ann Stromberg is technical director of the practical aspects of the work at the hospital.

BETTER VISION INSTITUTE

A record attendance of 81 members and guests marked the January 21st meeting of the Better Vision Institute in New York City. Mr. M. J. Julian, president, spoke of the new program which is being designed to combat the misinformation that has been spread regarding the practices of the ophthalmic industry, particularly along economic lines.

SOCIETIES

CLEVELAND MEETINGS

The guest speaker for the January dinner meeting of the Cleveland Ophthalmological Club was Dr. Richard G. Scobee, director of graduate study in ophthalmology, Washington University, Saint Louis, who spoke on "Versions: The case against prisms." Dr. Scobee's presentation was most instructive and interesting and was illustrated by excellent lantern slides.

Dr. James S. Shipman, clinical professor, Graduate School of Ophthalmology, University of Pennsylvania, and attending surgeon at Wills Hospital, was the speaker at the first dinner meeting of the club in November. Dr. Shipman spoke on "Some practical points regarding retinal detachment surgery." His talk was most practical and he brought out several new points in the treatment of detachment of the retina. A lively discussion followed his presentation.

BROOKLYN PROGRAM

Papers presented at the 107th regular meeting of the Brooklyn Ophthalmological Society on February 17th were: "Psychology of cataract sur-

gery considered from the standpoints of surgeon and patient," Dr. Daniel B. Kirby, New York; and "Some unusual optic nerve conditions which may be confused with papilledema," Dr. Frank B. Walsh, Baltimore. During the instruction session, Dr. Charles A. Perera, New York, spoke on "The pathology and treatment of retinal detachment."

SOUTHERN RESEARCH SECTION

On October 26, 1948, during the meeting of the Southern Medical Association in Miami, Florida, the southern section of the Association for Research in Ophthalmology was organized. Dr. Conrad Berens gave a brief resume of the development and achievements of the national association. Dr. George Haik presented further work on "Beta irradiation for glaucoma." Dr. Alston Callahan, Birmingham, Alabama, was asked to serve as chairman of the southern section for the coming year.

The following ophthalmologists attended: Dr. Conrad Berens, Dr. Shaler Richardson, Dr. George Haik, Dr. William Sayad, Dr. Don Boles, Dr. Johnson, Dr. William Hester, Dr. Karl Benkwith, Dr. Sam McPherson, Dr. Carl Dunaway, Dr. Stacy Howell, Dr. Curtis Benton, Jr., Dr. Hugh Parsons, Dr. E. R. Veirs, Dr. Frank Costenbader, Dr. Mason Baird, Dr. Philip M. Lewis, and Dr. Alston Callahan.

READING MEETINGS

The 88th and 89th regular meetings of the Reading Eye, Ear, Nose, and Throat Society were held on January 5th and 19th. Dr. N. A. Karakashian, of Philadelphia, spoke on "Practical perimetry," at the first meeting; Dr. E. Gerard Smith of Lancaster, Pennsylvania, discussed "The principles of gonioscopy," at the second meeting.

MILWAUKEE SPEAKER

Dr. I. E. Gaynon was the ophthalmic speaker at the January 25th meeting of the Milwaukee Oto-Ophthalmic Society. His subject was "Herpes zoster disciform keratitis."

FLORIDA ANNUAL MEETING

The 10th annual meeting of the Florida Society of Ophthalmology and Otolaryngology will take place at the Belleview-Biltmore Hotel, Belleair, Florida, on April 10th. The address of welcome will be delivered by the president, Dr. Bascom H. Palmer, Miami. A paper, "Benign tumors of the esophagus," will be given by Dr. Thomas M. Edwards, Tampa, and discussed by Dr. Joseph W. Taylor and Dr. C. Frank Chunn, Tampa.

Dr. Charles W. Boyd, Jacksonville, will present a paper on "Corneal section and suture in cataract operation," which will be discussed by Dr. Walton B. Wall, Jr., Orlando, and Dr. Sherman B. Forbes, Tampa. The annual report of the Florida Council for the Blind will be made by the executive secretary, M. Robert Barnett, of Tampa.

At the evening session, Dr. Algernon B. Reese of New York will present a paper on "The treatment of tumors of the eye and adnexa," and Dr. Louis H. Clerf of Philadelphia will speak on "Paralysis of the larynx."

ORTHOPTIC TECHNICIANS MEET

The western group of the American Association of Orthoptic Technicians met at the University of California Hospital, San Francisco, on February 18th and 19th.

PENNSYLVANIA PROGRAM

The annual meeting of the Pennsylvania Academy of Ophthalmology and Otolaryngology will be held April 22nd, 23rd and 24th, at the Penn Harris Hotel, Harrisburg.

Among the speakers who will present papers at this meeting will be Dr. A. D. Ruedemann, Dr. J. R. Lindsay, Dr. R. O. Rychener, Dr. C. S. Nash, Dr. J. G. Linn, Dr. Arno Town, and Dr. G. M. Coates.

In addition to formal presentations, the meeting will include a round table discussion on "Headaches" which will include representatives of all major specialties, and there will be a study club to discuss "Cataract problems," the discussers to include Dr. Ruedemann, Dr. Rychener, and Dr. Town.

The officers are: President, Dr. James J. Monahan; president elect, Dr. Daniel S. Destio; secretary, Dr. Benjamin F. Souders.

EGYPTIAN MEETING

The annual meeting of the Ophthalmological Society of Egypt was held at the Memorial Ophthalmic Library, Giza, Egypt, on March 4th and 5th.

PERSONALS

Dr. Everett L. Goar, Houston, Texas, presented the fifth annual Sanford R. Gifford Memorial Lecture before the Chicago Ophthalmological Society on January 17. The subject of Dr. Goar's paper was "Corneal dystrophies."

Dr. F. Herbert Haessler, Milwaukee, abstract editor of the JOURNAL, has been appointed professor of ophthalmology at the Marquette University School of Medicine.

Dr. Saul Kottler, Cleveland, announces the opening of his office in the Guardian Building. Dr. Kottler recently completed his internship in the ophthalmological division of the University Hospitals, Cleveland.

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measured 27 mm. and the left eye measured 19 mm. (fig. 1). The proptosis of the right eye was apparent grossly. There was no bruit and no pulsation of the right globe. The right globe could be pressed back into the orbit with no more than normal resistance. Pupillary responses to light and convergence-accommodation were prompt and equal in both eyes. There were no palsies of the extraocular muscles. The left fundus appeared normal and the right fundus showed temporal pallor of the nervehead.

Visual field studies of the right eye, with 3/330 white, 1/330 white, and 1/2,000 white, showed peripheral contraction, more marked temporally, with hemianopic characteristics. The left field was within normal limits to all visual angles.

It was the impression of Dr. Chamlin that the visual fields suggested interference with the right optic nerve retrobulbarly extending rather far back toward the chiasmal area (figs. 2 and 3).
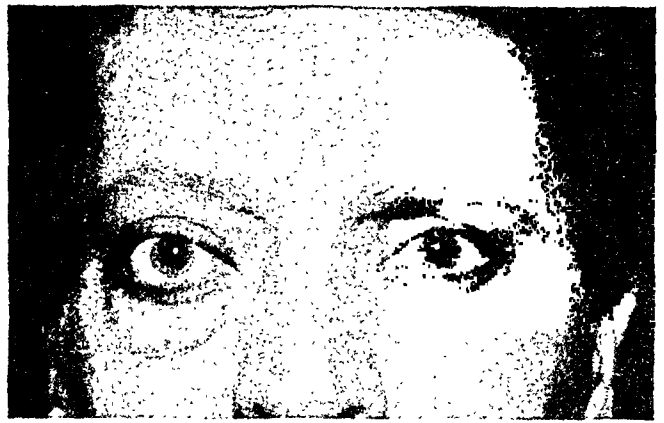
Fig. 1 (Grino and Billet). *Case 1.* Showing proptosis of the right eye.

Laboratory data. Urine was within normal limits. Blood hemoglobin was 13.5 gm.; R.B.C., 4.62 million; W.B.C., 6,600, with essentially normal differential; B.U.N., 14.9 mg. percent; blood sugar, 90 mg. percent; serum albumin, 4.4 mg. percent; serum globulin, 2.6 mg. percent; B.M.R. was —11.

Electrocardiography revealed a normal sinus rhythm. Electro-encephalography revealed a minor degree of change from the

Fig. 2 (Grino and Billet). *Case 1.* Visual fields on November 6, 1947, for 1/330 white. Visual acuity in the right eye was 15/100+1; in the left eye, 15/15.

...or was found
...done, including
...patient felt better but
...s recurred. About one
...edical Center, a biopsy

Fig. 3 (Grino and Billet). *Case 1.* Visual fields on March 15, 1948, for: R.E., 20/2,000 red; L.E., 1/2,000 white. Visual acuity: R.E., 15/70; L.E., 15/15.

Fig. 4 (Grino and Billet). *Case 1.* Right lateral roentgenogram. The slight bony alterations can be appreciated only in stereoscopic view.

electrical normal in an activity grossly influenced by the patient's drowsiness.

X-ray examination of the chest was within normal limits. X-ray examination of the skull revealed that both the superior orbital plate and the greater wing of the sphenoid consisted of denser but not apparently thicker bone on the right side; the optic foramina appeared normal (fig. 4).

On November 10, 1947, 18 cc. of air were injected behind the right globe. No resistance ... about 16 cc. were injected. ... injection was completed, ...arked ecchymosis of both ... s and of the periorbital

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X-ray examination of the orbits after air insufflation in the postero-anterior view did not disclose any air pockets. In the lateral position there was a very thin layer of air retrobulbarly in the superior portion of the orbital cavity. No tumor was outlined.

On November 12, 1947, a right common carotid arteriogram under general anesthesia was done percutaneously by one of us.

The venograms show a somewhat rounded density, measuring approximately 25 cm. in diameter, within the region of the right orbit posteriorly. A less well-defined density with rather indefinite borders is visible intracranially just above the lesser wing of the sphenoid on the right. These densities were not visible on the preliminary skull films and probably represent capillary circulation in neoplastic masses.

The arteriogram also reveals the just described masses in the region of the right orbit and behind the right lesser wing of the sphenoid. The retro-orbital density is rather poorly defined.

Conclusion. The changes described indicate the existence of a tumor mass in the right orbit, extending possibly retro-orbitally. The intraorbital portion of the mass appears to be highly vascularized (fig. 6). The patient was discharged from the hospital on November 17, 1947, with the diagnosis of retrobulbar tumor of the right eye, probably a hemangioma.

She received roentgen therapy—a total of 16,600r. over a period of one month, from November 28, 1947 to December 29, 1947— through right anterior and lateral portals to the right orbit. Repeated checks of visual acuity, visual fields, and Hertel exophthalmometer readings showed (February 10, 1948) no change in her ocular status.

Ocular examination on June 22, 1948, six months after X-ray treatment, revealed a marked improvement in visual acuity: O.D., from 15/100 to 15/40. There was no ...ession of the exophthalmos, and no ... in the fundus picture in this eye. ...'1 study with 20/2,000 red re-

Fig. 6 (Grino and Billet). *Case 1.* Right carotid angiography. Venogram showing tumor pointed by arrows. Arrow 2 shows the intracranial extension.

vealed macular sparing to account for the improved acuity (fig. 7).

CASE 2

History. O. H., a 55-year-old white man, had had a left nephrectomy about 8 years ago for painless gross hematuria. Four years ago, the patient developed blurring of vision and proptosis of the left eye. At that time, Dr. Davidoff performed a left exploratory frontal craniotomy. No tumor was found and a decompression was done, including orbital decompression.

For some time, the patient felt better but blurring and proptosis recurred. About one year ago at the Medical Center, a biopsy

Fig. 7 (Grino and Billet). *Case 1.* Visual fields on June 22, 1948, after roentgen therapy: R.E., 20/2,000 red; L.E., 1/2,000 white. Visual acuity: R.E., 15/40; L.E., 15/15.
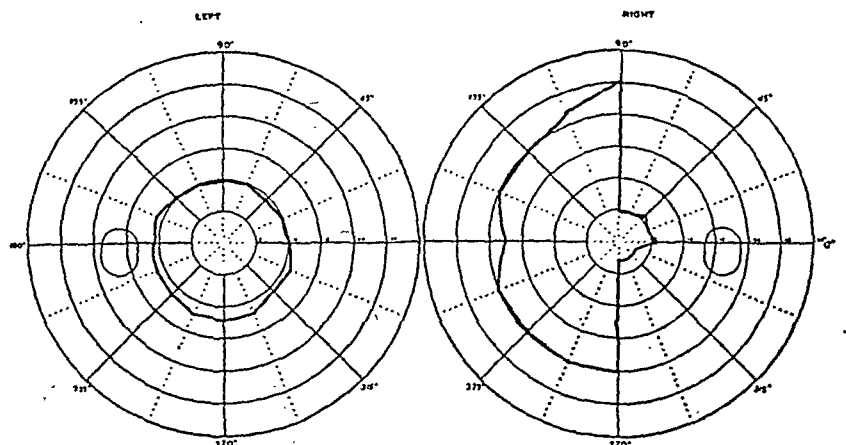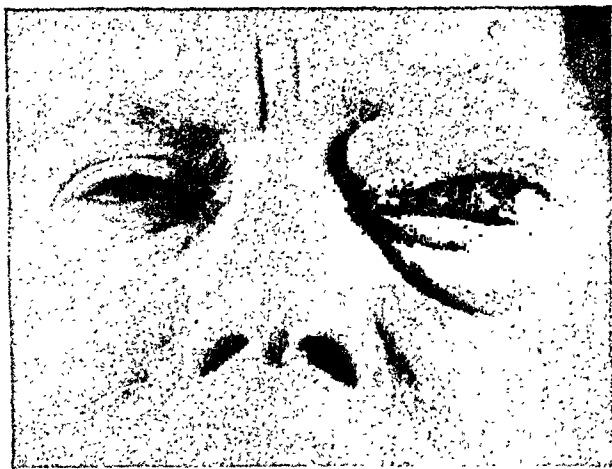
Fig. 8 (Grino and Billet). *Case 2*. Demonstrating proptosis and ophthalmoplegia of the left eye.

from a tumor behind the left eye (via inferior orbital route) was done and was reported to be a hemangioma.

Four months prior to admission to Montefiore Hospital, the patient developed weakness in the left arm and attacks of tachycardia. Three months before admission, his left leg became weak. For the last month prior to admission, it was necessary for the patient to rush to the bathroom in order to avoid soiling his clothes. For several weeks prior to admission, the patient complained of headaches.

Physical examination. The general physical examination revealed a fairly well-developed and well-nourished man. There was motor weakness of the left arm and leg. Left tendon reflexes were exaggerated. Left abdominal reflexes were absent.

Ocular examination. Visual acuity was:

O.D., 15/15; O.S., finger counting nasally. Hertel exophthalmometer readings with a base line of 103 were: O.D., 20; O.S., 35 (fig. 8). The right eye was wholly normal.
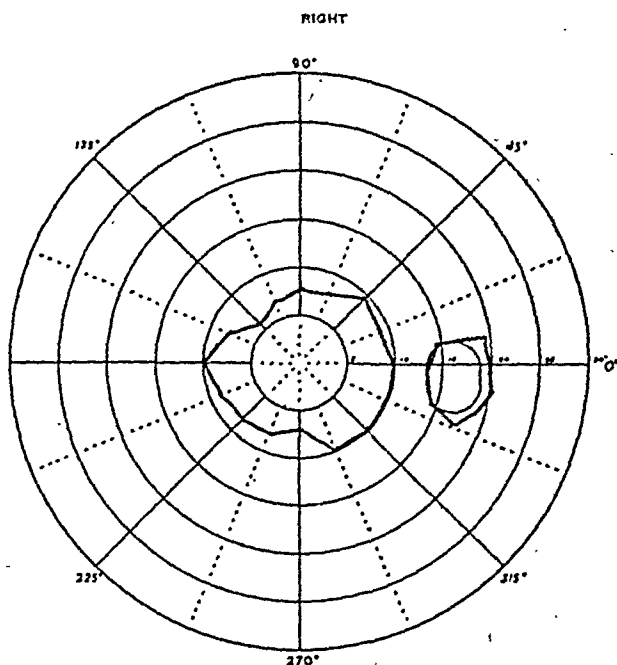
Fig. 9 (Grino and Billet). *Case 2*. Visual field for the right eye, March 10, 1948, 1/2,000 white; blindspot, 2/2,000 white. Visual acuity: 15/15.

The left eye showed restriction of the extraocular muscles in keeping with the proptosis. The left optic nervehead showed definite temporal pallor.

Visual field studies showed normal central and peripheral fields in the right eye, for 1/2,000, 1/330, and 2/330 white. The left eye retained only a small island of vision

Fig. 10 (Grino and Billet). *Case 2*. Visual fields, March 10, 1948: R.E., 1/330 white; 2/330 white; L.E., 10/330 white. Visual acuity: R.E., 15/15; L.E., finger counting.
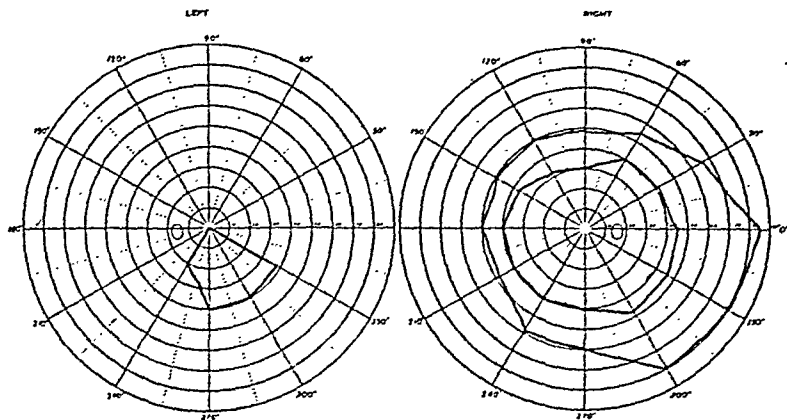
nasally and below for 10/330 white. These visual field findings suggested insult to the left optic nerve probably within the orbit and not in the cranium (figs. 9 and 10).

Electrocardiography showed a right bundle branch block without activity of any

Laboratory data. Urine and blood counts were normal, as were blood urea and sugar. Wassermann was negative.

Course in hospital. On March 22, 1948, under general anesthesia, a right posterosuperior frontal craniotomy for removal of

Fig. 11 (Grino and Billet). *Case 2.* Right carotid angiography, lateral view.
Capillarogram showing the shadow of the brain tumor.

coronary lesion. Electro-encephalography showed definite electrical abnormality with concentration of disturbances anteriorly to the right of the midline. Right angiographic studies localized the cerebral tumor as a highly vascularized lesion in the right parietal region near the vertex, measuring 3 by 4 cm. Left angiography disclosed a highly vascular lesion intraorbital in location (figs. 11 and 12).

Chest X-ray films showed three oval-shaped areas of homogeneous density in the lung.

the cranial lesion was performed. The brain itself bulged quite markedly through the defect in the dura mater. The lesion was disclosed to be fluorescent due to the injection of fluorescein before the operation. The tumor was removed and frozen sections revealed a hypernephroma.

Postoperatively, the patient remained drowsy. On the first postoperative day, he developed a fever of 105°F. He died on the second postoperative day. At autopsy, the left orbital contents were obtained in a body (fig. 13).

CASE 3

History. H. was a white woman, aged 46 years, who, in November, 1947, was told by an optometrist that he was unable to correct the vision in her right eye and that she should see an ophthalmologist. The patient had no subjective complaints but on direct

Laboratory data. Hemoglobin 13 gm.; R.B.C., 4.37 million; W.B.C., 10,900 (64-percent polys, 6-percent immatures, 24-percent lymphocytes, 4-percent monocytes, 2-percent eosinophils). Urinalysis was negative. B.U.N. 13.5 mg. percent; blood sugar, 82 mg. percent; total protein, 6.4 percent.
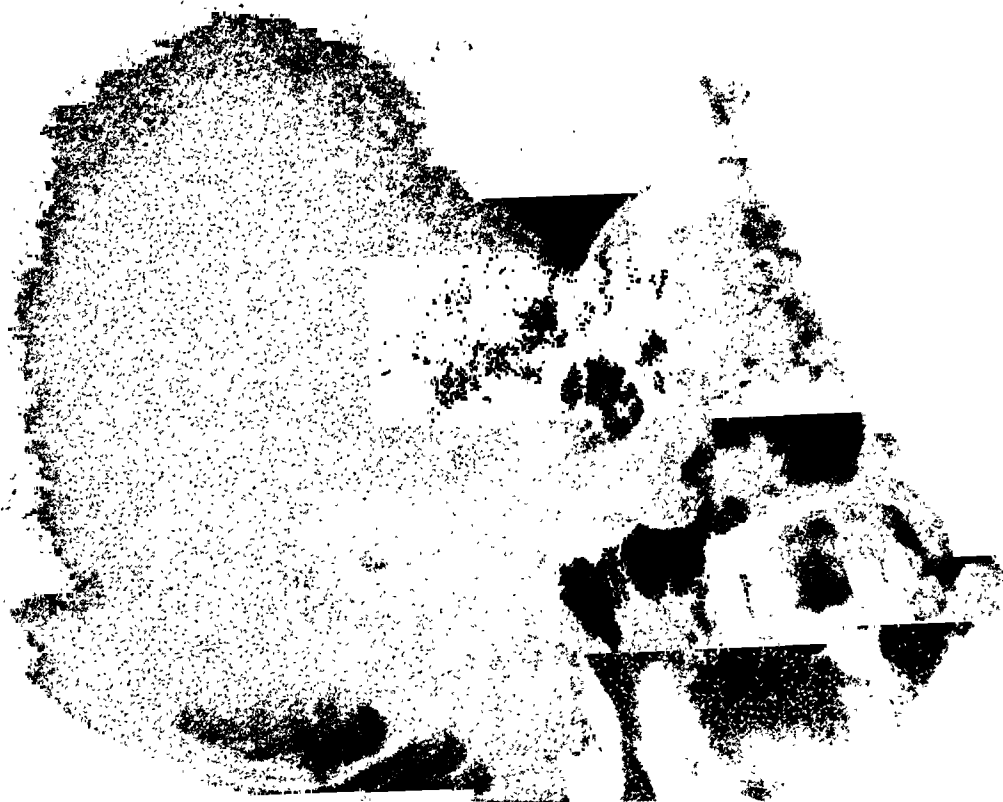
Fig. 12 (Grino and Billet). *Case 2.* Left carotid angiography, lateral view of arterial phase. The vessels of the orbital tumor are completely filled with diodrast.

questioning admitted that, when glasses were fitted in 1945, it seemed as if the lashes of the right eye brushed against the glass and that it took numerous adjustments to fit them. She, however, had noticed no prominence of the right eye. There was no history of headache, disturbances in smell, pain in the face, or endocrine disturbance. The past history was essentially noncontributory. Examination revealed a rather obese woman with a blood pressure of 160/90 mm. Hg, but no other abnormalities (fig. 14).

Visual field studies showed normal fields for the left eye. For the right eye, there was marked peripheral contraction encroaching on the central area with marked central involvement as indicated by central field studies (figs. 18 and 19).

Eye note. Visual acuity on February 9, 1948, was: O.D., 15/30; O.S., 15/15. The right eye was more prominent than the left. Hertel exophthalmometer measurements with base-line 100: O.D., 22; O.S., 17.5. Extraocular movements were unrestricted. Fundi; O.D., showed temporal pallor and

blurring of disc margins with some fullness of veins. O.S., showed upper nasal disc margin to be blurred, slight pallor temporally, veins full.

The blindspot of the right eye could not be properly evaluated even with 20/2,000

even in the region of the optic foramen or possibly even in the orbit.

X-ray studies of the skull, including postero-anterior and lateral stereoscopic views as well as views of the optic foramina showed thickening of the right sphenoid wing and
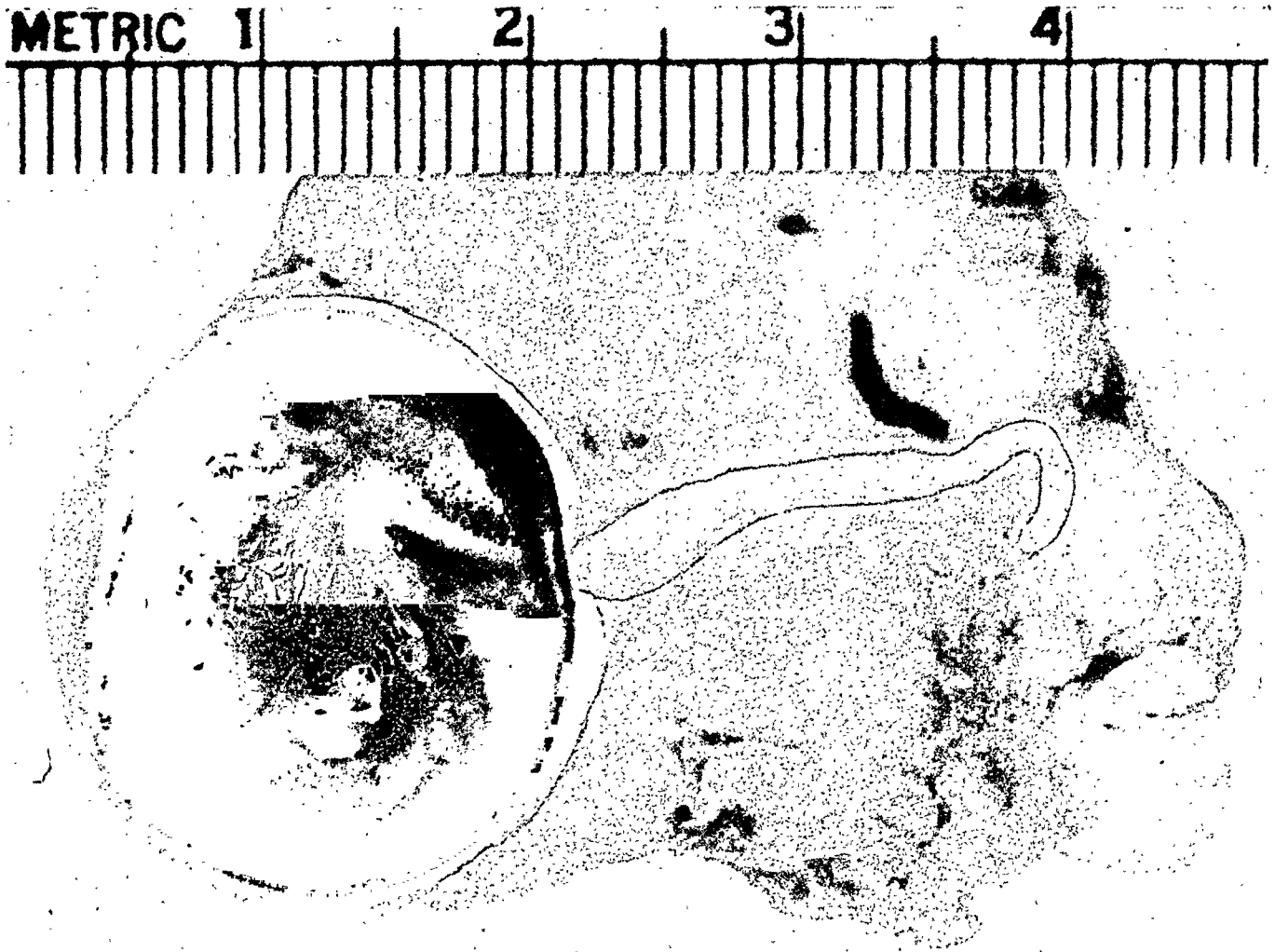

Fig. 13 (Grino and Billet). *Case 2.* Autopsy specimen. Sagittal section of the left orbit demonstrating the tumor.

white. The right eye showed practically no field for 1/2,000 white. With 15/2,000 red, there were no definite central hemianopic features in the right eye. In the left eye, the peripheral field for 2/330 white showed no substantiating criteria for upper defect in the field. The blindspot in the left eye was within normal limits.

Dr. Chamlin thought that, in view of the complete lack of involvement, one must assume that this interference with the visual pathway was limited to the right optic nerve, probably well anterior and possibly

of the orbital roof on that side. There was suggestion of spicule formation in the latter area. Dr. Davidoff reported that the appearance was typical of right sphenoidal ridge meningioma (fig. 15). Electro-encephalograms showed an essentially normal electrical pattern.

Angiography performed by percutaneous injection of the carotid showed a distinct semilunar posterior concave depression of the anterior cerebral artery in the region of the bony overgrowth in the sphenoidal ridge on the right, at the medial termination of the

Fig. 14 (Grino and Billet). *Case 3.* Demonstrating slight proptosis of right eye.

meningioma of the outer one third of the sphenoid ridge was fairly well established and operation was recommended. The patient at first was quite resistive to the idea of surgical intervention but eventually acquiesced and was discharged to return in about one month for surgery.

On April 15, 1948, a right frontotemporal craniotomy with orbital decompression was performed under endotracheal ether anesthesia. The bone overlying the base which was markedly thickened and vascular, was rongeured away back to the anterior clinoid process, thereby unroofing the orbit. The sphenoid ridge and part of the lesser wing of the sphenoid were removed by means of perforators, burrs, and the rongeurs.

sphenoidal ridge. The venogram showed the tumor by the injection of the blood vessels. The remainder of the angiogram was considered to be within normal limits (figs. 16 and 17).

The dura was then incised and a small hemispheric tumor, measuring about 3 to 4 cm. in diameter and ½ cm. in thickness, was encountered in the dura opposite the Sylvian vessels and removed.

Course in hospital. All investigative procedures were carried out with no untoward effects. The diagnosis of a sphenoidal ridge
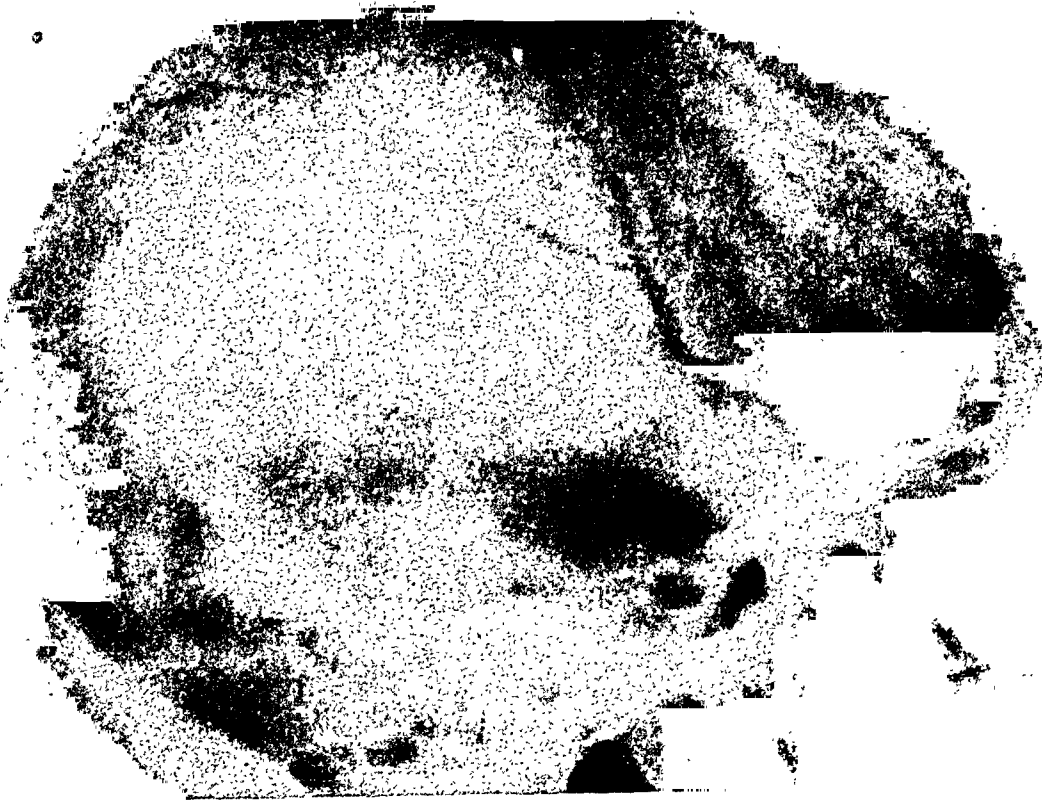

Fig. 15 (Grino and Billet). *Case 3.* Roentgenogram of the skull, right lateral view, showing some bony changes of the sphenoidal plate.

The orbital fascia was then incised and the orbital contents seemed to decompress themselves through the defect.

Postoperatively the patient did well and her wound healed by first intention. At the time of the patient's discharge, the visual acuity in the right eye was 15/15−2 as compared to 15/30 preoperatively. The exophthalmometer reading showed the same 5-mm. proptosis of the right eye.

of similarity. Unilateral exophthalmos and gradual loss of vision were the most prominent findings of the three, while roentgenologic changes also were present in greater or less degree in Cases 1 and 2.

That angiography has been not only useful but indispensable in making these diagnoses is evidenced by the accompanying angiograms, in which the tumors are clearly demonstrated, as well as by a close examina-
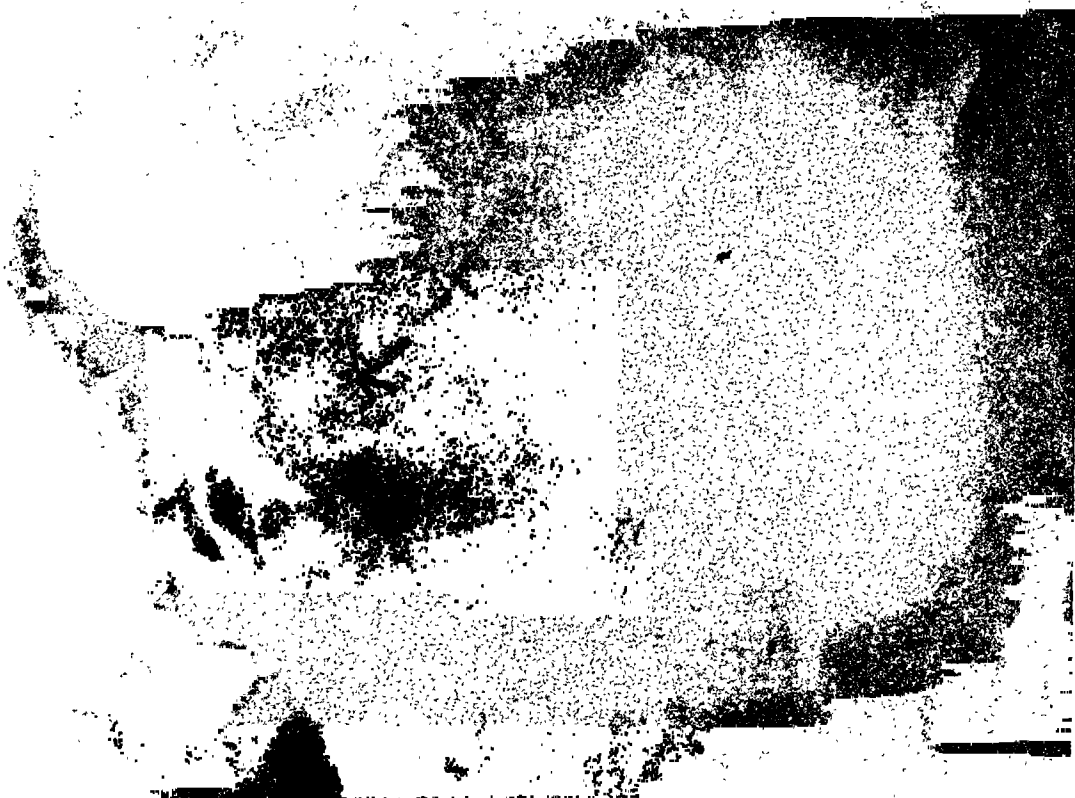
Fig. 16 (Grino and Billet). *Case 3.* Right carotid angiography, lateral view. Capillarogram showing vascular network of tumor filled with diodrast.

Pathologic report. The tumor was a meningocytic meningioma.

DISCUSSION

The three cases here presented, two orbital tumors (one primary, the other metastatic) and an intracranial tumor located at the sphenoidal wing, illustrate the difficulties in making the correct differential diagnosis in cases of unilateral exophthalmos. In spite of their different natures and locations, their histories, as well as their clinical and roentgenologic findings, show a marked degree

tion of the case histories (figs. 6, 11, 12, 16, and 17).

In Case 1, given the findings obtained by the various examinations—unilateral exophthalmos, partial loss of vision, bony changes in the sphenoidal wing of the affected side, and the aspects of the visual fields —one would suspect an intracranial lesion, which had to be ruled out. To this end, lateral and postero-anterior stereoscopic X rays of the skull were taken, as well as X rays of the optic foramina.

Although the latter were shown to be

normal, a suspicious increase in density was found at the level of the superior orbital plate and at the greater wing of the sphenoid of the affected side. An air injection behind the globe of the eye did not yield any data of diagnostic value, resulting only in marked cranial exploration (as was done in Case 2) or upon temporizing measures which could only result in further loss of vision.

Cerebral angiography was finally performed by the percutaneous method which showed unmistakably, in all three phases,

Fig. 17 (Grino and Billet). *Case 3*. Right carotid angiography, antero-posterior view, showing vascular bed of tumor filled with diodrast. The arrows point to the tumor.

ecchymosis of the eyelids, which caused the patient considerable pain and discomfort (fig. 5).

It is evident in this case that, because of inability to demonstrate an orbital tumor by the means at our disposal (angiography excepted), one would decide upon an intra-

the presence of an orbital tumor. This is one of the few cases in our series of angiographies in which general anesthesia was employed because, at that time, we were developing the percutaneous technique and we needed the maximum relaxation of the patient.

As can be seen by the angiogram (fig. 6), this tumor is eminently vascular. Although we were interested in determining its nature, we did not think that biopsy would be a safe procedure, especially in view of the untoward results of the air injection. Considering further the reluctance of the patient to accept more radical measures and the fact that a great percentage of orbital tumors are of hemangiomatous type (Reese[7]), we

toward the chiasmal area," can be easily correlated to the angiogram which shows a small number of abnormal vessels above the lesser wing of the sphenoid on the affected side.

When Case 2 was first seen by the neurosurgeon, the history (except for the nephrectomy) and the findings were almost identical to those described in the preceding case. Because a pathologic report could not be

Fig. 18 (Grino and Billet). *Case 3.* Visual fields on February 9, 1948: R.E., 2/2,000 white; L.E., 1/2,000 white. Visual acuity: R.E., 15/30; L.E., 15/15.
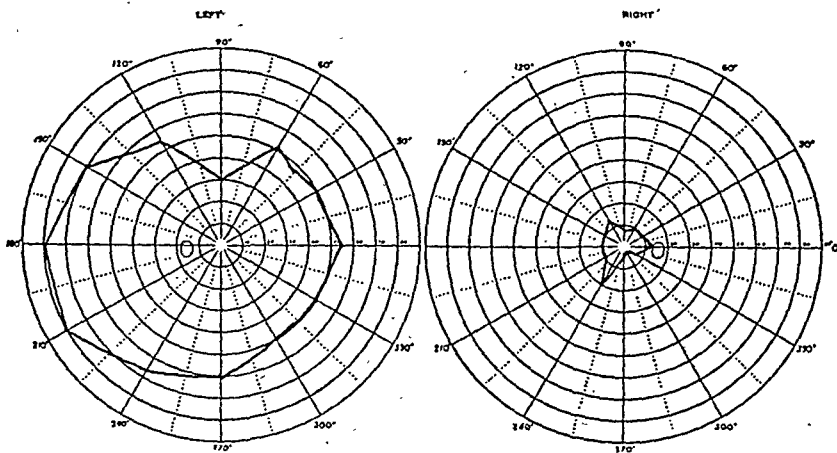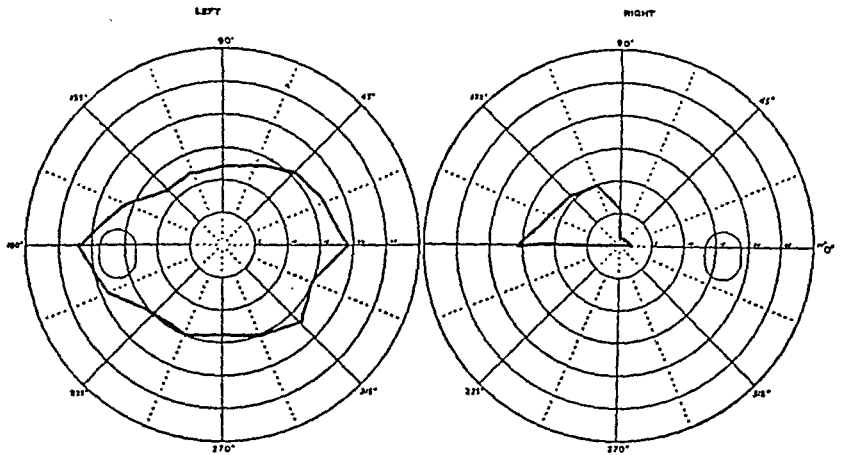

Fig. 19 (Grino and Billet). *Case 3.* Visual fields on February 9, 1948: R.E., 2/330 white; L.E., 2/330 white. Visual acuity: R.E., 15/30; L.E., 15/15.

agreed upon X-ray therapy and periodic examinations of the visual fields, anticipating, however, that we should have to insist upon surgical treatment, should the condition become worse.

A point of interest in this case is the relation of the ophthalmic findings to those of the angiographic. The visual fields, which suggest (in the words of Dr. Chamlin) "interference with the right optic nerve retrobulbarly, extending rather far back

obtained, the reasons for the nephrectomy were never established.

Although neither an intraorbital, nor an intracranial tumor could be ruled out on the basis of the clinical and radiologic findings alone, nevertheless an intracranial exploration was undoubtedly indicated, if only for the purpose of decompressing the optic nerve in the event that no tumor was found. This treatment would not change essentially, however strongly one might suspect the presence

of a metastasis, since we know that two different types of tumor can be present in the same individual, as has been emphasized lately by Feiring and Davidoff.[3]

Three years after the intracranial exploration, which was reported to be negative, the ocular signs were so obvious that the problem was not one of localization but of knowing the nature of the tumor. A biopsy was then performed, the report from which was "possible hemangioma."

Seven months later the patient developed a weakness on the left side of his body which was the immediate cause of his admission to Montefiore Hospital, where angiography of the left carotid system was performed in order to rule out any possible intracranial extension of the orbital tumor (fig. 12). Since this patient had neurologic signs which could be related to a possible lesion in the right cerebral hemisphere, the right carotid artery was also injected percutaneously two days afterward and a tumor was shown situated in the right frontal lobe (fig. 11).

In resume, this patient had, from the beginning, a metastatic lesion in his left orbit which was impossible to discover in its early stages and which probably could have been revealed by angiography, had angiography been available. As previously mentioned, the tumor mass removed at operation, as well as the orbital tumor obtained at necropsy, was shown to be a hypernephroma.

Case 3 had a history and presented clinical findings similar to those of the preceding cases. This patient had a unilateral exophthalmos with gradual loss of vision. Her radiologic findings, however, were compatible with an intracranial growth, showing bony changes commonly present in sphenoidal-wing meningiomas. Although the preoperative diagnosis was confirmed in the operation and was finally substantiated by the histologic report, it is evident that many doubts could have been cast upon that diagnosis without the documentary proof given by angiography (figs. 16 and 17).

More important still, from the point of view of the surgeon, was the fact that no intraorbital extension could be demonstrated angiographically. The steady improvement of the patient after the operation, in which the orbit was unroofed but not explored, testifies that no orbital tumor was present and confirms the assumption derived from the angiographic data.

At this point, we should like to mention that the absence of a tumor shadow in the angiogram does not preclude the existence of a tumor. Not all tumors have a well-developed vascular supply; astrocytomas and melanomas, for instance, are poorly vascularized and very rarely will be demonstrated by angiography. However, in these and allied cases, angiographic diagnosis is still made possible by the displacement of the vessels, as this is as much indicative of a growth as is a tumor's shadow.

However far from the scope of this paper it may seem to be, we wish to make some remarks upon the treatment of these cases, which will help to justify the emphasis that we place upon the differential diagnosis.

A complete removal of the tumor, here as elsewhere in the body, is the surgeon's aim. The removal of an intraorbital tumor or an intracranial tumor with orbital extension is, however, a major operation and not, by any means, an easy one, requiring perfect familiarity with the region, as well as knowledge of the suspected pathologic condition.

It is evident that, if the exact situation of the tumor is known and some hint of its pathology is obtained, the surgeon will be enabled to explore the intraorbital cavity with the least possible damage to the important structures that it contains.

That the removal of an intraorbital tumor by an intracranial approach is not only feasible but the route of choice in the majority of cases has been demonstrated by Cushing[1] and Dandy.[2] This approach is employed routinely by neurosurgeons. The operation consists of a frontal craniotomy, as for the

exploration of the pituitary gland, followed by the removal of the orbital roof. The capsule of the orbit is then opened widely, which allows a thorough exploration of the orbital cavity.

It is evident that one would feel reluctant to explore the orbital cavity unless the presence of a tumor were well demonstrated in advance, since the danger of damaging important structures cannot be overemphasized. Since one cannot, however, neglect such a tumor, it is of the utmost importance to have an accurate diagnosis. Although our experience is not extensive, we feel that angiography is the safest and most helpful method for differential diagnosis in cases which may show either intraorbital or intracranial tumors.

SUMMARY AND CONCLUSIONS

Two cases of orbital tumor and one of intracranial tumor are presented.

In all three cases the history and symptoms were similar.

Accurate localization was made possible by angiographic visualization of the tumors.

The importance of accurate localization as a prerequisite for proper surgical treatment is emphasized.

Cerebral angiography, by either the direct (percutaneous) or the open method, is presented as a harmless procedure, permitting radiologic visualization of orbital, as well as intracranial, tumors.

The technique of cerebral angiography is outlined.

We feel that cerebral angiography should be used in the diagnosis of cases exhibiting unilateral exophthalmos, in preference to more dangerous or less informative methods, as, for instance, pneumoencephalography, puncture biopsy, and intraorbital air injection.

71 East 77th Street (21).

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A SURGICAL TREATMENT FOR PTERYGIUM BASED ON NEW CONCEPTS AS TO ITS NATURE*

H. SAUL SUGAR, M.D.
Detroit, Michigan

Although much has been written regarding the cause of pterygium, the frequency of recurrence after surgical treatment is indicative of our profound ignorance of its true nature. As a result of clinical and histologic observations begun in 1944 on military personnel, and continued since, a theory of the nature of pterygium was formulated and a new method of surgical treatment devised. The results in approximately 50 cases have been such as to warrant this communication, even though follow-up in the early military cases was not possible.

According to Kamel,[1] "a true pterygium is a pathological encroachment of part of the bulbar conjunctiva exposed in the palpebral tissue over the cornea. This encroachment is in the form of a fold of the conjunctiva, triangular in shape, with the apex, called the head, on the cornea, the base merging imperceptibly in the caruncle region or the region of the outer canthus, and the sides formed of two folds of the conjunctiva, an upper and a lower." It is considered by Duke-Elder[2] to be a degenerative process which essentially affects the cornea.

These authors, like nearly all other writers on the subject, are concerned with the cornea and conjunctiva. I believe the layer of Tenon's capsule lying in the interpalpebral zone between the conjunctiva and sclera of cornea to be the essential element in the occurrence, extension, and recurrence of true pterygium.

CLINICAL OBSERVATIONS

The first clinical observations were made on eyes with pingueculae and early pterygia to determine the relationship between the two, and the earliest onset of pterygium. It was noted that all early pterygia were associated with pingueculae and that in each instance the pinguecula was elevated sufficiently to raise the epithelium mechanically from the end of Bowman's membrane. This suggested that the latter is the barrier separating the pinguecula from corneal encroachment when it is then termed pterygium. Once the barrier had been passed, the conjunctiva appeared to be pulled onto the cornea, as shown by the fact that the pinguecula becomes the apex of the pterygium (fig. 1) and by the folding of the conjunctiva which, when released surgically, returns to the normal conjunctival position.

The view that the pterygium develops from a pinguecula was first introduced by Zehender,[3] in 1869, although Horner[4] may deserve credit for originating this theory. Fuchs[5] championed this theory and, although Hubner[6] stated that pterygium could occur independently, it is difficult to be certain of this once a pterygium of sufficient size has formed, since the pinguecula is carried onto the cornea as the head of the pterygium and may leave no evidence of its previous presence in its usual position.
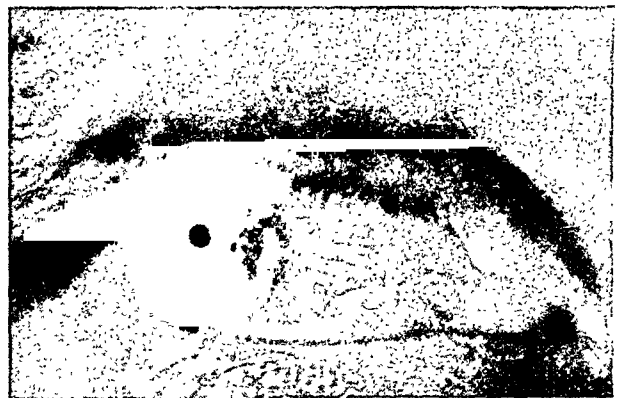

Fig. 1 (Sugar). Pterygium showing vascularity and pinguecula forming its head.

OBSERVATIONS MADE DURING SURGERY

Further observations made during surgical procedures on pterygiums showed that under the conjunctiva there is a definite layer of vascularized tissue (Tenon's capsule) which, in the horizontal meridian, has the appearance of a thin muscle tendon. It continues to be the very head of the pterygium.

Histologically, this tissue contains hypertrophic and hyperplastic elastic fibers which lie parallel to each other, thus giving rise to the "tendinous" appearance. This layer separates easily from the conjunctiva and is practically free from the sclera.

In addition, some of the prominent horizontal blood vessels extending from the inner canthal region toward the head of the pterygium lie in this tissue and not in the conjunctiva itself (fig. 1). It appears that these are anterior ciliary vessels, which lie just anterior to the rectus muscles in Tenon's capsule, which are pulled across the sclera and cornea with Tenon's capsule.

Just anterior to the head of the pterygium, there is a halo of grayish-white opacity, a short distance in front of which are islands of superficial opacities that, histologically, have been found to be small vesiclelike formations in Bowman's membrane at the points where the corneal nerves pierce the latter. Fuchs[5] has described these changes well.

When the head of the pterygium is removed, it is noted that there are dense adhesions between the pterygium tissue and cornea in some parts, while in other parts the two separate easily.

HISTOLOGIC OBSERVATIONS

Aside from clinical observations, there are important histologic observations which are well known and important in formulating the theory of the nature of pterygium. Most important is the histologic similarity between the pinguecula and the body of a pterygium. Both are covered by conjunctival epithelium with variations which are not essential to the process of extension of the pterygium.

Fig. 2 (Sugar). Photomicrograph showing the dense layer of Tenon's capsule (A) and calcified areas at (B). The thin strands which lie under Tenon's capsule are seen at (C).

Near the surface of its head and neck, the pterygium is covered by flat cells, with cylindrical cells in the folds and furrows and at the base. Bowman's membrane is destroyed in places and here the superficial corneal lamellae are involved in the pterygium.

The stroma of each shows a moderately vascular areolar tissue structure, loose in the early stages and more compact later (fig. 2). There is hyaline degeneration of fibrous tissue and deposition of amorphous hyaline and sometimes chalk deposits. Hypertrophy and hyperplasia of the elastic fibers are quite prominent.

DISCUSSION

These observations have led to the following incomplete theory: A pterygium develops from a pinguecula. The latter is a degenerative change in the subconjunctival fascia (Tenon's fascia). Two factors may be significant in this degeneration.

1. The closure movements of the lids squeezing the conjunctiva between them.

2. The movements of the horizontal rectus may cause intermittent pull on Tenon's fascia. That this factor alone could not be effective is shown by the absence of these changes in the region of the vertical recti.

The degenerative process leads to hyperplasia and hypertrophy of the elastic tissue and deposition of hyaline which causes an elevation that eventually separates the epithelium from Bowman's membrane. Then, probably because of a chemotactic force either in the nature of the changes occurring when tendinous tissue attaches itself to bone or other tissue, perhaps as a response to the pull of the "tendinous" Tenon's fascia, or as a response to a nutritional demand, changes occur in the cornea adjacent to the head of the pterygium and lead to the formation of connective tissue which contracts, slowly pulling the fascial layer onto the cornea. As the process repeats itself the tissue encroaches further onto the cornea, pulling the conjunctiva with it.

This theory explains the recurrences produced by all methods of pterygium surgery in which the subconjunctival tissue is permitted to remain.

This theory considers pterygium to be a purely degenerative process. On the other hand, Kamel believed the process to be inflammatory and D'Ombain[7] held that it is an irritative disease due to exposure and not primarily a degeneration, but he stressed that it is secondarily a degeneration. Kamel felt that a keratoconjunctivitis occurs, with the laying down of fibrous bands which contract and cause encroachment of conjunctiva onto the cornea. He treated pterygium by separating the conjunctiva from the underlying layer and cauterizing subconjunctivally with phenol on a toothpick.

New surgical procedure

On the basis of the theory herein presented, the following surgical procedure has been used successfully. No recurrence has been seen. None is expected, since the operation is based on the formation of a scleroconjunctival adhesion, 4-mm. wide adjacent to the limbus.

Anesthesia is induced by the use of 2 or 3 installations of 4-percent cocaine-hydrochloride solution at 2-minute intervals. Then,

a small amount of 2-percent procaine solution, enough to raise a thin bleb between the sclera and Tenon's capsule, is introduced through a hypodermic needle beneath the body of the pterygium about 4 to 5 mm. from the limbus.

Incision. After about five minutes, an incision (fig. 3) is made in the conjunctiva just posterior to the head of the pterygium, extending all the way from its lower to its upper border and then laterally at each border to the limbus.

This incision separates the conjunctiva from the cornea and permits tthe entire conjunctiva, forming the surface of the pterygium, to be undermined to the plica semilunaris, and to a couple of millimeters beyond its upper and lower borders. The conjunctiva is thus freed from attachment to the subconjunctival layer and may resume its normal position.

A second incision is now made at the same location as the first, this one being made through the "tendinous" layer of the Tenon's capsule tissue, from the lower to the upper border of the pterygium at this point.

A scissors is inserted between this layer and the cornea and sclera, and this layer is undermined for about 4.5 to 5.5 mm. from the limbus, and extending about a millimeter beyond the upper and lower borders of the pterygium. The portion of Tenon's capsule, which is thus undermined, is excised.

The head of the pterygium is now shaved from the cornea in such a manner as to remove as much of the scar tissue as possible, leaving the limbus free.

Suture. A double-armed silk suture is inserted through the superficial layers of the sclera about 3.5 mm. from the limbus and parallel to the latter, and each end is passed through the conjunctiva near its cut edge. The suture is tied over the conjunctiva, leaving a bare area of 3 mm. between the cornea and conjunctiva.

A patch is applied. Ointments are used after the first day. The suture is removed on the fourth day. The suture may be dis-
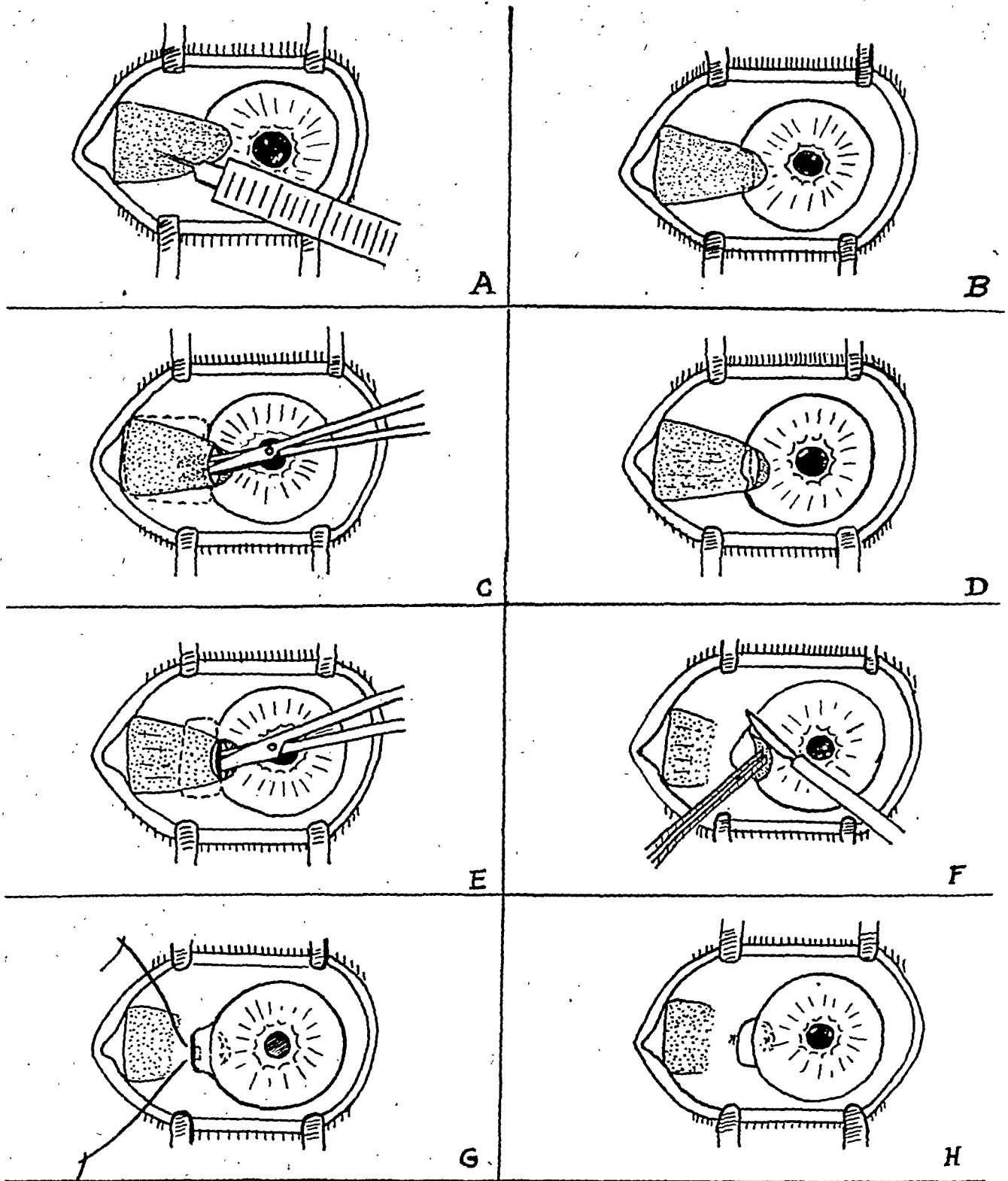
Fig. 3 (Sugar). *Steps in the operative procedure.* (A) Site of procaine injection for anesthesia. (B) Site of conjunctival incision. (C) Undermining of the conjunctiva. Broken lines indicate limits of undermining. (D) Site of incision in subconjunctival "tendinous" layer. (E) Broken lines indicate limits of area of subconjunctival layer undermined and excised. (F) Shaving of head of pterygium from cornea. (G) Insertion of suture (scleroconjunctival). (H) Suture tied leaving 3 mm. of bare sclera.

pensed with if the surgeon desires. This tends to lessen the tissue reaction considerably.

Comment. This procedure is simple enough to be done in the office, if adequate facilities for sterility are available. It is surgically sound as compared to the Mc-Reynold's operation, in which epithelium is

buried. The eye becomes pale much more quickly than with any operation in which the subconjunctival tissue is permitted to remain. The formation of the adhesion between the conjunctiva and sclera and the epithelization of the bare area are rapid.

In some cases, an adhesion of conjunctiva to the area of corneal scar, where the head of the pterygium had been, gives the impression of recurrence, but this has not been observed to continue further onto the cornea.

There has recently appeared another pterygium operation based on similar principles (D'Ombain[7]). In fact, it has been the stimulus of D'Ombain's paper which has led to the actual writing of this one.

In his procedure, the entire subconjunctival tissue is removed between the cornea and the plica semilunaris and a 5-mm., bare area of sclera left to epithelize the unsutured conjunctival edge. This procedure should lead to good results but has the disadvantage of possible injury to the horizontal rectus muscles while removing the Tenon's tissue since the internus inserts only 5.5 mm. from the limbus.

CONCLUSION

A theory is presented that the development of pterygium from pinguecula is a degenerative process in which the hypertrophic and degenerative changes in Tenon's capsule in the interpalpebral zone are considered to play the essential part. A simple, effective operative procedure based on this theory is presented.

311 Kales Building (26).

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HISTORICAL MINIATURE

Egyptian Ophthalmology

To "clear the pupil" a solution of saltpeter and ebony was used. The nature of this ailment is difficult to determine. The hieroglyphic sign for it was the crocodile (= the terrible). It may have been cataract.

Hirschberg, *Graefe-Saemisch Handbuch.*

RETROLENTAL FIBROPLASIA IN PREMATURELY BORN CHILDREN*

ANITA PEEK GILGER, M.D.
Cleveland, Ohio

The purpose of this study was twofold. The first was to determine the incidence of retrolental fibroplasia in prematurely born children, together with any factors in the development of the disease which such a survey might unearth. The second purpose was to attempt to gain a better knowledge of the clinical course of this condition by observing a group of prematurely born infants at regular intervals from birth.

Terry[1] stated that there was an apparent variation in the frequency of retrolental fibroplasia in different medical centers. It was, therefore, decided to conduct a survey in a middle-western community. In 1945, Terry[2] stated that Clifford had found in a series of less than 50 infants at the Boston Lying-In Hospital an incidence of retrolental fibroplasia of 12 percent in infants weighing 1,307 gm. or less at birth. In 1948, Clifford and Weller[3] quoted Allers as saying that 23 percent of the infants weighing between 2 to 3 pounds at birth, at the same hospital, develop retrolental fibroplasia. William and Ella Owens[4] found, in premature infants born between 1945 and 1947 at The Johns Hopkins Hospital, 5 cases of retrolental fibroplasia in 83 observed cases with birth weights of 1,899 gm. or less, an incidence of 6 percent.

Reese[5] states that there has been an apparent increase in retrolental fibroplasia in the last few years. This may possibly be due to improved survival of the babies whose birth weights were 1,814 gm. or less. He also states that 40 to 60 percent of the mothers of his patients with retrolental fibroplasia gave a history of uterine bleeding during pregnancy.

Vitamin A as a possible etiologic factor has been considered since Warkany[6] found a fibrous retrolenticular membrane in place of the vitreous in rats with maternal vitamin-A deficiency. Clifford and Weller[3] state that in their series of cases, the postnatal administration of absorbable, water-soluble vitamin A did not prevent the later development of retrolental fibroplasia.

Bakwin[7] suggested the possibility that retrolental fibroplasia was sex-linked because, out of 150 patients reported by Reese and Terry, 95 were males. Krause[8] described retrolental fibroplasia as a part of a congenital encephalo-ophthalmic dysplasia of unknown origin. He stated that, if the child was examined after the age of four years, the ocular disease rarely occurred without clinical signs of involvement of the brain.

METHOD

This survey included 229 children with a birth weight of less than 2,268 gm. (5 pounds) who were either born at, or admitted before the age of 24 hours to, the Cincinnati General Hospital during the 5-year period from January, 1943, to January, 1948. None of the infants born during this period was a private patient. Form letters or appointments on hospital discharge, seconded by home visits of public health nurses, were the methods of inducing the parents to bring the children to the clinic.

For a 6-month period, from July, 1947, to January, 1948, every infant born in the hospital weighing less than 2,268 gm. was examined within the first week of life and every week to two weeks thereafter during the hospital stay. After discharge, the babies of this group whose parents coöperated were examined at monthly intervals until the baby became at least six months of age.

In addition to this group, children born between January, 1943, and July, 1947, were

examined; but only one clinic visit was made and that at a time when the child had attained the age of one year or more.

In every case, examination consisted of inspection of the external segment of the

INCIDENCE

In the 5-year period, 1943 to 1948, there were 507 babies born at the Cincinnati General Hospital weighing less than 2,268 gm. at birth and presumably living at the

TABLE 1

INCIDENCE OF RETROLENTAL FIBROPLASIA IN PREMATURE CHILDREN

Year	Birth Weight (gm.)	Total Living	Lost or Moved		Infants Seen		Retrolental Fibroplasia	
			No.	%	No.	%	No.	%
1943	1,361 or less	1	0	25.0	0	0.0	0	
	1,362–1,814	11	3		3	27.3	0	
	1,815–2,000	33	7		6	18.2	0	
	2,001–2,268	51	8		16	31.4	0	
	Total	96	18	18.8	25	26.1	0	
1944	1,361 or less	4	1	47.3	3	75.0	0	
	1,362–1,814	15	8		6	40.0	0	
	1,815–2,000	13	3		6	46.2	0	
	2,001–2,268	23	9		8	34.8	0	
	Total	55	21	38.2	23	41.8	0	
1945	1,361 or less	4	1	18.5	3	75.0	0	7.1
	1,362–1,814	23	4		11	47.8	1	
	1,815–2,000	14	4		4	28.6	0	
	2,001–2,268	45	18		16	35.6	0	
	Total	86	27	31.4	34	39.5	1	2.9
1946	1,361 or less	14	1	12.0	12	85.7	1	5.6
	1,362–1,814	36	5		24	66.7	1	
	1,815–2,000	28	9		9	32.2	0	
	2,001–2,268	35	8		16	45.7	0	
	Total	114	23	20.2	61	53.5	2	3.3
1947	1,361 or less	6	2	17.0	4	66.7	1	11.8
	1,362–1,814	41	6		30	73.2	3	
	1,815–2,000	30	5		14	46.7	0	
	2,001–2,268	80	10		38	47.5	0	
	Total	157	23	14.7	85	54.2	4	4.7
TOTAL 1943 to 1948	1,361 or less	31	5	19.9	22	70.9	2	7.3
	1,362–1,814	125	26		74	59.2	5	
	1,815–2,000	118	28		39	33.1	0	
	2,001–2,268	233	53		94	40.3	0	
	Total	507	112	22.1	229	45.2	7	3.1

eyes and ophthalmoscopic examination following pupillary dilatation with either homatropine hydrobromide or neosynephrin hydrochloride (ophthalmic). Other examinations were performed as indicated. With very rare exceptions, the only sedation required for satisfactory examination of the infants was either formula or glucose water.

time of this study (table 1). Of this total, 156 weighed 1,814 gm. (4 pounds) or less. Of the total group, 229, or 45.2 percent, were examined; 96, or 61.5 percent of those with birth weights of 1,814 gm. or less were seen.

This higher incidence of returns was probably not due to the greater concern of the mothers of the smaller babies but to the

fact that in the lower-weight group repeated nurse visits or telephone calls were made when appointments were broken, a follow-up which time and personnel did not permit for the higher weight group. Of the total group, 112 or 22.1 percent had moved away from the Cincinnati or the post-office area and nurses had lost their addresses at the time of the study. The remaining 32.7 percent could not be persuaded to come to the clinic.

Retrolental fibroplasia occurred in 7 patients out of the total of 229 seen, an incidence of 3.1 percent. However, the disease was not seen in any children whose birth weights were above 1,814 gm. Its incidence in the 96 with birth weights of 1,814 gm. or less, who were examined, was 7.3 percent.

These percentages of incidence of retrolental fibroplasia are probably higher than they would have been if it had been possible to examine all the children available in the Cincinnati area. Of the children with birth weights of 1,814 gm. or less, there were 29 unobserved children, or 18.6 percent who were living within the Cincinnati area at known addresses at the time of the study and whose mothers received a minimum of two appointments which were broken.

These mothers had been visited by public health nurses who usually saw the children and reported no obvious gross defects of the eyes. Although it is impossible to exclude the existence of retrolental fibroplasia merely by external examination, it is unlikely that any of the 29 unexamined children had such an extensive retrolental membrane that the undilated pupillary area appeared white. If this hypothesis were taken to be true, the incidence of retrolental fibroplasia in the babies weighing 1,814 gm. or less at birth would be close to 7 out of 125, or 5.6 percent.

Of the 7 cases of retrolental fibroplasia, 2 had birth weights of less than 1,361 gm. (3 pounds) and 5 had birth weights between 1,362 and 1,814 gm. (table 2). In this study the data failed to reveal any significant difference in incidence between these two weight groups.*

TABLE 2

WEIGHT DISTRIBUTION OF OBSERVED PREMATURES

Birth Weight (gm.)	Cases Seen	Cases of Retrolental Fibroplasia
700– 799	1	0
800– 899	1	1
900– 999	2	0
1,000–1,099	2	1
1,100–1,199	5	0
1,200–1,299	7	0
1,300–1,399	8	1
1,400–1,499	10	0
1,500–1,599	13	0
1,600–1,699	17	0
1,700–1,799	24	3
1,800–1,899	24	1
1,900–1,999	18	0
2,000–2,099	29	0
2,100–2,199	41	0
2,200–2,268	27	0

Total 229

Although it may seem from Table 1 that the increase in incidence of retrolental fibroplasia from 0 to 11.8 percent in the lower weight group during the 5-year period of this study is significant, this is not the case. When a division of the examined prematures with birth weights of 1,814 gm. or less into later and earlier cases with respect to birth dates is made, the earlier half, or 48, had one case of retrolental fibroplasia; whereas, the latter half had 6 cases ($X^2 = 2.459$; $P = > 0.10 < 0.20$).

ETIOLOGIC FACTORS

In considering possible pre- and postnatal events which may affect the development of retrolental fibroplasia, only the smaller prematures (1,814 gm. or less) were investigated. This was done not only because of the fact that it was only in this group that the disease developed, but also because the heavier weight group was usually discharged from the hospital before the age of one week so that statistics concerning postnatal management and care would be dependent upon maternal memory.

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* Statistical significance has been determined in this study by the method of Chi square, using four-cell contingency tables wherever possible. Yate's correction was used in all four-cell contingency tables with small frequencies.

SURVIVAL RATES

The investigation of a possible increased survival rate in recent years of the smaller premature infants falls into two groups: (1) Survival of prematurely born infants to the time of discharge from the hospital, and (2) survival after hospital discharge to the age of six months or one year, by which time weights are broken down into three groups, it is found that the group of children with birth weights between 1,362 and 1,814 gm. does have a statistically significant increase of survivals to hospital discharge ($X^2 = 15.447$; for $n = 4$, $P = < 0.01$).

In Table 4, the known survival rate from hospital discharge to one year of age is

TABLE 3

SURVIVAL TO HOSPITAL DISCHARGE OF PREMATURES WITH BIRTH WEIGHTS OF 1,814 GRAMS OR LESS

Year Born	Birth Weight (gm.)	Infants Born Living	Infants Surviving to Hospital Discharge	% Surviving to Hospital Discharge
1943	907 or less	5	0	0
	908–1,361	16	1	6.2
	1,362–1,814	34	15	44.1
	Total	55	16	29.1
1944	907 or less	5	1	20.0
	908–1,361	13	3	23.1
	1,362–1,814	40	15	37.5
	Total	58	19	32.8
1945	907 or less	5	0	0
	908–1,361	16	5	31.2
	1,362–1,814	38	25	65.8
	Total	59	30	50.8
1946	907 or less	16	1	6.2
	908–1,361	30	13	43.3
	1,362–1,814	54	35	64.8
	Total	100	49	49.0
1947	907 or less	10	1	10.0
	908–1,361	23	5	21.7
	1,362–1,814	60	42	70.0
	Total	93	48	51.7

the existence of retrolental fibroplasia could be determined.

The rate of survival to discharge from the hospital for the 5-year period, 1943 to 1948, is shown in Table 3. Only liveborn premature infants are included, evidence of life being heart-beating or breathing. The percentage of living babies weighing 1,814 gm. or less increased from 29.1 percent in 1943 to 51.7 percent in 1947. This is not statistically significant but is suggestive that further analysis of the figures might show some significance ($X^2 = 12.310$; for $n = 4$ $P = > 0.01 < 0.02$). When the birth

shown. Those cases listed as surviving have been seen either by me or a public health nurse, or in a Babies' Milk Fund Association Clinic after the age of either six months or one year had been attained. Out of 162 discharges, 22, or 13.6 percent of the children either were lost or had moved out of the Cincinnati area before the age of one year. Only 6 or 4.3 percent of the children not lost are known to have died during the first year of life.

PRENATAL INFLUENCES

Because the observed infants who later

developed retrolental fibroplasia had normal eyes when seen in the first week of life, it has been said that the causative factor or factors would be more likely to occur during postnatal rather than prenatal life. However, the maternal histories of prematures with birth weights of 1,814 grams or less were studied for possible clues.

In Table 5, the history of bleeding prior to onset of labor is given for mothers of ob-

3. Occurrence of virus infections during pregnancy
4. Occurrence of chronic illness during pregnancy (cardiovascular disease, diabetes, tuberculosis, syphilis)
5. Cause of premature onset of labor
6. Race

When the known causes of premature onset of labor are separated, the probability

TABLE 4
SURVIVAL AFTER HOSPITAL DISCHARGE OF PREMATURES WITH BIRTH WEIGHTS OF 1,814 GRAMS OR LESS

Year Born	Infants Discharged from Hospital	Infants Known Dead before Age		% Known Deaths before 1 Year	Lost or Moved before 1 Year*
		6 months	1 Year		
1943	16	2	1	18.8†	2
1944	19	0	0		7
1945	30	1	1	6.7†	1
1946	49	0	0		5
1947	48	1	—	2.1	7
Total	162	4	2	3.7	22

* No record of deaths of these cases in city of Cincinnati.
† Two infants not included as deaths; one died at 13 and the other at 19 months of age.

served smaller prematures in the 5-year period of the study. Bleeding varied in degree from spotting to an amount requiring hospitalization and transfusion. Slight bleeding occurring at the onset of labor was not considered abnormal. The one case of retrolental fibroplasia with maternal bleeding had only two episodes of staining. In the observed group not having retrolental fibroplasia, 19.8 percent of the mothers gave a history of bleeding during pregnancy, while in the group with retrolental fibroplasia, the figure was 16.7 percent. The difference in incidence of bleeding between the two groups is not statistically significant.

The following conditions which may have something to do with the production of normal eyes or eyes with retrolental fibroplasia were studied, but the figures failed to reveal any statistically significant differences.

1. Age at delivery
2. Parity

that the difference between normal eyes and those with retrolental fibroplasia is due to any factor other than chance becomes even less than when the causes are grouped into known and idiopathic.

POSTNATAL AND OTHER FACTORS

It has been stated that the factor (or factors) causing retrolental fibroplasia probably occurs in early postnatal life. The smaller premature infant is placed in an environment which, in spite of pediatric advances in handling, is far different from the optimum which would have been maintained in utero.

In general, the smaller prematures in this study received similar management. The policy in the premature nursery has been one of adapting treatment, such as the administration of intravenous and subcutaneous fluids, to the individual case rather than one of following a routine procedure. The environment, method of regulation of temperature and humidity, and administration

TABLE 5
MATERNAL FACTORS IN RELATIONSHIP TO RETROLENTAL FIBROPLASIA[*]

	Normal	Retrolental Fibroplasia	Significance
Bleeding:			
Present	16	1	None
Absent	65	5	$X^2 = 0.122$
Not stated	3	1	$P = >.70<.80$
Age of Mother at Delivery (years)			
20 or less	28	2	None
21–30	40	5	$X^2 = 1.708$
31 or over	12	0	For $n = 2$, $P = >.30<.50$
Not stated	4	0	
Parity			
Primipara	31	0	None
Multipara	49	7	$X^2 = 2.682$
Not stated	4	0	$P = >.10<.20$
Virus Infection during Pregnancy			
Present	10	1	None
Absent	70	5	$X^2 = 0.856$
Not stated	4	1	$P = >.30<.50$
Chronic Illness			
Present	9	1	None
Absent	71	6	$X^2 = 0.748$
Not stated	4	0	$P >.30<.50$
Cause of Premature Onset of Labor			
Known	34	2	None
Idiopathic	47	5	$X^2 = 0.0832$
Not stated	3	0	$P = >.70<.80$
Race			
Colored	56	3	None
White	28	4	$X^2 = 0.734$
			$P = >.30<.50$

[*] Mothers of observed prematures with birth weights of 1,814 gm. or less, 1943 to 1948.

of oxygen and carbon dioxide have remained essentially the same during the 5-year period.

During the last three years, the diet has been changed from a usual one of breast milk or evaporated milk to a usual one of a formula relatively high in protein and low in fat according to the principles of Levine and Gordon.[9] The factor of type of diet showed no statistical significance between normal and retrolental fibroplasia cases.

During the last three years, increased amounts of vitamin K were administered following birth, but this also showed no statistically significant difference.

The infants routinely received a minimum of 2,000 units of oil-soluble vitamin D and a minimum of 100 mg. of ascorbic acid per day during their hospital stay. Neither spe-cific medications nor the presence or absence of recognized illness during the hospital stay showed statistically significant differences. Three differences occurred, however, which warrant more detailed report.

VITAMIN A

Most of the infants received added vita-min A during their hospital stay. However, from May through December, 1947, water-soluble vitamin D without vitamin A was given. The only vitamin A these babies re-ceived was that included in the formula, ap-proximately 590 units per day. This is less than the amount sometimes considered a minimum, although the actual requirements of vitamin A in the prematurely born infant are unknown.

Only the first month of life is considered in Table 6, since most of the babies had been discharged from the hospital before the age of two months. The choice of considering seven days as a dividing line was made because vitamin-A stores in the body are not so rapidly lost as are some other vitamins.[10]

TABLE 6

RELATIONSHIP OF VITAMIN A ADDED IN FIRST MONTH OF LIFE TO RETROLENTAL FIBROPLASIA IN PREMATURES WITH BIRTH WEIGHTS OF 1,814 GRAMS OR LESS, 1943 TO 1948

	Vitamin A Added 7 Days or More	Vitamin A Added 6 Days or Less*	Total
Normal	56	33	89
Retrolental Fibroplasia	1	6	7
Total	57	39	96

$X^2 = 4.4635$; $P = > 0.02 < 0.05$.
* In this group 30 prematures received no added vitamin A during the first month of life. The remaining three received oil soluble vitamin A as follows: (1) normal male, on the 30th postnatal day; (2) normal female, from the 26th to 30th postnatal day; and (3) male with retrolental fibroplasia, from the 27th to 30th postnatal day.

It could be expected that the administration of vitamin A for only seven days in the first part of the month would provide vitamin A for use in the body during the rest of the month. The difference in incidence between the groups given and not given additional vitamin A is not statistically significant.

All of the observed prematures in the series, who received vitamin A, were administered it in the oil-soluble form. Consequently, no comparison in results could be made between those receiving water-soluble and oil-soluble vitamin A.

SEX

In this survey, in the group of observed prematures with birth weights of 1,814 gm. or less 45.8 percent were males. Every case of observed retrolental fibroplasia was in a male. The predominance of the development

TABLE 7

RELATIONSHIP OF SEX TO OCCURRENCE OF RETROLENTAL FIBROPLASIA IN PREMATURES WITH BIRTH WEIGHTS OF 1,814 GRAMS OR LESS, 1943 TO 1948

	Boys	Girls	Total
Normal	37	52	89
Retrolental Fibroplasia	7	0	7
Total	44	52	96

$X^2 = 6.72$; $P = < 0.01$.
Identical twins were included in the table since affection of only one twin has been known. Only two pairs of identical twins, one boy and one girl, were observed in this weight group. If one member of each of these pairs is omitted, $X^2 = 6.77$; $P = < 0.01$.

of the disease in males in this study is statistically significant (table 7).

During the 5-year survey, only two prematures, both males, were administered testosterone (as an aid to bone maturation). Of these two, one developed retrolental fibroplasia and the other did not. Two cases are an insufficient foundation on which to draw any conclusions as to the role of testosterone. However, because of the fact that statistics indicate that retrolental fibroplasia is sex-linked, further investigation of the results of testosterone administration to prematures is indicated.

When the numbers of male prematures receiving additional vitamin A for seven days or more during the first month of life are compared with those who received less, the difference in incidence of retrolental fibroplasia is found to be not significant statistically (table 8).

TABLE 8

RELATIONSHIP OF ADDED VITAMIN A TO RETROLENTAL FIBROPLASIA IN MALE PREMATURES*

	Vitamin A Added 7 Days or More	Vitamin A Added 6 Days or Less	Total
Normal	20	17	37
Retrolental Fibroplasia	1	6	7
Total	21	23	44

$X^2 = 2.305$; $P = > 0.10 < 0.20$.
* Only first postnatal month and male prematures with birth weights of 1,814 gm. or less, 1943 to 1948, included.

	Normal Development	Probably Normal	Retarded	Total
Normal Eyes	34	5	3	42
Retrolental Fibroplasia	4	0	1	5
Total	38	5	4	47

With probably normal considered as normal, $X^2 = 3.29$; $P = > 0.05 < 0.10$.
* All children included had birth weights of 1,814 gm. or less and were less than four years of age at time of examination.

ASSOCIATED INTRACRANIAL DISEASE

Dr. James Fisher[11] examined an unselected portion of the observed children with birth weights of 1,814 gm. or less and compared them with the Yale Developmental Scale. All were less than four years of age. His results are shown in Table 9. Only 1 of the 5 children with retrolental fibroplasia whom he examined was mentally retarded. The difference between the normal cases and the retrolental fibroplasia cases is not statistically significant in this group.

REPORT OF CASES

After a retrolental membrane has developed to its final extent and especially after the eye has become phthisical, it is difficult, clinically, to distinguish this condition from other pathologic conditions. Furthermore, at these stages the appearance may offer false or no clues as to the preceding course of events. Since routine ophthalmoscopic examinations from the time of birth to the development of retrolental fibroplasia have rarely been made, the descriptions of three cases are given in detail.

The normal eye in a newborn infant is very different in appearance from eyes of children who have reached the age of one year. Pigmentation, with the exception of most Negro babies, is usually clinically absent so that the irides are a grayish "infant" blue, and choroidal vessels are prominently seen in a reddish, hazy fundus. Discs have either no cupping, or slight elevation due to the presence of Bergmeister's papilla, and they are usually a dead-white in color. Disc margins are frequently not distinct. The macula is not discernible until about the fourth postnatal month; this time is usually the same in prematurely born and full-term infants. Depending on the degree of prematurity, various degrees of persistence of the fetal vascular system are seen; in most cases these atrophy completely in the course of time.

CASE 1

History. This Negro boy, born on July 15, 1947, had a birth weight (at one-half hour of age) of 1,715 gm. (3 lbs. 12½ oz.). The mother, aged 25 years, had two full-term, normal living children, aged 6 and 7 years.

On June 4, 1947, she was admitted to a tuberculosis sanitarium with far-advanced tuberculosis of the lungs. During the pregnancy she had no history of uterine bleeding or virus infection. Kahn and Hinton serologic tests were negative, and she denied history of syphilis. She had no chronic illness other than tuberculosis. Delivery was precipitous and occurred after an estimated 7-month gestation. The mother died from tuberculosis 12 days after the birth of the baby.

The baby had no recognized illnesses during his hospital stay. Management was routine except that he received no vitamin A other than that contained in his formula for the first two months and evaporated milk for the remainder of his stay. He was discharged at the age of 3 months, 18 days, with a weight of 4,370 gm.

Eye Examinations. (Aged 10 days). External. O.U.: Lids, lacrimal apparatus, conjunctivas, corneas, pupillary size and reaction to light, and scleras were normal. Horizontal corneal diameters were 8.5 mm. Irides were pigmented.

Ophthalmoscopic. O.U.: Atrophic tags of the pupillary membranes were present. There was a good red reflex everywhere. The discs were pale, without cupping, and the margins were slightly blurred. No remnants of the hyaloid artery or tunica vasculosa lentis were seen. The retinas showed very early pigmentation. The retinal vessels were normal. There was no evidence of any retrolental fibrous tissue.

(Aged 3 weeks). External. O.U.: No change. Ophthalmoscopic. O.U.: The disc margins were now distinct, although there was no pigment outlining them. Otherwise no change.

(Aged 5 weeks). External. O.U.: No change. Ophthalmoscopic. O.U.: The color of the discs was now a normal pink and slight cupping could be seen. There was a slight increase in the retinal pigmentation. The retinal vessels, both arteries and veins, had become very tortuous; in the midperiphery many were corkscrew in shape. No aneurysmal dilatations were seen.

Since tortuosity of the retinal vessels is seen in

sickle cell anemia, a sickling preparation was made; there was no sickling.

(Aged 2 months, 11 days). External. O.U.: There was no change except for a possible faint whitish sheen in the pupillary area behind the lens.

Ophthalmoscopic. R.E.: With a plus 8D. lens, a pinkish gray tissue containing many fine blood vessels was seen in the lower half of the eye. This tissue had the clinical appearance of a detached retina. At the 6-o'clock position, projecting anteriorly from this tissue, there was a bright-red area of fresh hemorrhage. Above there was a gray area, which appeared to be thickened retina rather than detached retina; in this area no vessels could be seen, but the vitreous was hazy, obscuring it.

L.E.: Except for the area from the 10- to 12-o'clock positions a pinkish gray tissue could be seen behind the lens. From the 6- to 10-o'clock positions this was most clearly seen with a plus 10D. lens. The remainder was best seen with a plus 7D. lens. The tissue contained fine blood vessels and many fresh small hemorrhages. From the 10- to 12-o'clock positions, a gray tissue could be distinguished with a plano lens; the vitreous over this area was hazy. The interpretation was the same as that made for the right eye—thickened retina from the 10- to 12-o'clock positions and detached retina elsewhere.

In neither eye could the discs be seen. No elongated ciliary processes were seen. Tension to fingers was within normal limits. Tension was (local anesthesia, baby not crying): R.E., 25 mm. Hg with 5.5 gm. weight; L.E., 22 mm. with a 5.5 gm. weight (Schiøtz). The vessels of the retrolental membrane were not tortuous.

(Aged 3 months). External. O.U.: No change.

Ophthalmoscopic. R.E.: With a plus 10D. lens, there was a gray tissue containing fine blood vessels and old and fresh hemorrhages everywhere just behind the lens. L.E.: In the far periphery at the 8-o'clock position there was a little normal-appearing retina. Elsewhere there was a grayish vascularized tissue with fresh and old hemorrhages.

(Aged 3 months, 2 weeks). External. R.E.: For the first time a grayish white tissue with a few hemorrhages could be definitely distinguished filling the pupillary space behind the lens. L.E.: No change.

Ophthalmoscopic. R.E.: There had been no change except that the retrolental tissue had become whiter and appeared to be thicker. L.E.: The entire retina appeared to be detached, but the vitreous was so cloudy that details could not be seen.

(Aged 4½ months). External. R.E.: Tension to fingers was softer than normal. The pupil was bound down by a white secondary pupillary membrane with an irregular surface and could not be dilated with neosynephrin. L.E.: No change.

Ophthalmoscopic. R.E.: Examination could not be made. L.E.: Temporally, at the 9-o'clock position there was a grayish white tissue elevated 10 diopters. The vitreous was less hazy so that some retinal details could be distinguished. The retina was seen with a plus 1D. lens. The retinal vessels seen were not tortuous. On the surface of the

retina extending forward into the vitreous, there were grayish white areas resembling either glial or connective-tissue proliferation. There were many fresh preretinal hemorrhages.

(Aged 5½ months). External. R.E.: In the center of the cornea there was a dense white opacity about 1.5 mm. in diameter. There was iris bombé. Tension to fingers was mushy soft, and the pupil would not dilate because of the secondary pupillary membrane. L.E.: No change.

Ophthalmoscopic. L.E.: The vitreous was so cloudy that undetached retina, if present, could not be visualized. There was an old hemorrhage behind the lens.

The foster mother reported that there were transient episodes of redness of the right eye during which time the baby would rub his eye and cry. At no time while the baby was under my observation was there either conjunctival injection or positive aqueous ray.

(Aged 7 months). External. Horizontal corneal diameters were 9.5 mm. A moderately rapid searching nystagmus had developed. R.E.: The corneal opacity had enlarged. Otherwise there was no change. L.E.: Tension to fingers was soft. Otherwise no change.

Ophthalmoscopic. L.E.: The vitreous was still very cloudy.

(Aged 8 months). External. R.E.: The corneal opacity was 5 mm. in diameter. In the upper temporal quadrant of the iris there was a brush of newly formed dilated vessels. L.E.: White tissue could be seen in the pupillary area. There was no pupillary reaction to light.

Ophthalmoscopic. L.E.: There was no red reflex. The dense white triangle of tissue at the 9-o'clock position was persisting. Elsewhere there was a grayish-white tissue elevated 10 diopters and containing fine blood vessels. A complete retinal detachment appeared to have occurred in this eye also.

The baby was sent to Boston to a home for preschool blind children. He was moderately retarded physically and mentally.

CASE 2

History. This white boy, born on November 3, 1947, had a birth weight of 1,715 gm. (3 lbs. 12½ oz.). The mother was aged 34 years at the time of delivery. She had one full-term, normal child, aged 5 years.

During this pregnancy she had had staining twice, once in the third month and once a week before the onset of labor. She had no history of virus infection, chronic disease, or syphilis. The Kahn test was negative. Labor occurred spontaneously at the end of an estimated 7½-month period of gestation, was of 3 hours' duration, and presentation was right occipito-anterior. There was no known cause for the premature onset of the labor.

At birth, the left side of the baby's face appeared bruised and blue. One week after birth the infant had a moderate jaundice. He had had a fracture of his 7th rib in delivery. On December 13, 1947, the baby developed gastro-enteritis due to an un-

known cause. The baby's management during his hospital stay was routine with the exception that he received no added vitamin A, other than that in his formula. He was discharged at the age of 2 months, 11 days, with a weight of 2,325 gm.

Eye Examinations. (Aged 3 days). External. O.U.: Lids, lacrimal apparatus, and conjunctivas were normal. Corneas were very slightly cloudy, probably due to silver nitrate administered at birth. Irides were an "infant" blue, or unpigmented. Pupillary size and reaction to light and scleras were normal.

Ophthalmoscopic. O.U.: Nonpatent pupillary membranes with three arcades were present. There was a good red reflex everywhere. Discs were the same shade as the retina which was clinically unpigmented. Disc margins were very indistinct, and there was no cupping. Retinal vessels were normal. No retinal hemorrhages, remnants of hyaloid artery or posterior tunica vasculosa lentis, or abnormal retrolental tissue were seen.

(Aged 2 weeks). External. O.U.: The corneas were quite clear. Otherwise no change.

Ophthalmoscopic. O.U.: The pupillary membranes had atrophied considerably so that only a portion of the first layer of arcades was well developed. Otherwise no change.

(Aged 1 month). External. O.U.: No change. Ophthalmoscopic. O.U.: Pigment was developing in the fundus so that the choroidal vessels were no longer plainly seen except in the periphery of the fundus. Otherwise no change.

(Aged 2 months). External and ophthalmoscopic. O.U.: No change.

(Aged 3½ months). External. O.U.: No change. Irides were blue but had lost their grayish, "infant" blue appearance. Tactile tension was normal. The anterior chambers were of normal depth, and no iris synechias were present.

Ophthalmoscopic. O.U.: The pupillary membranes had not changed in appearance. Nasally, in both eyes, there was a retrolental gray tissue containing small blood vessels and elevated 10 diopters. There were no hemorrhages on the surface of this membrane which extended over a fourth of the eye and appeared to be detached retina. Elsewhere there was a poor red reflex, but vitreous opacities inhibited a detailed examination of the retina. No elongated ciliary processes were seen.

(Aged 4 months). External. O.U.: No change. The corneas were 8.5 mm. in horizontal diameter. Ophthalmoscopic. O.U.: The nasal retrolental membranes had extended to the midline. Temporally, there was no membrane, but vitreous cloudiness obscured fundus details. Otherwise no change.

(Aged 4¾ months). External and ophthalmoscopic. O.U.: No change.

(Aged 5¾ months). External. O.U.: The retrolental membranes could be seen by focal illumination. Ophthalmoscopic. O.U. There had been a little clearing of the membrane in the far nasal periphery of the right eye. Otherwise no change.

(Aged 7 months). External and opthalmoscopic. O.U.: No change.

(Aged 7¾ months). External. O.U.: The baby usually held his eyes in a depressed position, but had no searching nystagmus. Both pupils reacted to light. Otherwise no change. Ophthalmoscopic. O.U.: No further change. Vitreous cloudiness persisted.

The baby's mental development was normal. He had still not attained the physical development of a full-term infant of comparable age.

CASE 3

History. This Negro boy, born November 23, 1947, had a birth weight (at one-half hour of age) of 1,086 gm. (2 lbs. 6 oz.).

The mother, aged 27 years, had had one abortion and had one full-term, normal daughter, aged 2 years. During this pregnancy she had no uterine bleeding or virus infections. In 1946, she was told that she had syphilis and she had 60 injections during that year. Her Kahn test was negative during this pregnancy, and there was no evidence of syphilitic infection of this baby. The mother had no other chronic diseases. Labor and delivery occurred spontaneously outside the hospital, after a 5½-month gestation, as estimated by the mother.

The baby was admitted to the hospital at the age of one-half hour. His development was poor; in the first month he gained only one ounce over his birth weight. On January 27, 1948, he developed atelectasis due to bronchial obstruction of right upper and lower lobes. Suction of the trachea and bronchi caused marked improvement.

His management was routine with two exceptions. From November 24th to December 20th he received testosterone (2.5 mgm., twice daily). He did not receive vitamin A, other than that contained in his formula until he was 49 days old. He was discharged at the age of 2¾ months with a weight of 2,380 gm.

Eye Examinations. (Aged 1 day). External. O.U.: Lids, lacrimal apparatus, conjunctivas, corneas, pupillary size and reaction to light, and scleras were normal. Irides were pigmented.

Ophthalmoscopic. O.U.: Completely formed pupillary membranes persisted. There was a good red reflex everywhere through dilated pupils. Detailed fundus examination was postponed, since the baby was in very poor condition.

(Aged 2 weeks). External. O.U.: No change. Ophthalmoscopic. O.U.: The pupillary membranes had atrophied slightly. A good red reflex was present everywhere. The discs were pale with no cupping but with distinct margins. The fundi were not clinically pigmented. Retinal vessels were normal. The maculas had not yet developed. No remnants of the hyaloid artery, or posterior tunica vasculosa lentis, or retrolental fibroplasia were seen.

(Aged 1 month). External and ophthalmoscopic. O.U.: No change except for further atrophy of the pupillary membranes.

(Aged 1 month, 2 weeks). External and ophthalmoscopic. O.U.: Fundi were pigmented. Otherwise no change.

(Aged 2 months). External and ophthalmoscopic. O.U.: Only slight tags of the pupillary membrane remained. Otherwise no change.

The patient's first appointment for examination after discharge and several others were broken because of his mother's illness; so he was not seen as frequently as desired.

(Aged 4½ months). A public health nurse had noticed an occasional nystagmoid movement the preceding week.

External. O.U.: No change. Horizontal corneal diameters were 10 mm. Pupillary size and reaction to light were normal. Anterior chambers and tactile tension were normal.

Ophthalmoscopic. R.E.: The pupillary membrane remnants had completely atrophied. There was a good red reflex everywhere. The disc had distinct margins, good color, and a little cupping. The macula had developed and was normal. Vessels and peripheral retina were normal. No retrolental membrane was present.

L.E.: Pupillary membrane remnants had atrophied. In the far temporal periphery behind the lens, there was a crescent-shaped hemorrhage bounded posteriorly by retinal detachment about one-half disc diameter in width and 10 diopters in elevation. Elsewhere, there was a good red reflex. The vitreous was clear; disc and retina were as in the right eye. The retinal vessels were not tortuous.

(Aged 6 months). The mother stated that she had been noticing a difference in the size of the two eyes.

External. O.U.: The horizontal corneal diameter of the right eye was 11 mm.; that of the left, 10 mm. Otherwise no change.

Ophthalmoscopic. R.E.: No change; normal. L.E.: In the far temporal periphery, hemorrhage was still present. The detached retina had become white in color, as if fibrosis and thickening had occurred, but the extent of the detachment had increased only slightly. The vitreous was still clear. Temporally, the retina contained many white streaks. The retinal vessels were not tortuous. The disc and nasal retina were normal.

(Aged 6½ months). External. O.U.: The left pupil did not react to light, but the right did.

Ophthalmoscopic. R.E.: No change. L.E.: The vitreous had become slightly cloudy. The temporal retinal detachment had increased. Temporally up to the disc, the retina was wrinkled and elevated 2 to 3 diopters. The nasal periphery was normal.

The mental and physical development of this infant was normal.

DISCUSSION

The incidence of retrolental fibroplasia in this study appears lower than that found in Boston; however, since the percentage incidences of the Boston groups are the only figures cited, a statistical comparison cannot be made. A comparison with the incidence found by Dr. William and Dr. Ella Owens in Baltimore shows almost identical findings. In their observed cases with birth weights of 1,899 gm. or less, the incidence of retrolental fibroplasia was 6.0 percent. In this study, 7 cases of retrolental fibroplasia were found in 114 examined cases with birth weights of 1,899 gm. or less, an incidence of 6.1 percent (table 2. $X^2 = 0.00131$; $P = > 0.98 < 0.99$). In the observed groups in Baltimore and Cincinnati, the incidence of the disease is the same.

At the Cincinnati General Hospital there was a statistically significant increase in survival to hospital discharge of prematures with birth weights between 1,362 and 1,814 gm. from 1943 to 1948. However, this was not accompanied by a statistically significant increase in the number of cases of retrolental fibroplasia for the same period of time.

The incidence of retrolental fibroplasia in children given and not given additional vitamin A in the first month of life is not statistically significant in this study. However, since the probability of the observed difference being due to chance is less than 0.05, the figures indicate that a conclusive statement that vitamin A does not play a role in the development of retrolental fibroplasia in this study cannot be drawn.

The fact that in this survey more boys than girls developed retrolental fibroplasia is statistically significant. It evokes the question as to whether or not testosterone should be administered to prematurely born infants for therapeutic purposes.

Other possible etiologic factors were studied but were not found to have differences which were statistically significant. These factors were: uterine bleeding during pregnancy, age and parity of mother at delivery, occurrence during pregnancy of virus infections or chronic illness, cause of premature onset of labor, race, associated intracranial disease, vitamin A received by boys and early postnatal management and course other than those factors previously discussed.

The three cases of retrolental fibroplasia followed from birth have the following noteworthy findings:

1. External and ophthalmoscopic examinations of each baby during the first two weeks of life revealed no findings varying from those usually seen in the normal newborn premature infant. It is possible that at the very extreme periphery of the retina some pathologic process may have been present at birth. However, from the succeeding events this possibility would seem highly unlikely.

2. None of the three infants had a hyaloid artery or posterior tunica vasculosa lentis or their remnants present after the first two weeks of life. The cases observed from birth are too few to exclude the development of retrolental fibroplasia in eyes in which the hyaloid artery or posterior tunica vasculosa lentis or their remnants persist; however, it does exclude the suggested[2] role of these fetal vessels as structures producing the development of retrolental fibroplasia.

3. In one case, the first indication of any abnormality was the development of considerable tortuosity of the retinal vessels. The clinical appearance may resemble that seen in von Hippel's disease.

4. In each case, preceding the development of a retrolental membrane, elevation and detachment of the retina occurred. In two cases, hemorrhages were present on the surface of the detached retina, probably indicating some vascular disorder. After retinal detachment had persisted, the eye became white in appearance instead of gray, as if a little fibrous tissue had developed. The sequence of events in these cases seems to indicate that the retina is primarily involved in the formation of the membrane rather than secondarily involved, which was the earlier conception.[12, 13]

5. In all three cases varying degrees of vitreous cloudiness were observed. This may indicate the existence of an underlying retinitis or choroiditis.

6. In no cases, except after the development of shallow anterior chambers, synechias, and glaucoma, was there any injection of the conjunctival vessels or positive aqueous ray. This would seem, in the three followed cases, to indicate the absence of an anterior uveitis in the development of retrolental fibroplasia.

Elongated ciliary processes were seen only in the patients examined after the retrolental membrane was completely developed.

SUMMARY

1. A survey for retrolental fibroplasia in 229 prematurely born children weighing less than 2,268 gm. at birth during a 5-year period was made in Cincinnati. No cases of retrolental fibroplasia were found in the group weighing above 1,814 gm. at birth. In 96 cases with birth weights of 1,814 gm. or less, 7 cases, or 7.3 percent, were found to have retrolental fibroplasia.

2. In this study the predominance of boys over girls among the infants affected with retrolental fibroplasia was statistically significant.

3. The following factors were considered in the etiology of retrolental fibroplasia: uterine bleeding during pregnancy, age and parity of the mother at delivery, occurrence of virus infections or chronic illness during pregnancy, cause of premature onset of labor, race, associated intracranial disease, administration of vitamin A in early postnatal life, and other factors in early postnatal management and course. The difference in the influence of these factors in affected and nonaffected prematures was not sufficient to be statistically significant and, therefore, the development of retrolental fibroplasia in this series cannot be attributed to them.

4. A description was given of three cases followed from birth until the development of retrolental fibroplasia.

2065 Adelbert Road (6).

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AMPUTATION NEUROMA IN THE ORBIT*

FREDERICK C. BLODI, M.D.
New York

Although true neuromas are rather uncommon, amputation or traumatic neuromas not infrequently develop at the severed end of a nerve trunk. These neuromas are really only a proliferation of the nerve fibers and of the connective tissue. They represent a clubbed overgrowth of coiled trunks at the extremity of the severed nerve. The local thickening may simulate a neoplasm.

When it was first proved that these amputation neuromas were not true neuromas, they were believed to be connective-tissue tumors, in which the nerve fibers play a minor and completely passive role. This theory (Goldmann,[1] Finotti[2]) assumed that only the connective-tissue fibers proliferate, while the nerve fibers, at the most, only elongate.

We know now that the connective tissue of the nerve is the first to proliferate. This connective tissue of the endo-, peri-, and epineurium is usually the main part of these neuromas. But into this mass of mesodermal tissue the nerve fibers push their way. The axis cylinders elongate, branch, and ramify into the connective tissue. As they are prevented by the surrounding tissue from growing straight forward, they form twisted bundles of medullated or nonmedullated fibers. The newly formed axis cylinders may be provided with myelin sheaths, because the nuclei of this sheath multiply also. The amputation neuroma, therefore, is essentially a regenerative overgrowth, similar to changes in simple regeneration of nerve trunks. Some authors nevertheless attribute to it a certain neoplastic character.

Amputation neuromas are always present after a certain time in an amputated limb. They are painful only when they are constantly pressed upon or pulled by the surrounding tissue. Not only the severed nerve of an extremity can give rise to such a neuroma, but also the cut nerves of the trunk, such as the intercostal nerves (Gouverneur[3]) and the sympathetic nerve

(Leriche and Fontaine[4]).

There are few reports of amputation neuromas in the orbit. This is surprising, since the nerves of the orbit are often cut in various operations. They should especially be expected to occur after enucleation of the bulb and after exenteration of the orbit. There is no reason why the ciliary nerves should be an exception in this regard. Apparently these neuromas are seldom the cause of neuralgias in the orbit, as they are not exposed to any mechanical trauma. Also histologic examinations of the orbit are rarely made after enucleation or exenteration. The histologic examinations which have been reported (Bock,[5] Sattler[6]) were performed too early after the operation to allow the development of an amputation neuroma.

REVIEW OF LITERATURE

The first case of an intraorbital traumatic neuroma was described by Bietti,[7] in 1900. He discussed the regeneration of the nerves after opticociliary neurectomies. In one of his histologically examined cases he found a retrobulbar neuroma in the scar tissue. It was composed of connective tissue and thick, mostly myelinated, intertwined nerve trunks, forming a nodule.

Ten years later Loehlein[8] examined histologically a series of patients after opticociliary resection performed because of pain or as a prophylaxis against sympathetic ophthalmia. In 2 of his 6 cases he found an amputation neuroma behind the globe.

Adamantiadis[9] found an amputation neuroma in the orbit five years after an operation for a hydatid cyst. This neuroma caused considerable pain and was the size of a big hazelnut. The nerve fibers of the neuroma were mostly myelinated.

Recently Babel and Valerio[10] reported the first case of an amputation neuroma after an enucleation. It caused neuralgia four years after the operation. The tumor was the size of a small nut and was connected with the optic-nerve stump. All the fibers were nonmyelinated.

REPORT OF A CASE

A 3-year-old Negro boy, J. W., was admitted to the Institute of Ophthalmology on the service of Dr. A. B. Reese. For the previous 6 or 7 months, his grandmother had noted that the right eye looked peculiar. Except for the eye, examination showed the child to be healthy.

Ophthalmic findings. Right eye: The cornea was somewhat steamy. The anterior chamber was shallow and in its lower angle, in the region between the 5- and 6-o'clock positions, were some grayish white nodules. The iris was atrophic and several similar nodules were scattered over its anterior surface. Back of the lens was an orange reflex that occupied the whole pupillary area. The lens was clear, but pushed forward. The right globe was larger than the left one and showed a mild ciliary injection.

The left eye was normal; the fundus examined under general anesthesia showed no lesions.

X-ray films showed the typical mottled shadow of calcium density in the right orbit and none in the left. The optic canals were normal (Dr. R. L. Pfeiffer).

The diagnosis of retinoblastoma of the right eye was made and the globe with about 12 mm. of the optic nerve was enucleated. No implant was placed in the orbit.

The microscopic section revealed a retinoblastoma with total destruction of the retina. The choroid was invaded near the disc and near the ora serrata. Tumor cells were seen in the anterior chamber. The papilla of the optic nerve was densely infiltrated with tumor cells, which also grew through the lamina cribrosa. Additional islands of these cells were found farther behind the bulb in the optic nerve but the operative section was beyond the nerve invasion.

Postoperative course. Two months after the enucleation, there was noted in the apex of the right orbit a fullness which seemed to be somewhat more than could be accounted for by the muscle funnel. As the microscopic slides of the bulb did not show
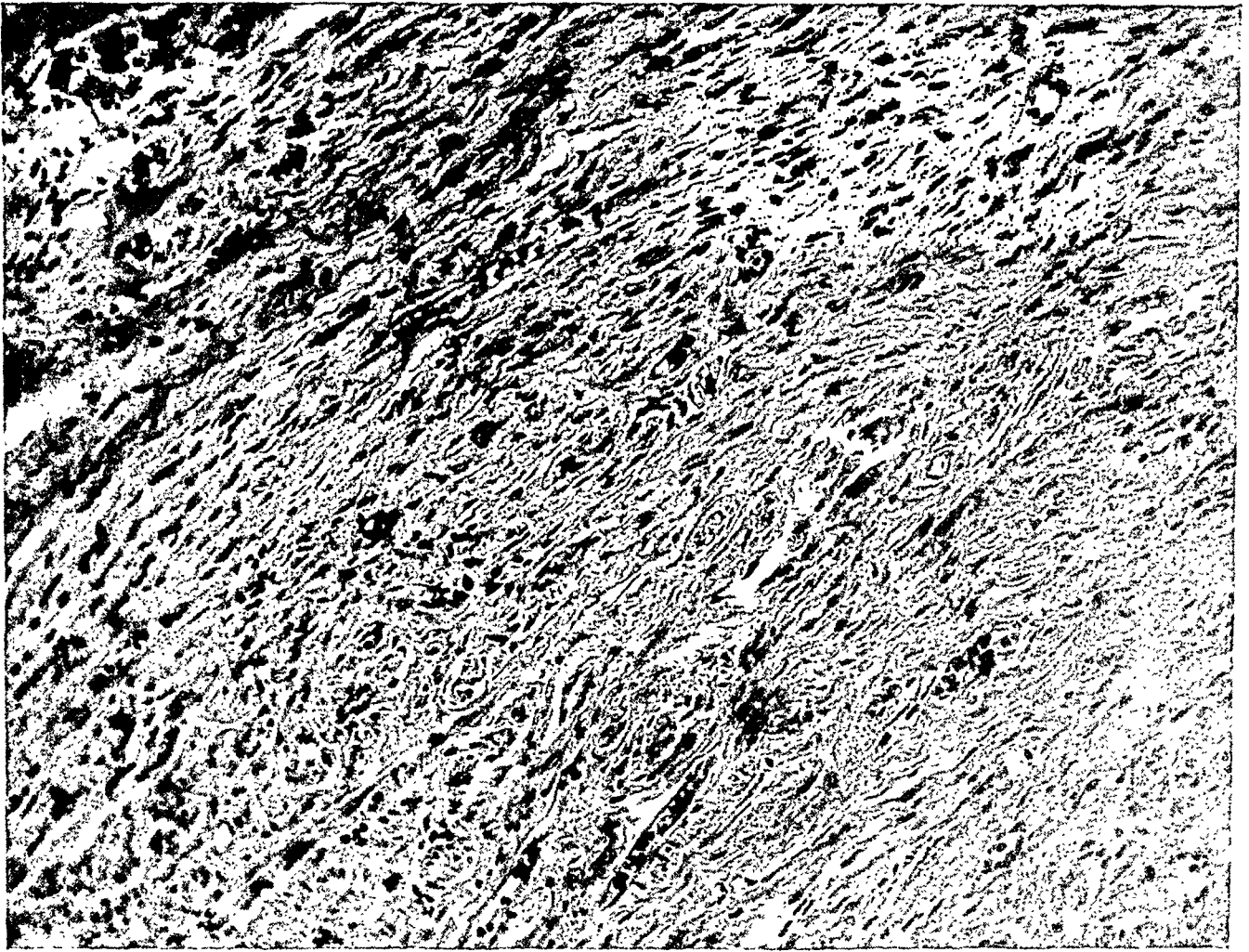
Fig. 1 (Blodi). Microphotograph of a section through the amputation neuroma.

any extraocular extensions and the operative section was beyond the tumor invasion of the optic nerve, a recurrence did not seem probable.

The boy was not back for observation at the appointed time and only returned again to the clinic four months later. At this time a large, firm, sharply demarcated, freely movable mass was palpable in the middle of the right orbit. This mass measured about 30 to 35 mm. in diameter and was not painful. It lay in the muscle funnel and was not attached to the bone or surrounding structures. No preauricular or cervical lymph nodes were palpable. A recurrence of the retinoblastoma was diagnosed and the boy was again admitted to the hospital.

An exenteration of the right orbit with skin graft was performed. The postoperative course was uneventful. A part of the spec-

imen of the exenteration was prepared as a biopsy. It was the part of the tissue adjacent to the apex and it did not differ in consistency from the rest of the intraorbital contents.

The microscopic examination of the specimen revealed, to our great surprise, that this part was not a recurrence of the retinoblastoma, but an amputation neuroma (fig. 1). The nodule consisted of a mass of connective tissue and nerve fibers.

Centrally, the nerve fibers built up thinner trunks, which were densely interwoven with the connective-tissue fibers. These nerve trunks were twisted in all directions and crossed each other, so that on every slide they were cut transversely, longitudinally, and obliquely.

The connective tissue was dense and consisted of bundles of fibers, which were

similarly twisted. Toward the periphery of the nodule there was a preponderance of connective tissue which became denser and contained many capillaries and larger vessels. The nerve fibers were here arranged in larger trunks.

The nodule was poorly demarcated and had no capsule. It was surrounded by muscle tissue and by vessels. The muscle tissue was sharply demarcated from the nodule only in some places. In most parts the nerve fibers invaded the muscle tissue and spread among the muscle fibers, sometimes forming larger nerve trunks.

The major part of the intraorbital mass was prepared in the usual way. It showed a typical recurrence of a retinoblastoma. The tumor formed two nodules just beneath the conjunctiva. In the inferior periphery was a markedly thickened nerve running backward and becoming twisted. Apparently this was the place from which the biopsy was taken.

DISCUSSION

The formation of an amputation neuroma in the orbit is certainly not as rare as is generally supposed. Such a neuroma might arise after any operation during which larger nerves are severed. In the orbit, it is presumably generally small and rarely causes neuralgic pain. The reason it is not more often found is that it does not cause symptoms and histologic examinations of the orbit after an operation are rarely performed. Amputation neuroma can easily be overlooked, especially in those cases in which the enucleation was not performed because of a malignant tumor and there is no reason to examine the orbit postoperatively. It is also probably difficult to palpate such a small tumor when there is an implant in the orbit.

In our case, the amputation neuroma reached a considerable size within seven months after the enucleation, which is rather early. Amputation neuromas have been recorded developing between 16 months and 54 years after an operation (Jedwabnick[11]). It may be that the youth of the patient and the keloid tendency of his race were related to the rapid growth of the regenerative process. The early detection of the tumor was due to the fact that the patient was watched for a recurrence after an enucleation for retinoblastoma.

SUMMARY

The literature of amputation neuromas in the orbit is reviewed.

A case of amputation neuroma following an enucleation for retinoblastoma is reported.

635 West 165th Street (32).

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HERNIATION OF THE ANTERIOR HYALOID MEMBRANE FOLLOWING UNCOMPLICATED INTRACAPSULAR CATARACT EXTRACTION*

ALGERNON B. REESE, M.D.
New York

Following an uncomplicated intracapsular cataract extraction the anterior hyaloid membrane may herniate toward the anterior chamber. If the membrane rests against the cornea or pushes the iris forward, there may arise various sequelae which will be discussed in this paper. It should be emphasized that the observations given are based on intracapsular extractions with no complications at the time of the operation and with normal restoration of the anterior chamber.

At the time of the first dressing or later there may be a central, poorly demarcated, disc-shaped opacity of the cornea. The opacity is located around the posterior surface and is accompanied by wrinkling of Descemet's membrane and some edema of the stroma.

If the anterior chamber is extremely shallow or absent, the opacity may be more extensive and not confined to only the central portion of the cornea. An examination of these cases under magnification and preferably with a slitlamp reveals the hyaloid membrane to be in apposition to the cornea. The contact of the hyaloid membrane with the cornea is a cause of so-called "striate keratitis" following intracapsular cataract extraction.

In these cases, particularly if there has been a round-pupil extraction, a strong miotic such as D.F.P. (di-isopropyl-fluorophosphate) should be used. If the herination is large, the miotic may not accomplish a complete regression of the hyaloid membrane but may leave a collar-button-shaped knuckle extending through the pupillary area. In such a case the patient should be in bed, lying on the back, and the pupil should be dilated with neosynephrin (10 percent) and reconstricted with the miotic. These measures usually accomplish a complete regression of the membrane and a clearing of the corneal opacity, edema, and wrinkling of Descemet's membrane, as well as a prompt whitening of the eye.

If the case proves intractable, the patient should be put to bed lying on the back, the pupil should be dilated with neosynephrin, and air or Ringer's solution should be injected into the anterior chamber followed by the instillation of D.F.P. The latter is indicated in the presence of a round pupil in order to lock the hyaloid membrane out of the anterior chamber.

This type of "striate keratitis" does not occur in cases of round-pupil extraction so long as the pupil is well constricted. In these cases the condition appears after the first dressing when the pupil has been dilated with atropine or some other mydriatic. In order to overcome the atropine promptly, we have employed D.F.P.

A pupil which has been small may dilate when the herniation of the membrane occurs, and a pupil dilated by a herniated membrane may not easily constrict.

When the membrane touches the cornea, it usually causes some irritation of the eye, giving the clinical appearance of a very mild iridocyclitis. Besides the slight redness of the eye and the corneal changes, lacrimation and, to a lesser extent, photophobia are noted. This combination is often interpreted as a mild postoperative iridocyclitis and is treated by mydriatics, especially atropine. The use of miotics and other measures when necessary causes the condition to clear promptly.

The apposition of the hyaloid membrane to the corneal surface seems to disturb the endothelium sufficiently to permit aqueous

to enter the cornea and thus produce edema of the stroma and overlying epithelium, particularly over the site where the hyaloid touches the cornea. Also, at the site of the apposition and in the region immediately adjacent to it, there is clouding and wrinkling of Descemet's membrane. If cornea guttata is present, so that the eye has the potentialities of an endothelial dystrophy, the apposition of the hyaloid causes more corneal changes than otherwise and may even lead to some permanent opacification.

Usually the herniation of the hyaloid membrane disappears spontaneously, and the membrane assumes a normal position in the pupillary area. When the membrane lies at the level of, or back of, the pupil, it usually shows a wrinkling. When it herniates into the anterior chamber, it usually presents a smooth, rather tense surface.

Kubik,[1] from an examination at the time of discharge of 526 cases of intracapsular extractions, found in 169 cases that the anterior hyaloid membrane projected flatly or in the form of a hemisphere. In the follow-up examinations he frequently could no longer see the protrusion of the hyaloid membrane. Vannas[2] could not give exact information regarding the frequency and rapidity of the recession of the herniation of the hyaloid membrane because he did not have a sufficient number of follow-up examinations.

In studying the anterior hyaloid membrane following intracapsular cataract extraction, there occurred an occasional instance in which a spontaneous rent in the membrane was noted months after the extraction. The membrane thinned out and, in the central portion where it was missing entirely, the vitreous protruded into the anterior chamber and over the surface of the iris.

Straight vitreous in the anterior chamber in these cases, or in those cases in which vitreous is lost at the time of operation, has not in my experience led to corneal changes.

From an examination of 32 eyes which had had intracapsular cataract extraction without loss of vitreous, Vannas found 10 cases with tears or holes in the anterior hyaloid membrane during a period of from 2 months to 4 years following the extraction. He felt that the hyaloid membrane more often showed a spontaneous rent in eyes in which the vitreous was diseased because a vitreous which became liquefied could manifest the same process by a weakening or even liquefaction of its hyaloid membrane. As most of the rents in the hyaloid membrane were located in the region of the pupillary margin, he speculated as to whether or not the action of the pupil could have had a slowly progressive traumatic effect.

Vannas found in 23 percent of the eyes with uncomplicated intracapsular cataract extraction that the anterior hyaloid membrane showed a concave surface and remained at the level of the pupil or even behind the pupillary border, and that in 61 percent of the eyes the height of the postoperative herniation of the anterior hyaloid membrane ranged from one fourth to one half the depth of the anterior chamber. In 9 percent of the eyes the anterior hyaloid membrane reached the posterior corneal surface. This author makes no mention, however, of corneal changes consequent to this herniation. His observations were made from the 7th to the 9th postoperative day.

Vannas also observed in his series of cases three instances in which during the period of observation with the slitlamp there was rapid alteration in the position of the anterior hyaloid membrane. For no apparent reason the membrane would alter its position from a state of herniation extending half the depth of the anterior chamber to a recession behind the pupillary border, forming a groove directed backward as deep as the hernia had been forward. He considered it possible that these fluctuations might be due to contraction and dilatation of the sphincter muscle of the iris, but that a more probable explanation was the state of contraction of the muscles composing the muscle funnel. He stated, however, that when these to-and-

fro movements of the vitreous are observed with the slitlamp, they seem to be entirely spontaneous.

The failure of the anterior chamber to restore, or the loss of the anterior chamber after it has been restored, following an intracapsular cataract extraction, may be due to advancement of the hyaloid membrane into the anterior chamber. Often a leaky wound is thought to be the cause of the absent chamber, but proof that this is not always the case is the fact that, if measures are taken to promote a retraction of the hyaloid membrane, the anterior chamber promptly restores, the corneal changes clear, and the symptoms subside.

An illustrative case is a round-pupil intracapsular extraction in which the anterior chamber was lost after it had been present for 12 postoperative days. Coincident with the loss of the chamber, there was increased redness of the eye, photophobia, lacrimation, and cloudiness of the cornea with wrinkling of Descemet's membrane. Examination with the slitlamp showed the hyaloid membrane against the posterior surface of the cornea. D.F.P. was instilled in the eye, the pupil contracted, the hyaloid membrane receded from the cornea, and, within five hours, the anterior chamber was restored, the cornea had cleared, and the symptoms had subsided.

After the cornea cleared, a choroidal detachment could be seen. The following day the pupil was dilated somewhat and the hyaloid membrane protruded but not so far as the cornea. D.F.P. was employed again and it has not been required since. The ability to influence a herniated hyaloid membrane by an intact iris is a distinct advantage of a round-pupil extraction. In cases of combined extraction the situation must be met by an injection of air into the anterior chamber.

There are rare instances in which recurrent herniations of the hyaloid membrane occur across the anterior chamber. These may take place any time, even up to years following the operation. When the membrane touches the posterior surface of the cornea, it causes a slight irritation of the eye with lacrimation, some photophobia, and even some discomfort or slight pain. The herniation may regress spontaneously, may recur, or may become permanent. These eyes usually show vitreous opacities and other indications of a very mild iridocyclitis which has apparently occurred as the result of the herniated membrane. Secondary glaucoma may ensue.

In one uncomplicated intracapsular cataract extraction there occurred even five years after the operation a slight congestion of the eye, vitreous opacities from a mild iridocyclitis, and reduction of the vision from 20/15 to 20/70. The only explanation I could find for this occurrence was that the anterior hyaloid membrane touched the cornea in the upper outer quadrant and produced corneal edema with epithelial stippling. The fact that there was some cornea guttata present may have aggravated matters. The hyaloid membrane became permanently adherent to the cornea over one area, and four years later the corneal edema and epithelial stippling had increased, some permanent scarring had ensued, and the intraocular pressure was elevated to 35 mm. of Hg (Schiøtz).

If the anterior hyaloid membrane does not retract spontaneously, or as the result of therapeutic measures, a permanent corneal opacity develops. This occurs because of the protracted period in which the membrane is in apposition to the cornea. Supposedly it may be facilitated by some trauma to the endothelium at the time of the operation. This trauma may be in the nature of corneal buckling when the lens is delivered, undue rubbing of the lens capsule across the posterior corneal surface at the time of the extraction or injuring of the endothelium with forceps or other instruments at the time of the operation. Thus, permanent scarring of the cornea ensues and the edema of the corneal stroma, as well as of the overlying epithelium, may persist indefinitely.

One case was observed in which the mem-

brane was in contact with the cornea for 3 months and caused corneal changes which cleared entirely when the membrane retracted. This eye was treated as a mild postoperative iridocyclitis and so atropine was employed. After the nature of the condition was appreciated, D.F.P. was used alternately with neosynephrin. The membrane retracted, the eye promptly whitened, and the cornea cleared.

When the membrane is permanently adherent to the corneal surface, the membrane may become thicker and denser adjacent to the site of the adhesion. This is thought to result from proliferation of the corneal endothelium over the surface of the adjacent hyaloid membrane.

If a permanent corneal opacity seems imminent in the pupillary area or adjacent to it, I think an attempt should be made to free the hyaloid membrane from the posterior surface of the cornea with a spatula. After this is done, air or Ringer's solution should be injected into the anterior chamber. If a round pupil is present, D.F.P. or some other strong miotic should be used with the patient in bed lying on the back. If the membrane cannot be freed from the cornea, I believe a deliberate rupture of the membrane would be beneficial.

Besides the usual type of iris prolapse* following cataract extraction, there is another type caused by the herniation of the anterior hyaloid membrane which pushes the iris ahead of it into the separated edges of the wound. The onset is insidious: it is not accompanied by pain and seldom by hyphemia. This may occur any time following the operation and tends not to be progressive. If operative measures are employed to correct it, an excision of the prolapsed

iris is accompanied by little or no escape of aqueous and, behind the iris, can be seen the anterior hyaloid membrane herniating toward the wound. Unless care is taken, this membrane may be ruptured. There is some doubt in my mind as to whether or not this type of iris prolapse requires a surgical repair.

If the anterior hyaloid membrane herniates toward the operative wound over the site of an iris coloboma, there results merely some degree of separation of the wound lips. Frequently there is also some cloudiness of the cornea adjacent to the wound. Calhoun[2] believes this is sometimes confused with early epithelization of the anterior chamber. After a round-pupil, uncomplicated, intracapsular extraction the iris will sometimes develop a coloboma at one site some weeks to months following the extraction. In such cases there has been no iris prolapse but merely a gradual development of a coloboma. At least in some instances this is due to a herniation of the anterior hyaloid membrane which pushes the iris peripherally, causing some degree of inversion or recession.

Secondary glaucoma may ensue because the anterior hyaloid membrane herniates sufficiently at the periphery to advance the iris and block the angle, or because the membrane itself blocks the angle over the site of a coloboma of the iris. When the anterior chamber fails to reëstablish or is lost following the extraction due to the forward protrusion of the hyaloid membrane, glaucoma may occur because anterior synechias are produced.

In these cases the rational treatment seems to be the freeing of the membrane from the corneal surface with a spatula, a cyclodialysis operation with injection of air into the chamber, and the use of a strong miotic when a round pupil is present. If the membrane cannot be freed from the cornea by the above measures, I am not sure that it would not be wise deliberately to rupture the anterior hyaloid membrane.

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*I refer to the type which occurs characteristically from the 4th to the 6th postoperative day and is caused by the fact that the wound cannot withstand the restored intraocular pressure and ruptures with escape of aqueous which pushes the iris into the wound. This is accompanied by sudden pain and usually by a hyphemia. If the prolapsed iris is not repaired, the prolapse becomes more extensive. An excision of the iris is followed by a gush of aqueous.

The glaucoma that may ensue following a round-pupil extraction may be due to the fact that the membrane protrudes in a pyramidal fashion through the pupillary area and thus causes the ball-and-valve effect described by Chandler.[4] The observation in one case supports this mechanism: in this case the hyaloid membrane herniated through the pupillary area but not so far as the posterior surface of the cornea. Glaucoma was present and there was an iris bombé so that, particularly in the periphery, the iris extended forward almost to the posterior surface of the cornea.

In such a case a dilatation of the pupil, followed if possible by a constriction of the pupil, may suffice to relieve the glaucoma provided it has not been of too long standing.

The incidence of glaucoma is said to be less following a simple intracapsular extraction than following a combined intracapsular extraction.[5] Following a combined extraction, the hyaloid membrane herniates more frequently and farther into the anterior chamber than following a simple extraction. This seems to be due to the fact that the intact iris offers support to the membrane. This, therefore, may be a factor in the lower incidence of glaucoma following simple extraction.

In order to establish the representative character of the cases from which these observations have been made, I have analyzed 100 consecutive cataract extractions performed by me just prior to writing this paper. This series includes, therefore, the complicated as well as the uncomplicated cases.

There were 10 glaucomatous eyes, 7 of which had had 1 or more filtering operations; 4 radiation cataracts; 2 eyes with old uveitis; 2 eyes with neurodermatogenous cataract; 1 cataract complicating retinitis pigmentosa; 1 cataract associated with detachment of the retina; and 1 cataract complicating malignant myopia. The complicated cataracts, therefore, were 21 percent. Ninety-two percent of the lenses were delivered in

capsule. This includes 2 cases in which the capsule ruptured as the lens came through the wound. No capsule and no soft lens matter remained in the eye, and this was confirmed by the postoperative course. A third case in which the capsule ruptured as the lens came through the wound was not considered a delivery in capsule because some capsule remained in the eye and necessitated reëntering the anterior chamber to remove it.

Vitreous was lost at 4 operations, or 4 percent. Two of these were in the complicated group, one being a case of malignant myopia of over 20 diopters in which watery vitreous appeared at the time of the keratome section.

DISCUSSION

The anterior hyaloid membrane normally extends from the base of the vitreous around the posterior chamber and makes contact with the lens at a site termed the "ligamentum hyaloidea capsularis." This membrane, which is much thicker than the posterior membrane, is a definite, rather dense, thick structure composed of a condensation of the vitreous elements. There is some histologic evidence to indicate that the membrane has a somewhat laminated structure. Outstanding characteristics of the membrane are its distensible and elastic properties.

At the time of a cataract extraction the membrane may bulge through the operative section. As the result of proper maneuvers, this herniation may retract and assume its normal or near-normal position. Following a contusion to the eye, the zonules may be ruptured and the anterior hyaloid membrane may herniate into the anterior chamber, the resultant appearance being one of a well-demarcated, globular mass which may recede or remain.

The anterior hyaloid membrane is normally in contact with the lens at the site of the ligamentum hyaloidea capsularis. It must be assumed that ordinarily this union is

merely one of apposition. Otherwise, if there were a firm ligamentous union, a rent would be torn in the anterior hyaloid membrane when an intracapsular extraction was done. There must, however, be variations in the degree of union between the membrane and the lens capsule. Even though in the majority of instances it may be merely one of apposition, there must be instances when an actual union of the two exists.

Thus, in these cases, when an intracapsular extraction is performed, the removal of the lens pulls away at least some of the lamellae of the anterior hyaloid membrane. If, then, this should occur, it may weaken the anterior hyaloid membrane and, therefore, predispose it to ectasia even under the normal vitreous pressure.

Likewise, there must be rarer instances in which a firm adhesion exists between the two. In these cases the removal of the lens causes an actual tear in the hyaloid, and this may account for the times when the delivery of the lens is followed by normal-appearing vitreous not under pressure.

For our discussion here, however, we are interested in the possibility that such a lens extraction may reduce the lamination of the hyaloid and thus weaken it. Clinically, evidence in support of this occurrence is the fact that under the slitlamp the thickness of the anterior hyaloid membrane following intracapsular extraction seems to vary considerably. In some instances it is even difficult to see. In others it is absent over an area where the vitreous is seen protruding into the anterior chamber through a rent or hole in the membrane.

Vannas found upon examination of 100 recent cases of intracapsular cataract extraction without loss of vitreous that there were 8 instances in which he could detect with the slitlamp a tear in the anterior hyaloid membrane.

It appears, therefore, that the anterior hyaloid membrane may be torn at the time of operation without loss of vitreous provided there is no vitreous pressure present. This tear or hole must be caused by an adhesion at the site of the ligamentum hyaloidea capsularis.

There are rare examples, particularly in complicated cataracts, perhaps as a result of inflammatory adhesion, in which there is a very firm adhesion between the posterior lens capsule and the anterior face of the hyaloid membrane. When such a union is firm, the surgeon appreciates it at the time of the intracapsular extraction because, as the lens comes forward, there is a feeling of an advancement of the entire vitreous body with it. In such an instance it may be necessary to peel or separate the hyaloid membrane from the lens capsule in order to remove the lens.

In the herniation of the anterior hyaloid membrane following an intracapsular cataract extraction, I believe an important factor is the change in the vitreous volume. It is necessary to assume such an occurrence to explain the transitory and even recurrent nature of the herniation. Lindner[5] claims that, following every cataract extraction as well as in all fistulizing eyes, there is a posterior detachment of the vitreous due to shrinkage.

The shrinkage of the vitreous may be due to aqueous replacement which in the aphakic eye is greater than in the phakic eye. Later, if the vitreous takes on fluid and regains its former volume, or even a portion of it, the anterior hyaloid membrane may protrude into the anterior chamber if the posterior vitreous detachment still persists.

It seems to me that a decrease in the lamination of the anterior hyaloid membrane (thus a thinning) as well as an increase in the vitreous volume must be assumed to explain the various manifestations of the herniation. The increase in the vitreous volume might explain the usual cases in which the hyaloid membrane protrudes straight through the pupillary area, but alone it would not explain the other cases in which the hyaloid membrane protrudes at a site away from the pupillary area. In these cases

it appears that a localized weakening of the membrane must also be assumed.

An instructive case was one in which the capsule broke after the lens had been dislocated over the lower one third. Postoperatively the patient developed a herniation of the anterior hyaloid membrane over the lower one third at the site where there was no remaining capsule. The membrane touched the cornea and produced a corneal opacity and edema at this site. The explanation must be that the anterior hyaloid membrane bulged at the site of least resistance when the vitreous volume was regained.

There are many who believe that, following a cataract extraction or a fistulizing operation, a choroidal detachment occurs secondary to a shrinking of the vitreous. If such is the case, the incidence of choroidal detachment should be less in extracapsular extraction than in intracapsular extraction. This is assumed because, when the vitreous regains its volume, the presence of the capsulozonular barrier prevents it from protruding into the anterior chamber. Therefore, it must expand posteriorly and decrease the posterior vitreous detachment, and thus the choroidal detachment. In other words, the anterior hyaloid membrane protrudes into the anterior chamber because this is the course of least resistance when the vitreous volume is replaced.

Von Sallmann[7] made some interesting observations on the behavior of the anterior hyaloid membrane following uncomplicated intracapsular cataract extraction. He noted that at the time when a detachment of the choroid is fully developed there is a definite herniation of the hyaloid membrane into the anterior chamber. When the choroidal detachment begins to subside, the bulging of the anterior hyaloid membrane recedes. This recession of the choroidal detachment and the recession of the herniated anterior hyaloid membrane go hand in hand until finally there is an actual depression or concavity of the hyaloid membrane behind the plane of the iris. This phenomenon was not noted in all cases of detachment of the choroid but only in those which regressed rapidly.

After the choroid becomes completely reattached, the recession of the anterior hyaloid membrane disappears, and the membrane assumes a normal position. The changes in the position of the anterior hyaloid membrane are coincident with those of the choroidal detachment and take place over a short period, the longest being several days.

Von Sallmann explains the recession of the previously protruding hyaloid membrane coincident with the reattachment of the choroid as follows: When the reattachment of an extensive detachment of the choroid proceeds rapidly, the regulation of the fluid absorption by the vitreous is not sufficiently rapid to prevent a temporary reduction in the vitreous volume. In this process the vitreous, which is adherent to the internal ocular structures, follows the receding choroidal surface, and this is manifested on the face of the vitreous by a retraction.

Lindner[6] integrates this phenomenon with his conception of a detachment of the choroid produced by a shrunken vitreous body in the following manner: The action of the vitreous on the choroid is generally horizontal, thus giving rise to the well-known manifestation of a choroidal detachment nasally and temporally. When the filtration of the operated eye, and therefore the abnormal production of aqueous, ceases, the pressure within the eye returns to normal. The vitreous thus tends to regain its normal volume. At this stage, however, any choroidal detachment present begins to recede, and the absorption of the subchoroidal transudate is apparently more rapid than the increase in vitreous volume, so that the anterior hyaloid membrane temporarily is retracted.

Further interesting observations were made by von Sallmann:[7] In a patient with secondary glaucoma following an uncomplicated intracapsular extraction, a cyclodialysis operation was performed and, at the time when the intraocular pressure was normalized as a result of the glaucoma op-

eration, he noted a herniation of the anterior hyaloid membrane into the anterior chamber.

Moderate pressure upon the eye through the upper lid caused the herniation to project farther forward, and fine wrinkles in the surface of the membrane disappeared. Following massage of the eye for one minute, the hyaloid herniation bulged farther and the membrane appeared more tense. Five minutes later the hyaloid membrane had receded behind the plane of the iris and showed wrinkling. Twenty-five minutes later the membrane had receded still farther behind the plane of the iris. One hour later the hyaloid membrane again herniated to the same degree to which it had before the massage was done.

The drainage of aqueous occasioned by the cyclodialysis operation ceased to function later, and the intraocular pressure rose to 50 mm. Hg (Schiøtz). The anterior hyaloid membrane lay behind the plane of the pupil. Pressure upon the globe through the upper lid caused the membrane to bulge markedly into the anterior chamber, but upon release of the pressure the hernia returned slowly to the level of the pupil. After massage of one minute the membrane still remained at the level of the pupil.

These observations indicated that, during the time in which the cyclodialysis operation was effective, the pressure upon the eye, as well as the massage, caused a definite increase in the extent of the already bulging hyaloid membrane. When the cyclodialysis operation became ineffective, the pressure and the massage on the eye produced no appreciable bulging of the membrane into the anterior chamber. Immediately following the massage, when the filtering operation was functioning, there was a rapid recession of the membrane. As a result of the communication between the anterior chamber and the suprachoroidal space, pressure and massage upon the eye forced the aqueous into the suprachoroidal space. As the aqueous from the anterior chamber decreased, the vitreous hernia could bulge farther into the anterior chamber. When the cyclodialysis was draining, the pressure and massage on the eye caused fluid to be forced out of the vitreous, and from 30 to 45 minutes was required for the vitreous volume to be replaced.

SUMMARY

The contact of the anterior hyaloid membrane with the posterior corneal surface following uncomplicated intracapsular cataract extraction causes symptoms and signs which disappear if therapeutic measures are successful in causing the herniated membrane to recede from the corneal surface.

73 East 71st Street (21).

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DISCUSSION

DR. EDWIN B. DUNPHY (Boston): Dr. Reese's thorough presentation of this interesting subject has given us much food for thought. It emphasizes the harmful potentialities of the vitreous when this substance leaves its normal confines and spreads forward to new boundaries. Although many ophthalmologists are aware that vitreous in contact with the corneal endothelium for any length of time may give rise to edema of the

cornea, its occurrence in my experience has been extremely rare, considering the prevalence of vitreous herniation.

Dr. Reese apparently feels that this contact is the chief cause of the so-called striate keratitis seen postoperatively, although he mentions that it may be facilitated by damage to the corneal endothelium. It has always been my impression that damage to the endothelium at the time of operation is the *main* factor, since striate keratitis occurs just as frequently after extracapsular extraction where there is no possibility of vitreous touching the cornea.

It is my endeavor in intracapsular cataract surgery to deliver the lens by the Verhoeff sliding technique, the capsule being grasped at or near the upper equator with smooth forceps and pressure being made at the limbus below. A small iridectomy including the sphincter is performed before the delivery. The wound is closed by two Verhoeff corneoscleral tract sutures. By this method of extraction I feel that minimal damage to the cornea occurs.

The anterior chamber is reformed at the first dressing (24 hours). It is extremely rare to see any gross striate keratitis either then or subsequently, although slitlamp examination is not done until the 6th or 7th postoperative day, and it is possible, of course, that it might have been present earlier to a slight degree. At this examination vitreous is invariably found herniating through the pupillary space, sometimes practically in contact with the cornea, although not attached thereto. Wrinkling of Descemet's membrane is present in all cases, even when the hyaloid is nowhere near the cornea. In a few cases in which the reformation of the anterior chamber is delayed for a few days, I have not seen the saucer-shaped corneal opacity which Dr. Reese describes, although there is usually a lot of wrinkling of Descemet's membrane due to the hypotony.

I was interested in the quotation of Vannas's statistics to the effect that, in 23 percent of eyes with uncomplicated intracapsular

extractions, the anterior hyaloid membrane showed a concave surface and remained at the level of the pupil, or even behind the pupillary border. In my uncomplicated cases I would estimate that practically 100 percent show some protrusion of the hyaloid in front of the pupillary border, in most instances extending halfway across the anterior chamber, and in some of them the vitreous is almost in contact with the cornea. Even when observed several years postoperatively this is true, although there tends to be a gradual retraction of the hyaloid. It is quite probable that, if I did round-pupil extractions, the incidence of extensive herniation would be less.

There is no doubt, of course, that corneal edema and opacification can be caused by adherence of the vitreous to the endothelium, particularly if the latter is damaged. Dr. Cogan of the Howe Laboratory, who has been making a special study of corneal edema, considers vitreous adherence to be an important contributory cause. Unlike Dr. Reese, he feels that the presence of the intact hyaloid is not essential; in other words, the edema may result from free vitreous in contact with the cornea following vitreous loss at operation. The condition of the endothelium is the determining factor. If it is in bad shape, either because of trauma at the time of operation or because of inherent degeneration, then the vitreous may stick to it with all the dire effects that Dr. Reese describes.

The injection of air to free the adhesion of vitreous to cornea has been attempted recently in one case at the Massachusetts Eye and Ear Infirmary. The patient, a man aged 68 years, had had intracapsular cataract extractions in each eye three years previously. Vitreous had been lost in one eye but not in the other. Both eyes showed vitreous herniating through the pupils and attached to the upper part of the endothelium at the line of incision. Edema of each cornea was present over the point of vitreous adherence. A shelving incision was made in the cornea

below just inside the limbus with a cataract knife. A good blast of air injected through this incision by a small needle and glass syringe succeeded in freeing the vitreous from the endothelium with subsequent clearing of the cornea to a large extent. The same process was successfully repeated in the other eye.

I am not familiar with the special type of iris prolapse caused by the vitreous pushing the iris into the edges of the wound as described by Dr. Reese, but see no reason why it should not occur, particularly in round-pupil extractions.

In similar fashion secondary glaucoma might be caused by vitreous pushing the iris root against the angle.

I have seen several cases in which the glaucoma was due to vitreous blocking the pupil according to the mechanism recently described by Chandler. In these cases there was a tendency to iris bombé, and a transfixion of the iris in the periphery relieved the situation by reëstablishing communication of aqueous between the posterior and anterior chambers.

The technique advocated by Dr. Reese of dilating the pupil, placing the patient on his back, and then constricting the pupil with a strong miotic might well be helpful in this type of case, particularly after round-pupil extractions.

The creation of a coloboma by the herniating vitreous pushing the iris peripherally has been observed by me on several occasions. A round pupil is not necessary for its production. Apparently in these cases the hyaloid ruptures, or thins out, not in the center of the pupillary zone, but to one side, so that the vitreous bulges through just behind the pupillary margin, shoving it toward the periphery. I have recently had such a case. During delivery of the lens some difficulty had been encountered in getting it to dislocate. Suddenly it gave way nasally, popping up into the wound. Extraction in capsule was completed without loss of vitreous. The next day

the chamber was reformed and the operative result appeared to be perfect. On the third postoperative day I noticed a coloboma of the iris developing nasally. This increased slowly during the next three days. Slitlamp examination on the sixth postoperative day showed the picture just as Dr. Reese describes—the vitreous was bulging nasally, the adjacent pupillary border being displaced toward the periphery.

The author's supposition of a partial adhesion between the anterior hyaloid and the posterior surface of the lens to explain the weakening and bulging of the hyaloid following extraction is a reasonable one, and answers the question why this bulging sometimes takes place on one side and not in the center of the pupillary space.

The other factor he mentioned concerning the shrinkage of vitreous with choroidal detachment, and the correlation of changes in the position of the anterior hyaloid with the changes in vitreous volume, is an interesting one, and helps us understand the mechanism of vitreous herniation.

I have learned a lot from this paper, and am indebted to Dr. Reese for clearing up in my mind some things I never understood about herniation of the vitreous.

DR. F. H. VERHOEFF (Boston): I am much interested in this paper of Dr. Reese's and think it is a very important communication. I agree with most of the things he brought out, but it would take me about an hour to discuss all the aspects of the subject so I shall confine myself to just one, the permanent serious opacification of the cornea which results from adhesion of the vitreous to the back of the cornea. Some of us at the Massachusetts Eye and Ear Infirmary have known about this for at least 15 years. I would like to think I was the first one to get the idea, but my impression is that Dr. Gundersen is entitled to most of the credit.

For a good many years I had in mind a method of combating this opacification of the cornea but it was not until 1944 that I used

the method. I began to write up the case, but when I looked up the literature I could not find that anyone else knew anything about the condition, so it seemed foolish to report an operation for combating a danger that was almost unknown. I was, therefore, very much pleased to learn that Dr. Reese had established the fact that it was a serious condition with which I was dealing.

In March, 1944, I operated on the right eye of the patient, doing an intracapsular cataract extraction without loss of vitreous. She had 20/20 vision in this eye and wished me to operate upon the other eye, which I did three months later. She acted very well in the first operation, but in the second she was not a good patient, or at least that is to what I attribute the fact that I lost vitreous. The loss of vitreous was so slight that the pupil was not drawn up, but vitreous became adherent to the back of the cornea over a large area, about two thirds of the cornea. She began to get definite corneal opacification which, according to my experience, has been permanent and serious.

She was so well pleased with the right eye that she had the utmost confidence in me, very fortunately, otherwise I could not have done what I did for the left eye. She had edema of the cornea and opacification, so I decided that eye would be ruined if I did not do something. I made a keratome incision, let out all the vitreous that would come, and then I even put an irrigating tip in the anterior chamber, but irrigation did not bring out much more vitreous. I used only one suture this time. The wound healed very well and the anterior chamber was free of vitreous. The cornea cleared up except for a slight opacity high up, which is there today. But, as usually happens after a primary large loss of vitreous, the pupil became drawn up so high that one could hardly see it, and the eye remained irritable for months. The eye therefore had very little vision at that time. The patient stuck by me all this time in spite of photophobia and discomfort.

At the end of nine months, when the eye had become white and quiet, I did a small iridotomy with a Ziegler knife and obtained 20/30 vision, which she still has.

I suspect that a slight loss of vitreous is more likely to produce the condition than a large loss. After a large loss I think most often the vitreous goes back to the level of the pupil. I do not think it is necessary for the hyaloid to be in front of the vitreous. It is the contact of the vitreous with the cornea that produces the opacification. Dr. Cogan thought possibly opacification would be more likely to occur if there was cornea guttata. Cornea guttata was present in both eyes of my patient. I have not had many of these cases myself, but I have seen the condition a number of times in eyes operated upon by other surgeons.

I recall one case especially in which I wish I had done this operation of vitreous removal. The patient had been operated upon in Hartford by one of the members of this society and had opacification of the cornea. I thought the operation must have been badly done, and I would do a better one, so I operated on the other eye and had exactly the same thing happen. The man was a very "bad actor"; I lost vitreous and I imagine my colleague in Hartford did also. Both eyes had such opacification of the corneas that the patient could only count fingers. I feel sure that if I had removed the vitreous from the anterior chamber before serious opacification of the cornea had occurred, this patient would have obtained good vision.

DR. WILLIAM P. BEETHAM (Boston): I would like to say a few words in behalf of the injection of air into the anterior chamber at the time of cataract extraction. Some of us in Boston have been somewhat disappointed with the injection of air into the anterior chamber in some of the late cases of this complication which we are talking about. By late cases I mean those with serious corneal damage in which adherence of the vitreous to the posterior surface of the

cornea has occurred at a rather late date following cataract extraction. The vitreous, either free or with the hyaloid intact, can be pushed back from the posterior surface of the cornea, but usually by the time this is done the corneal changes are severe and irreversible, and the situation proceeds, namely, edema, bullous keratitis, and corneal opacities.

Since vitreous prolapse can occur postoperatively from hours to days following operation, it does not seem reasonable that anyone can predict which eyes will be affected, and when. The chances are that, when these people appear for treatment, they will have seriously damaged corneas or irreversible changes. In contradistinction to that group for which little can be done are the early cases, for which I think considerable can be done, namely, prevention, and by prevention I mean preventing the occurrence of the adherence of the vitreous to the posterior surface of the cornea by doing something at the time of operation.

I think at this point we ought to thank Dr. Reese for admirably describing this condition and bringing it to our attention. For 6 or 7 years I have made it my routine procedure to inject not a bubble of air but if possible to fill the anterior chamber with air at the time the cataract is removed through my iridodialysis opening after two Verhoeff stitches have been tied.

Last week I inspected the records of 300 operations done during the last three years, and I found one case which fufilled Dr. Reese's description. That patient was one in whom striate opacity was noted at the first postoperative dressing. It has persisted for two years with a maintained acuity of 6/12; vitreous is still adherent to the posterior surface of the cornea. In my description of the record of that operation, believe it or not, I make the statement "no air was injected into the anterior chamber." Why, I do not know, but I operated on the other eye of that patient two years before that operation and air was injected into that anterior chamber,

and she had a good result, so it is interesting to me that the eye in which air was presumably injected did not develop this complication.

My point is merely this, that for some time I have believed that the injection of air into the anterior chamber immediately following cataract extraction is an important addition to the modern cataract operation, and I think Dr. Reese's paper has made me feel more decisive about it.

DR. CHARLES A. PERERA (New York): I wish to agree with Dr. Dunphy in his remarks in regard to the cause of striate opacification. I think Dr. Reese's thesis on herniation of the anterior hyaloid membrane is only one of the causes, and perhaps not the main cause in most cases. I wish to report an example of this condition following a cataract operation with round pupil and a peripheral iridectomy. This was done on an 81-year-old man; the postoperative course was uneventful, and air was injected into the anterior chamber at the close of the operation as Dr. Beetham has done for years. The night after the operation the patient got out of bed and wandered about until he was finally put back to bed.

At the first postoperative dressing the anterior chamber was filled with blood which extended under the conjunctival flap. When the blood was sufficiently absorbed a small iris prolapse was seen temporally; the cornea in this quadrant showed striate opacification and the blood-filled vitreous pressed against the cornea in this quadrant. After consultation with Dr. Reese, and in accordance with his suggestion that air injection might be worth while, I performed this procedure as Dr. Dunphy described it. The vitreous was pushed back from the cornea, the corneal opacification rapidly disappeared, and the vitreous is now clearing.

DR. RALPH O. RYCHENER (Memphis): I enjoyed Dr. Reese's paper and its very timely explanation of a number of things which I have been puzzled about, and I want to add a little confusion to it. With regard

to air injection immediately following intracapsular cataract extraction for uncomplicated cataract, in the past two years I did that routinely, employing the method suggested by Dr. MacMillan in which I put in a lot of air, enough to depress the iris, and it was during that period I ran into all the complications of herniation of the vitreous against the endothelium which I have encountered in my limited practice. So after reviewing my operations I decided perhaps the air was responsible for the opacification of the cornea and have now stopped air injection. I would like to ask Dr. Reese, when he dilates with neosynephrin and employs strong miotics, how long does he employ the miotic, and what happens after he stops it?

DR. ALFRED COWAN (Philadelphia): I have been interested in this subject for many years, and particularly in the acceptance of the term "anterior hyaloid membrane." In 1931, I presented a paper before this society describing the anterior hyaloid membrane; in 1932, Dr. Fry and I gave what we thought was conclusive evidence that there is such a thing as an anterior hyaloid membrane and, in 1939, before this society again, Robb McDonald and I presented a report of a series of cases of postoperative aphakics.

In this series was a group in which the lens and its capsule were supposed to have been extracted—intracapsular extractions. In nearly every one of these cases, immediately after the operation, the anterior hyaloid protruded far into the anterior chamber, and in many instances it was in contact with the posterior surface of the cornea over quite a large area. I should say in most of the cases we examined protrusion of the hyaloid into the anterior chamber persisted until the 5th or 6th day.

After that—now I am describing those in which the operation was successful, in that the hyaloid membrane was intact—after that, the hyaloid retracted gradually and, in the majority of instances, later on it would lie in the plane behind the iris without anything having been done for it. It seems to me after all this time (and I have studied a great many of these conditions) that it is not a matter of pressure from behind that causes the hyaloid to protrude but rather it is due to a lack of pressure or support in front.

As far as striate keratitis is concerned, I think it is possible that herniation of the hyaloid is a factor; but I do not think it is an important factor, because in almost every case after you open the globe you will find some indication of folds in Descemet's membrane or in the posterior portion of the cornea. I should like to show a slide which contains illustrations from an article by me and of one by McDonald and me. The first drawing illustrates a case that can be considered a narrow slitlamp appearance of the hyaloid membrane which is concave from before backward and lies behind the plane of the iris. This is what is considered a successful extraction of a lens with its capsule after 6 or 7 days. There is a drawing of a case in which a permanent herniation resulted; it is hemispheric. This is not a rare result. Another represents an instance in which the hyaloid lies in horizontal folds. One drawing illustrates a case in which blood in the vitreous is contained in the hyaloid which protrudes into the anterior chamber over the lower border of the pupil. After the blood became absorbed, the hyaloid membrane contracted behind the plane of the iris. Another is an illustration of an instance in which the hyaloid became incarcerated in the wound. It seems to me that such cases are not due to pressure from the force behind but that the hyaloid is drawn into the wound as the knife is withdrawn.

DR. ARTHUR J. BEDELL (Albany, New York): I wish to show one slide which has some historical interest because it was exhibited almost a quarter of a century ago. You can see the vitreous prolapse in each drawing. Dr. Reese told me he had not seen the article which was presented before the English-speaking Congress in 1925. It is for that reason I present it to those who may be unaware of this early work.

DR. ALGERNON B. REESE (closing): Dr. Dunphy mentioned the fact that he and also Dr. Cogan feel that the condition of the endothelium is an important factor in the corneal changes. I agree with them. I mention in the paper that if cornea guttata is present the corneal changes are more severe.

Dr. Dunphy also mentions the fact that herniation of the hyaloid may produce a coloboma of the iris. This point is also discussed in the paper.

A feature of Dr. Dunphy's and Dr. Verhoeff's discussion with which I am not entirely in accord is that dealing with the ill effects of straight vitreous on the cornea. I am not sure that vitreous alone produces corneal changes. I think the changes I have observed have occurred as the result of the hyaloid membrane. This membrane has a definite structure and it is the effect of this against the cornea which promotes symptoms and signs.

I was glad to hear Dr. Verhoeff state that he felt a deliberate rupture of the hyaloid membrane is indicated sometimes. I have thought that this might be beneficial sometimes in cases with permanent adhesion of the membrane to the cornea, and in cases with secondary glaucoma.

Dr. Beetham mentions the value of air injections. I think they have value not only in pushing the iris back but in pushing the hyaloid back. I recall the case which Dr. Perera quoted, and I feel, as he did, that the injection of air was beneficial.

Dr. Rychener asks how long miotics are used. I think a period of about 2 to 3 days is adequate.

I know of Dr. Cowan's work. I referred to the hyaloid as a membrane which is in agreement with his ideas. I thank Dr. Bedell for calling my attention to the article which he wrote in 1925 pertinent to this subject.

OPHTHALMIC MINIATURE

Blumen

(Dem Augenarzt von seinen Kranken.)

Sie kommen aus dem Schoss der Nacht:
Doch waren unten sie geblieben,
Wenn nicht das Licht mit seiner Macht
Hinauf ins Leben sie getrieben.

Holdselig aus der Erde bricht's,
Und blüht nun über allen Schranken;
Du bist der Freund des holden Lichtes:
Lass dir des Lichtes Kinder danken!

Theodor Storm (1817-1888).

THE ROLE OF CILIARY AND SUPERIOR CERVICAL GANGLIA IN OCULAR TENSION*

Ernst Schmerl,[†] M.D., and Bernhard Steinberg, M.D.
Toledo, Ohio

This study is a part of a general investigation of the factors which affect intraocular pressure. In a previous report it was indicated that the diencephalon contained a center or centers which exercised a regulatory control of intraocular pressure.[1] In a subsequent paper[2] it was shown that the central control of tension involved the pituitary body. The presence of two active principles, probably hormonal in nature, was found in the region of the posterior lobe of the pituitary. One of these principles increases and the other decreases the tension. In a normal state they are in an equilibrium. Apparently, these active principles are secreted into the spinal fluid and they act upon the diencephalic center or centers.

It was postulated that stimuli which are induced in the diencephalon are transmitted through the medium of the autonomic nerve fibers to the eyeball. These stimuli dilate or constrict capillaries depending upon the predominance of either of the two principles. There is ample clinical and experimental proof that capillary action represents one mechanism which determines ocular tension.[3]

The present study concerns itself with the role of the ciliary and superior cervical ganglia in ocular tension and the postulated mechanism which is outlined in this paper.

Saitoh[4] extirpated the ciliary ganglion and found an immediate decrease of intraocular pressure which returned to normal in an hour. The tension was low again the second day and returned to normal within two weeks. Peschel[5] described a procedure for removal of the ciliary ganglion and noted a decrease in tension. Givner,[6] among others, pointed out the occurrence of accessory cili-

ary ganglia. Linksz[7] observed the effect of the sympathetic pathways on ocular tension.

EXPERIMENTAL PROCEDURES

Rabbits were used as experimental animals. The ciliary ganglion was reached by a bipolar electrode which was insulated except for the tip. The electrode could either stimulate or cauterize. The tip of the electrode was introduced through an incision in the anterior lower part of the eyelid after removal of the tear and Harder glands. The electrode was guided by the trigeminal nerve to the region of the ciliary ganglion. Contact with the ganglion was recognized by contraction of the pupil and a rise in the ocular tension after stimulation. Stimulation was followed by cauterization. The method was not universally successful. Only those animals were used in the experiments in which the pupils were dilated, the pupillary reflex was absent, the wink reflex was retained, the corneal sensation remained intact, and the fundi were normal.

The left ciliary and the superior cervical sympathetic ganglia were stimulated and cauterized in 10 rabbits. The ocular tension was determined prior to the action upon the ganglia and immediately after stimulation and up to 21 days following cauterization. In 4 animals with cauterized ciliary ganglion, ocular tension was determined after administration of distilled water for 60 to 90 minutes.

In 7 rabbits, following either cauterization of the ciliary ganglion or excision of the superior cervical, spinal fluid, in volumes of 0.5 to 0.8 cc., of animals exposed to dark or to light was injected. The tension was determined for 60 to 90 minutes following the injection. Normal animals were injected with identical spinal fluid and were used as controls. As in our former studies, changes

in tension of 3 or more mm. Hg (Schiøtz) were considered significant.

RESULTS

Stimulation of the ciliary ganglion in 5 animals resulted in an immediate increase of

TABLE 1

EFFECT OF FARADIC STIMULATION OF THE CILIARY OR SUPERIOR CERVICAL GANGLION UPON INTRAOCULAR PRESSURE

No. of Rabbit	Area Stimulated	Ocular Tension in mm. of Hg in Relation to Stimulation	
		Before	After
1	Ciliary Ganglion	16	33
2		20	31
3		21	31
4		17	33
5		28	36
6	Superior Cervical Ganglion	25	14
7		21	14
8		23	16

intraocular pressure of from 8 to 17 mm. Hg (table 1). Other changes consisted in pupillary contraction, marked hyperemia of the iris, flattening of the anterior chamber, and haziness of the iris. These changes are indicative of stimulation of the parasympathetic fibers of the oculomotor nerve with a resultant capillary dilation and increased permeability.

Cauterization of the ciliary ganglion in 6 animals resulted in a decrease of intraocular pressure of from 8 to 13 mm. Hg (table 2).

The readings were taken at intervals of from 1 to 28 days. Generally, the ocular tension showed a tendency to slight recovery after several days. Other changes which were observed consisted of pupillary dilatation and loss of light reflex.

Cauterization of the ciliary ganglion followed a month later by ingestion of 40 cc. of distilled water per kilo body weight resulted in little or no change. Under normal conditions, with an intact ciliary ganglion, the tension rises (table 2).

Cauterization of the ciliary ganglion followed 5 to 7 months later by intravenous injection of spinal fluid from animals kept in the dark showed a reduction of ocular tension equal to that found in normal animals (table 3). The reduction occurred within 15 to 20 minutes and persisted for the subsequent 30 to 60 minutes. Injection of spinal fluid from animals exposed to light showed no change. On the other hand, the intraocular pressure was elevated in the control animals (table 3).

These changes indicate that removal of the parasympathetic pathway results in a failure to transmit those stimuli which cause an increase in tension. At the same time, there is indication that there is no interference with the active principle which causes a decrease in tension.

Stimulation of the superior cervical ganglion resulted in a lowering of the intraocular

TABLE 2

EFFECT OF CAUTERIZATION OF CILIARY GANGLION UPON INTRAOCULAR PRESSURE

No. of Rabbit	Ocular Tension in Relation to Cauterization			Ocular Tension in Relation to Cauterization after Administration of Distilled Water		Ocular Tension of the Eye with Intact Ciliary Ganglion in Relation to Water Intake	
	Before	After		Before Water	After Water	Before	After
		1 Day	14–28 Days				
1	16	8	15	14	14	18	22
1	—	—	—	15	10	17	18
2	21	12	18	18	19	18	27
3	17	4	17	17	21	19	27
4	21	9	12	12	14	17	22
5	20	9	10	—	—	—	—
6	28	16	—	—	—	—	—

TABLE 3

EFFECT UPON INTRAOCULAR PRESSURE AFTER CAUTERIZATION OF LEFT CILIARY GANGLION FOLLOWED BY INJECTION OF SPINAL FLUID FROM RABBITS EXPOSED EITHER TO LIGHT OR DARKNESS

No. of Animal	Left or Right Eye	Type of Spinal Fluid	Ocular Tension in Relation to Injection of Spinal Fluid		Control Animals with Intact Ganglion and Injected with Spinal Fluid	
			Before	After	Before	After
1	R	From Light-Exposed Animals	18	18	21	25
	L		15	15	21	24
2	R	"	18	18	25	28
	L		18	18.5	25	28
3	R	"	18	18	26	30
	L		14	15	26	28
4	R	From Dark-Exposed Animals	16.5	14	19	15
	L		16	12	19	17
5	R	"	19.5	16	21	17
	L		19.5	16.5	21	18
6	R	"	21	18	—	—
	L		19	16	—	—

pressure of from 7 to 11 mm. Hg (Schiøtz). Removal of the superior cervical ganglion followed 5 to 6 months later by injections of

spinal fluid from animals exposed to light showed an increase in tension of from 3 to 9 mm. Hg. Injection of spinal fluid from

TABLE 4

EFFECT UPON INTRAOCULAR PRESSURE AFTER REMOVAL OF LEFT SUPERIOR CERVICAL GANGLION FOLLOWED BY INJECTION OF SPINAL FLUID FROM RABBITS EXPOSED EITHER TO LIGHT OR TO DARKNESS

No. of Rabbit	Left or Right Eye	Type of Spinal Fluid	Ocular Tension in Relation to Injected Spinal Fluid		Ocular Tension in Control Animal with Intact Ganglion in relation to Injected Spinal Fluid	
			Before	After	Before	After
1	R	From Light-Exposed Animals	25	28	—	—
	L		25	28	—	—
2	R	"	26	29	—	—
	L		26	30	—	—
3	R	"	20	27	21	25
	L		20	29	21	23
4	R	From Dark-Exposed Animals	24	25	19	16
	L		25	25	20	17
5	R	"	25	24	19	15
	L		25	26	19	17
6	R	"	20	21	21	17
	L		22	23	21	18
7	R	"	22	22	25	20
	L		21	23	25	21
8	R	"	24	24	24	20
	L		24	27	23	19

rabbits exposed to darkness showed no significant change in tension (table 4). These changes indicate that removal of the sympathetic pathway results in a failure to transmit those stimuli which cause a decrease in tension. At the same time there is indication that there is no interference with the active principle which causes an increase in tension.

SUMMARY

Under the conditions and on the basis of these experiments, it may be postulated that stimuli travel from the diencephalon by way of the ciliary ganglion, which is essentially of parasympathetic nature, and produce vascular dilatation with a consequent increase in ocular tension.

On the other hand, those stimuli from the diencephalon which travel by way of the superior cervical ganglion, a sympathetic conveyer, contract capillaries and produce a lowering of intraocular pressure. Light and darkness incite the production of active principles in the pituitary. These principles act upon the diencephalon and initiate nervous stimuli which are transmitted to the periphery along the autonomic pathways.

2805 Oatis Avenue (6).

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OPHTHALMIC MINIATURE

Celsus contains a summary of all that was known in his time. Although he was ignorant of the seat of cataract, he has described the operation of couching excellently and concisely, not omitting the important subjects of previous preparation and after treatment, for which his directions are judicious.

Sir William Lawrence, *A Treatise on the Diseases of the Eye,* 1833.

THE EPIDEMIOLOGY OF EPIDEMIC KERATOCONJUNCTIVITIS*

PHILLIPS THYGESON, M.D.

San Jose, California

The recurrence of epidemic keratoconjunctivitis in California in epidemic form in 1947 and 1948 indicates that this disease, which first became widespread in the United States in 1941, is probably to be a permanent problem. Although it failed to have the expected military significance during the war years, it did become an industrial problem and would seem to be potentially capable of causing major disturbances in the future.

In view of the office transmissions which occurred in both the 1941-1942 and the 1947-1948 epidemics, and in the course of which many ophthalmologists became infected, it would seem pertinent at this time to reëxamine the epidemiology of this important disease. The present clinical study is based on my personal observations, on the observations of a number of colleagues, and on epidemiologic studies previously recorded in the literature.

CLINICAL CHARACTERISTICS

The clinical characteristics of the disease as it appeared in the 1941-1942 epidemic have been well described by Hogan and Crawford,[1] Braley,[2] and Holmes.[3] My own experience has been limited to approximately 90 cases about equally divided between the two epidemics. In these cases the disease was characterized by an acute onset with preauricular adenopathy, by the nonpurulent character of the exudate, and by the development in most cases of small, round, subepithelial corneal opacities after an interval of from 7 to 10 days.

The conjunctival involvement varied from a follicular hypertrophy in mild cases to a severe pseudomembranous, or occasionally membranous, conjunctivitis in severe cases. The corneal complications varied similarly from mild involvement without visual impairment to severe involvement with reduction of vision to 20/200 or even less. The severity of the corneal involvement did not always parallel the severity of the conjunctival involvement.

In most cases the vision eventually returned to normal but occasionally the lowered acuity persisted. This was apparently related to the diffuseness of the infiltration since persistent round infiltrates were often associated with normal vision.

There were a number of severe cases in which multiple petechial hemorrhages in the skin occurred. Coincidental respiratory symptoms were observed in a small percentage of cases and the complaint of headache at onset was common enough to suggest the possibility of meningeal irritation. In the 1947-1948 epidemic in California there was a noteworthy degree of mental depression among the patients during the first few weeks of illness.

The clinical diagnosis of epidemic keratoconjunctivitis can be made with certainty only after the development of the characteristic round, subepithelial infiltrates, but a presumptive diagnosis can be made on the basis of the clinical picture of an acute follicular conjunctivitis with grossly visible preauricular adenopathy, combined with the laboratory finding of a mononuclear cell exudate without significant bacteria.

Differential diagnosis must be made from the following disease entities: (1) Acute herpetic keratoconjunctivitis, (2) acute follicular conjunctivitis (Beal), (3) nummular keratitis (Dimmer), (4) inclusion conjunctivitis, and (5) acute trachoma. Table 1 illustrates the essential points of difference among these conditions. It will be observed that acute herpetic keratocon-

junctivitis offers the greatest difficulty. Its gross resemblance to epidemic keratoconjunctivitis is striking but differential diagnosis can be made readily on the basis of slit-lamp examination since the corneal lesions in the herpetic disease are invariably epithelial and those of epidemic keratoconjunctivitis invariably subepithelial.

disease in his family or among his immediate contacts, but the incidence was no greater among the epidemic keratoconjunctivitis cases than it was in a similar series of patients without the disease. It is noteworthy that the great majority of patients in this group were young, active adults who were in contact with numerous people in

TABLE 1
DIFFERENTIAL DIAGNOSIS OF EPIDEMIC KERATOCONJUNCTIVITIS

	Epidemic Kerato-conjunctivitis	Herpetic Kerato-conjunctivitis	Inclusion Conjunctivitis	Beal's Conjunctivitis	Nummular Keratitis	Acute Trachoma
Preauricular adenopathy	++++	++++	+	+	0	±
Follicular hypertrophy	++++	++++	++++	++++	0	++
Pseudomembranes	++	++	0	0	0	±
Keratitis	Subepithelial round infiltrates	Epithelial infiltrates; dendritic figure	0	0	Round subepithelial infiltrates; facet formation	Pannus; irregular infiltrates
Visual disturbance	++++	++++	0	0	Variable	Late
Cytology of conjunctival exudate	Mononuclear cell exudate	Mononuclear cell exudate	Polymorphonuclear cell exudate	Mononuclear cell exudate	Not known	Polymorphonuclear cell exudate

PERSONAL OBSERVATIONS ON EPIDEMIOLOGY

An attempt was made in every case observed to work out the source of infection. The fact that the incubation period is usually from 7 to 10 days helped in tracing possible contacts. The cases could be divided into five epidemiologic groups, as follows:

1. SOURCE OF INFECTION UNKNOWN

Patients in this group could not recall having been in contact with anyone with inflamed eyes, nor had they, within the period of incubation, been in attendance at any doctor's office where they might have been accidentally exposed. In view of the possibility that the infection may be carried in the respiratory tract, each patient was questioned as to the presence of respiratory

their work or in traveling to and from their work; there was not one who was not exposed repeatedly to persons other than those in his immediate family.

2. FINGER-TO-EYE TRANSMISSION

This type of transmission was presumed to be the cause of the infection of three ophthalmologists, each of whom contracted the disease after treating one or more typical cases of it.

Case 1. Ophthalmologist A had 17 cases in his practice and developed a fulminating case of epidemic keratoconjunctivitis with thick membranes. The character of the membranes was such as to suggest diphtheria, but repeated cultures failed to reveal pathogenic bacteria. It was not until the typical corneal picture of the disease developed that

a definite diagnosis was made. In handling his cases, this ophthalmologist had used the ordinary hand-washing technique. No solutions had been used in his eyes. His wife subsequently contracted a mild case of the disease.

Case 2. Ophthalmologist B had five cases of typical epidemic keratoconjunctivitis in his practice and developed a severe case of the disease shortly after going on vacation. He had employed the usual soap and water hand wash after treating his cases. No secondary cases developed in his family.

Case 3. Ophthalmologist C developed a severe case of epidemic keratoconjunctivitis after seeing only one case, the nature of which he had not recognized until corneal signs developed. He also had employed the usual soap and water hand-washing technique. No secondary cases developed in his family.

None of the three ophthalmologists recalls rubbing his eyes after seeing cases, but this is a very common gesture and often an unconscious one. Fingers-to-eyes is believed to have been the most likely route of infection.

In addition to these three ophthalmologists seen by me personally in the 1947-1948 epidemic, I know of eight other such cases and there must surely have been still others. With reference to the 1941-1942 epidemic, I was able to obtain from colleagues and from the literature the history of seven infections in ophthalmologists. Except for one doctor whose eyes were accidentally sprayed with irrigating fluid, all were apparently the result of finger-to-eye transmission.

3. FAMILIAL TRANSMISSION

Three cases were observed in which it was clear that the husband had transmitted the disease to his wife. One of these transmissions was from one of the ophthalmologists mentioned above. The infection developed in his wife 17 days after the onset of his own disease. The wife had not treated her husband's disease in any way but she

was in intimate contact with him during the period of his illness. The exact mode of transmission could not of course be determined, but of the articles handled by both, sheets and pillowcases would seem to have been the most likely agents of transmission in view of the abundant tearing characteristic of the infection.

The other two husband-to-wife transmissions were comparable. Both couples slept in double beds where contaminated linen would have offered a likely means of transmission.

4. INDUSTRIAL INFECTIONS

During 1947 and the first four months of 1948, I observed only one individual with the disease who was employed in the shipbuilding industry. There were no other cases in this man's shop and he is believed to have contracted the disease while being treated for chronic conjunctivitis in a doctor's office in which numerous typical cases of epidemic keratoconjunctivitis were being seen.

Other patients with the disease were engaged in the following occupations: canning, meat packing, plumbing, merchandising, agriculture, law, insurance, grocery store clerking, secretarial work, and nursing. Except in the case of the one nurse and one secretary, no history of contact with other cases in connection with the patient's work could be obtained. The nurse was a public health worker who was exposed to a number of individuals with inflamed eyes but she did not know that a diagnosis of epidemic keratoconjunctivitis had been made in any of them. The secretary was employed in an internist's office and was in contact with several patients infected with the disease.

In returns from questionnaires sent to representative ophthalmologists throughout the country, there were no histories of outbreaks in any occupational group except the physician group. I was unable to elicit any history of the disease in welders or shipyard workers. This was, of course, sharply at variance with the situation in 1941-1942

when the disease was epidemic among ship-yard workers, and in particular among weld-ers.

5. OFFICE INFECTIONS

Transmission of epidemic keratoconjunc-tivitis in offices and industrial clinics has been noted repeatedly in the literature. Such

these the only common factor was the ad-ministration of a 0.5-percent pontocaine solu-tion from a dropper bottle. Tonometry and hand contamination could also have been factors in some of the transmissions. The majority of the 14 were glaucoma cases in which tonometry had been performed, but all 14 had received the pontocaine solution

TABLE 2

CASES OF EPIDEMIC KERATOCONJUNCTIVITIS DEVELOPING IN OFFICES A AND B

	Office A		Office B	
Patients developing epidemic keratoconjunc-tivitis after receiving 0.5-percent ponto-caine solution from dropper bottle	14		42	
Percentage of those exposed to solution who developed infection	90 to 100%?		98%	
Patients developing infection who had *not* been exposed to contaminated solution	5		0	
Secondary cases arising from office infections	2		0	
Total number of cases	21		42	
Incubation period	9 days		7 to 10 days	
Patients developing (a) keratitis (b) pseudomembranes (c) preauricular adenopathy (d) bilateral disease (e) secondary infection (f) dendritic keratitis or lid vesicles	21 2 21 18 0 1	100% 10 100 90 0 5	42 3 36 37 0 0	100% 3 85 90 0 0
Role of trauma	Tonometry, meibomian gland expression, removal of su-tures, or other manipulation in all but one case		Tonometry in majority of cases	

accidental transmissions were not uncommon in the 1941-1942 epidemic and they occurred again with important frequency in the 1947-1948 outbreak. I have seen in consultation patients from four series of accidental office transmissions and have been informed of a number of other series. Three colleagues were kind enough to furnish details of office transmissions in which the mechanism of transmission could be worked out with rea-sonable reliability. These are reported as fol-lows:

Office A. In Office A (table 2) there were 19 infections, all believed to have been de-rived from a single case. In the first 14 of

and some the pontocaine only. How long the pontocaine remained infective could not be determined as the solutions were discarded and the bottles sterilized at irregular but frequent intervals. Unfortunately there was no record of the day upon which this had been done. However, the epidemiologic data indicate that all infections occurred on one day, since the first 14 cases were seen on a single day and all developed first symptoms nine days later.

On the ninth day several of the 14 cases appeared in the office for treatment. When the first appeared, the probable source of his infection was surmised and the dropper bot-

tle technique of administering the pontocaine solution was promptly discarded. In spite of this precaution, five new cases developed after another 9-day interval. Neither pontocaine solution nor tonometry could have been the agents of transmission in any of these cases. The hands of the attending ophthalmologist could have been responsible, or possibly the arms of the treatment chairs could have been contaminated. One of the five cases did not enter a treatment room, however, but received euphthalmine drops for funduscopy in the darkroom where it is believed none of the infected patients had been.

Two additional cases were treated in this office at this time, both of them contracted secondarily by the spouses of 2 of the 19 office infections.

Office B. The accidental infections which occurred in Office B (table 2) numbered 42 and, unlike those in Office A, all cases had received 0.5-percent pontocaine solution from a single dropper bottle over a period of eight days. A good many cases had been subjected to tonometry but the only factors common to all were the use of pontocaine and examination in the treatment room. Since no patient examined in the treatment room who did not receive pontocaine developed the infection, it would seem reasonable to eliminate these other factors from consideration.

Unlike the situation in Office A, there were no known secondary infections from any of the office cases. The reported incubation period of 7 to 10 days is at variance with the sharp 9 days observed in Office A, but more careful scrutiny of the data on this point might yield closer agreement.

Office C. The infections which occurred in Office C furnished particularly valuable data on the epidemiology of the disease. The incubation period varied from 8 to 13 days in the 11 cases in which it was known, as follows: 8 days in 3 cases, 10 days in 3, 11 days in 3, 12 days in 1, and 13 days in 1. It is of interest that in those cases in which

only one eye was treated in the office, only that eye initially developed the disease; whereas, in the patients who had had both eyes treated, bilateral infection occurred. This would seem to indicate a high degree of susceptibility to the virus. All the cases which developed in this office had preauricular adenopathy and keratitis. If the cocaine-adrenalin used in the first office patient with epidemic keratoconjunctivitis was contaminated with the virus, the duration of its infectivity must have been protracted, since the first office infection did not receive the drops until 11 days later and the last infection in the first series did not receive them until 41 days later.

The following paragraphs present the reconstructed history of the 3 small outbreaks of the disease which occurred in Office C:

Series 1 (1941)

Case 1. September 7th. Patient was treated for what appeared to be an acute catarrhal conjunctivitis, left eye. The eye was cocainized and conjunctival scraping taken and found to be negative. Patient was not seen again until October 19th when there were numerous infiltrates, left eye, typical of epidemic keratoconjunctivitis. It is probable that this infection had just developed when patient was first seen in early September.

Case 2. September 18th. Patient was refracted in the office. Eleven days later (October 1th), onset of typical epidemic keratoconjunctivitis with preauricular adenopathy and corneal infiltration, both eyes.

Case 3. September 24th. Foreign body removed from upper tarsal conjunctiva. Eight days later (October 2nd), onset of conjunctivitis; developed into typical epidemic keratoconjunctivitis.

Case 4. September 25th. Conjunctival concretions in the right eye were removed. Eight days later (October 3rd), onset of conjunctivitis, right eye; developed into typical epidemic keratoconjunctivitis, later spread to left eye.

Case 5. October 6th. Abrasion of con-

junctival follicles, left eye. October 14th (8 days later) conjunctivitis started in left eye, developed into typical epidemic keratoconjunctivitis.

Case 6. October 8th. Chalazion operation, right eye. Eleven days later (October 19th), typical epidemic keratoconjunctivitis developed.

Case 7. October 18th. Mild conjunctivitis, both eyes. October 29th (11 days later) epidemic keratoconjunctivitis developed in both eyes.

Between November 1st and January 1st there were four more cases, seemingly not connected with one another, but in this period there were no office infections.

Cases 3, 4, 5, and 6 received cocaine-adrenalin drops which could have been from the same source as those used on September 7th on Case 1. However, Cases 5 and 6 had minor surgery and Case 7 an examination for conjunctivitis on days when Cases 2, 3, and 4 also made office calls. Cocaine-adrenalin drops were used in Cases 1, 3, 4, 5, and 6, and in all 7 cases there was manipulation of the lids.

Series 2 (1947)

Case 1. June 17th to 21st. An eye physician with bilateral epidemic keratoconjunctivitis was seen in consultation in Office C.

Case 2. June 17th. Tear duct, right eye, irrigated because of complaint of tearing. First sight of conjunctivitis, right eye, June 26th. Typical epidemic keratoconjunctivitis developed.

Case 3. June 21st. Patient prepared for cataract operation: tear duct irrigated, tension taken, meibomian glands massaged. Cataract operation, June 22nd. Conjunctivitis started July 1st, developed into typical epidemic keratoconjunctivitis.

Case 4. June 21st. Exactly like Case 3.

All four cases received cocaine-adrenalin drops. Evidently Cases 2, 3, and 4 were office infections, from these drops or from contaminated hands. However, since the attending ophthalmologist had diagnosed

Case 1 as epidemic keratoconjunctivitis, he was very careful about his hand washing technique and therefore considers the infectious agent to have been in the drops or on the nipple of the dropper bottle. It is his opinion that the virus probably stays viable for hours or days on the rubber nipple, in the drops, or on the hands.

Series 3 (1947)

Case 1. September 20th. Right eye became inflamed about 10 days after an eye examination by an ophthalmologist in Office X; vision became blurred around October 1st. Observed in Office C on October 19th when there were numerous subepithelial infiltrates, both eyes.

Case 2. October 26th. Friend of Case 1 consulted same ophthalmologist in Office X. First observed in Office C on November 7th when numerous corneal infiltrates had developed in both eyes.

Case 3. November 23rd. Patient examined in Office X. First observed in Office C on December 13th when there were a few superficial punctate infiltrates.

All three of these patients developed typical epidemic keratoconjunctivitis which in all probability they acquired in Office X between September 10th and November 23rd.

EPIDEMIOLOGIC CONTROL

The information regarding the epidemiology of epidemic keratoconjunctivitis is admittedly incomplete due to lack of laboratory controls. Until the incidence of neutralizing antibodies for the virus in the general population is known, little can be said concerning inapparent or subclinical infections. It is believed, however, that one attack confers a permanent immunity and it is noteworthy that it has been impossible to obtain a history of a second attack from any of my own cases or from the records of my colleagues. The data from the office infections reported above indicate that there is a high degree of susceptibility in the gen-

eral population and would suggest that subclinical infections are rare.

On the basis of the experience gained in the 1941-1942 epidemic, a number of recommendations for the prevention of the disease were promulgated[4-7] but unfortunately were not generally adopted. Of these recommendations, the following would seem to be the most important:

1. Not only ophthalmologists, but general physicians and nurses, particularly those connected with industrial dispensaries, should become thoroughly familiar with the clinical characteristics of the disease in order to facilitate early diagnosis.

2. Physicians and nurses should be meticulous in the washing of their hands between examinations. This washing should be with soap and water and could well include scrubbing with a brush.

3. Dropper bottles should be discarded from all eye offices and industrial dispensaries. Individual sterilizable droppers should be used routinely.

4. Office procedures should be modified so that epidemic keratoconjunctivitis cases can be seen apart from other cases. Protection against contamination of treatment chair arms and doorknobs should be instituted.

5. All instruments, including tonometers and contact lenses, which are used on patients should be sterilized.

6. Patients with epidemic keratoconjunctivitis should receive instruction in the use of tissues in eye care to prevent hand contamination. Separate sleeping arrangements should serve to diminish husband-and-wife infections.

7. Common use of masks and goggles in industry should be discouraged.

DISCUSSION

The literature on epidemic keratoconjunctivitis reveals a considerable degree of confusion as to the relationship of the disease to superficial punctate keratitis, nummular keratitis, acute follicular conjunctivitis

(Beal), and herpetic keratoconjunctivitis. The work of Sanders[3] has shown clearly that epidemic keratoconjunctivitis is a specific virus disease. Future laboratory studies will no doubt clarify the picture, but on clinical grounds alone a reasonable differentiation is possible at the present time.

Superficial punctate keratitis, as we are familiar with it in the United States, is an entirely different disease,[9] with minimal conjunctival symptoms and a chronic course. The punctate corneal lesions are not grossly visible like the round infiltrates of epidemic keratoconjunctivitis and are epithelial rather than subepithelial. It is true that epidemic keratoconjunctivitis was originally described by Fuchs[10] under the name "superficial punctate keratitis," but usage in this country has identified this name with a disease entity of which it is more closely descriptive.

The term "keratitis nummularis," although originally identified with the entity now known as epidemic keratoconjunctivitis, has since been used to describe a quite different disease[11] with insignificant conjunctival lesions compared with the corneal lesions, and with a tendency of many of the corneal infiltrates to form facets and even ulcers, a tendency entirely lacking in epidemic keratoconjunctivitis.

Acute follicular conjunctivitis (Beal) has, in my experience, never been complicated with keratitis. It has a shorter course than epidemic keratoconjunctivitis (never longer than three weeks), moreover, and has never been known to develop pseudomembranes or grossly visible preauricular adenopathy.

Herpetic keratoconjunctivitis is a rare disease in which the conjunctival signs exactly simulate those of epidemic keratoconjunctivitis but in which the corneal signs develop without the delay characteristic of epidemic keratoconjunctivitis and are epithelial rather than subepithelial. The occurrence of a dendritic figure is of course differentiating. The studies of Maumenee and his associates[12] suggest a relationship between

this herpetic disease and epidemic keratoconjunctivitis but their work has yet to be confirmed.

Epidemic keratoconjunctivitis is not the only infection in which transmission has occurred in offices and clinics. The role of the tonometer in the transmission of inclusion conjunctivitis has been described (Thygeson and Stone[13]) and the role of the contaminated solution bottle in the production of pyocyaneus ulcers has been well established (McCulloch[14]). No other infection has produced such widespread office outbreaks, however, and no other disease has produced a comparable number of infections in doctors and nurses. It is obvious that a thorough reëxamination of office and dispensary techniques is indicated.[6]

The mechanism of spread in office outbreaks is not difficult to work out but the epidemiology of sporadic cases is obscure. Does the lack of known contact with typical cases indicate that subclinical disease is a factor? Elucidation of this question must await further laboratory studies on the general population. On purely clinical grounds, however, it seems within the realm of the possible that a single case of epidemic keratoconjunctivitis could contaminate enough doorknobs, toilet levers, washbasin faucet handles, drinking fountain handles, and so on, to account for sporadic cases of the disease over a wide territory.

SUMMARY AND CONCLUSIONS

1. Epidemic keratoconjunctivitis, which first appeared in the western United States in epidemic form in the fall of 1941, became widespread throughout the country in 1942. During the war years of 1943-1946 only sporadic cases were seen and, contrary to expectation, the disease did not become a military problem. In 1947, the disease again became epidemic in California and, to a lesser extent, in other parts of the country.

2. The American disease is believed to be identical with the keratoconjunctivitis first described in Vienna, in 1889, under different names by Adler, Fuchs, and others. It should be differentiated from acute herpetic keratoconjunctivitis, nummular keratitis (Dimmer), acute follicular conjunctivitis (Beal), acute trachoma, and so on. It bears no relationship to superficial punctate keratitis, an entity which has been widespread in this country.

3. The high communicability of the disease appears to be due to the ability of the virus to survive drying and dilution. In this respect it differs from other potentially epidemic types of keratoconjunctivitis such as gonorrheal ophthalmia and trachoma.

4. In the present study, transmission of the disease has been shown to have occurred by the following means: (a) contaminated tonometers, (b) contaminated solutions, including pontocaine, cocaine-adrenalin, and homatropine, (c) direct finger-to-eye transmission, and (d) fomites, especially welders' masks, goggles, and common tools.

5. No satisfactory evidence was obtained to indicate the presence of asymptomatic conjunctival carriers or respiratory carriers.

6. In view of the high frequency of office transmissions, routine office practice should be reëxamined in order to prevent this and other infections. The following prophylactic measures are to be recommended: (1) The discarding of all dropper bottles, (2) the use of individual sterilizable droppers, (3) adequate hand washing before and after treatments, (4) the use of disposable treatment chair arm covers, and (5) individual masks and goggles for workers in industry, with early recognition and isolation of cases.

87 North 6th Street.

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ACCOMMODATIVE DEFECT FOLLOWING ATMOSPHERIC CONCUSSION*

HOMER E. SMITH,† M.D.

Salt Lake City, Utah

The effects of atmospheric concussion on the ocular structures have long been recognized. Stoewer,[1] as cited by Wurdemann,[2] described a multiplicity of ocular pathologic findings resulting from concussion following the terrific explosion at the Roburit factory long before World War I. During and following World War I, Lagrange,[3] McKee,[4] Tooke,[5, 6] deSchweinitz,[7] Doherty,[8] Anderson,[9] Lister,[10] Slight and Haughey,[11] and others[12, 13] rather extensively covered the subject matter pertaining to ocular lesions resulting from atmospheric concussion in military and civilian casualties seen by them during that war.

The effects of atmospheric concussion on the eye during World War II have been described by Stallard,[14] Mathews,[15] Tyrrell,[16] and others.[17-29] However, in spite of the extensive writings to date, manifestations of doubt as to the efficiency of atmospheric concussion (windage) in producing ocular damage appear in the literature.[28-29]

The studies of Theis,[30] Sutherland,[31] and others,[32-35] have shown the essential damaging physical qualities of atmospheric blast to be: (1) An excessively intense longitudinal compression wave of short duration travelling at a velocity of 5,000 to 25,000 feet per second, with a pressure component up to 200 atmospheres (3,000 pounds) per square inch, followed by (2) a phase of rarefaction (suction component) which is never less than 15 pounds per square nich (perfect vacuum). Both components are capable of producing injury.

It is natural that the eye should share, with other organs, the damage sustained by concussion. In the absence of gross lesions, minor changes may be found in the ocular structures which are of value to the ophthalmologist in his clinical evaluation of patients who fall into this postconcussion class.

Many articles have been presented recently[36-45] describing the cerebral and mental effects following atmospheric or blunt traumatic concussion, and their manifestation following such exposure has become known as the "postconcussion state."[44] The essential symptoms that have been described in this syndrome are: headache, dizziness, fatigability, impairment of memory, poor concentration, sensitivity to temperature change, character changes, emotional instability, and antisocial behavior.

Among service personnel (the source of this material) other motivating factors were effective in precipitating similar emotional and personality disturbances. To rule out these in patients who had a history of exposure to atmospheric concussion, a search was made for objective evidence of ocular pathologic conditions which might have resulted from such trauma.

While I was on active duty in the U.S. Navy Medical Corps, many such postconcussion cases were observed in which relatively minor pathologic ocular findings appeared to substantiate a history of exposure to atmospheric concussion of traumatizing degrees. The patients had been hospitalized on the neuropsychiatric service with the complaints of irritability, restlessness, inability to concentrate, lassitude, periodic emotional swings, memory deficiency, headaches, rapid ocular fatigue and pain upon reading, blurred vision, ocular pains, and ear symptoms of tinnitus and pain. They were referred to the department of ophthalmology by the neuropsychiatric service for evaluation of their eye complaints. These cases presented evidence of mild but definite ocular changes in comparison with those seen in severe concussion injuries. Although minor in degree of severity, they were uniformly consistent and of such constancy as to offer definite aid in their analysis for the neuropsychiatric service.

CASE REPORTS

Four such cases are presented and, in Case 1, a 20-month follow-up examination was made.

CASE 1

History. A 35-year-old lieutenant was admitted to the hospital on October 10, 1943, with the complaints of diminished hearing, numbness, marked fatigue, stuttering, memory defect, mental lethargy, emotional instability, insomnia, speech difficulty, occipital headaches, blurred distant and near vision, poor night vision, and bilateral eye pains since exposure to a severe bomb blast on October 1, 1943.

The physical examination was essentially negative except for the significant aural, neuropsychiatric, and ocular findings. His hearing was reduced

and bone conduction exceeded air conduction.

The neurologic findings revealed an increase in the deep tendon reflexes on the left, a questionable positive Babinski on the right, some impairment of coördination in the use of the upper extremity muscles, mental slowness, confusion in executing instructions, and hesitancy in selecting words for speech. It was the opinion of the neurologist that there was present a diffuse organic condition simulating the picture of multiple sclerosis which could have been due to multiple areas of edema or hemorrhage resulting from the concussive effects of the explosion.

The psychiatric consultant reported, "In my opinion this man shows a very appreciable personality change of the type associated with concussion. These changes are regressing, but I am certain a Rorschach test, even at the present time, would reveal an organic pattern. I believe this man is unfit for combat duty, and should be under prolonged neuropsychiatric observation because of the possibility of (1) marked personality changes and (2) convulsive episode."

The eye findings revealed a mild degree of episcleral injection near the limbus of each eye. Vision was: O.D., 20/25; O.S., 20/30. With a pinhole disc the vision of each eye was reduced to 20/40. Unfortunately, accommodation measurements were not taken. The homatropine cycloplegic refraction revealed: O.D., with a +0.75D. sph. $\subset$ +0.5D. cyl. ax. 80° = 20/20; O.S., with a +0.75D. sph. $\subset$ +0.25D. cyl. ax. 100° = 20/30.

The ophthalmoscopic examination revealed hazy media, pigment clumps on the anterior lens capsule, and fine products of inflammation in the vitreous. The discs were slightly elevated, the margins blurred, and the central excavation was filled with white edematous tissue. The retinas showed diffuse edema throughout the whole of the fundi, being especially marked in the equatorial and peripheral regions. In these regions there were also areas of mild exudative choroiditis. In the right fundus, one disc diameter temporal and down from the macula there was a one-fourth torsion of the edematous retina and its vessels with a small hole. The maculas showed fine edema, distortion of the foveal reflex, and mild retinal pigment epithelium proliferation.

The visual fields revealed a peripheral constriction to a 2-mm. white target at 330-mm. distance which varied from 15 to 25 degrees in extent (fig. 1). X-ray films of the skull were negative.

Course. Three weeks later the patient was transferred to another hospital and was returned to full duty on December 31, 1943.

Follow-up study. On August 14, 1945, the patient was again admitted to a naval hospital with the chief symptoms of emotional swings, mood changes, lack of interest, and personality changes. The physical examination was essentially negative.

Eye findings. Corrected vision was 20/20 in each eye with the homatropine cycloplegic refraction findings of: O.D., +0.25D. sph. $\subset$ +0.75D. cyl. ax. 75° = 20/20; O.S., −0.25D. sph. $\subset$ +1.0D.

cyl. ax. 95° = 20/20. The amplitude of accommodation was: R.E., 3.3 diopters (30 cm.); L.E., 5.9 diopters (17 cm.). The peripheral and central fields to a 3-mm. white target were normal. A slight ptosis of the right upper lid existed, and the right pupil responded more to cocaine pupillary studies than the left. Versions and phorias were within normal limits.

The fundi revealed the discs to be round, flat, with distinct margins and tissue proliferation in the physiologic cups. The vascular structure appeared to be normal. The maculas showed fine pigmentary changes, distorted foveal reflexes, and

1945, with the complaints of frontal headaches, chest pains, antisocial attitude, restlessness, nightmares, inability to concentrate, blurred vision on detailed use of the eyes, and earache.

The past history (medical records substantiated the patient's story) revealed that on February 19, 1945, while on Iwo Jima, the patient was knocked unconscious for an indefinite period as a result of blast concussion (mortar-shell explosion). Upon awakening, the patient was unable to hear or speak and noticed great difficulty in reading. The hearing began to improve in 24 hours, but the speech defect persisted for 6 days. The record states that
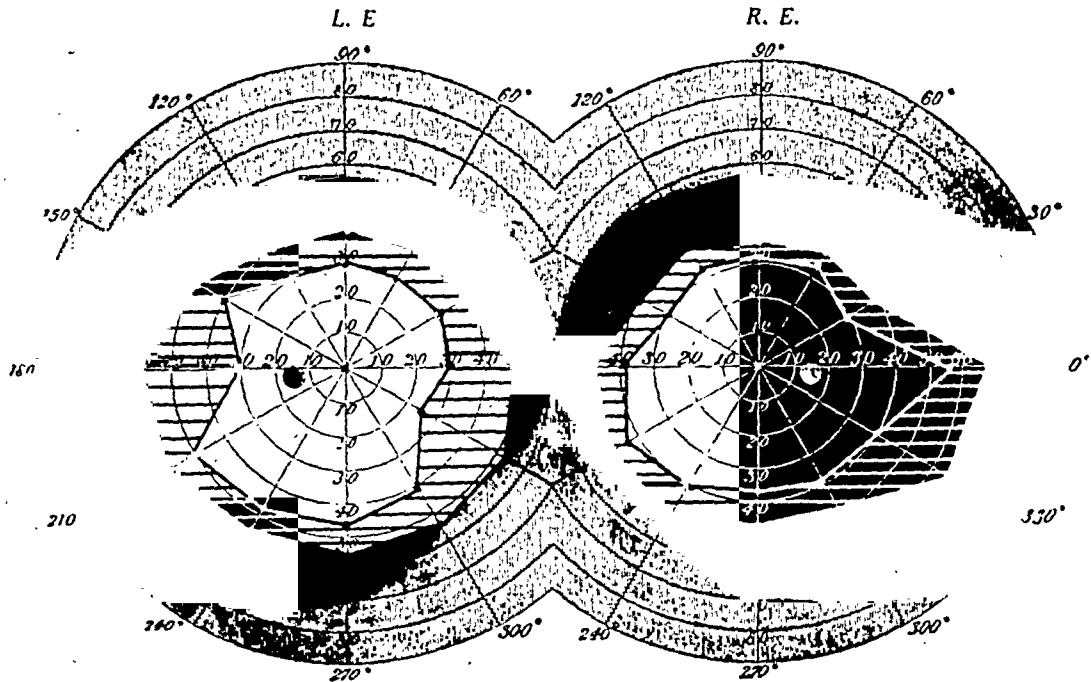
Fig. 1 (Smith). *Case 1*. Visual fields, taken on November 2, 1943, revealed a peripheral constriction to 2/330 white.

reflexes radiating out from their center like spokes in a wheel.

The retina in the right eye revealed a small proliferating retinal scar lying between two anomalously directed blood vessels that were incorporated in the "whorl" of the previous findings. From this scar, radiated additional spokelike reflexes.

In the equatorial region and periphery there were diffuse omnipresent fine retinal pigmentary changes of dispersion and proliferation. Associated with them were definite, fine changes in the retina which appeared to be cystic in nature and which rendered the tissue somewhat translucent.

The laboratory findings were essentially normal. The spinal fluid showed: W.B.C., 2; R.B.C., 3; sugar, 62 mg. per 100 c.c.; protein, 30.2 mg.; chlorides, 790 mg.; globulin, faint trace; negative Kahn; colloidal gold curve, 1,123,210,000. An electroencephalogram tracing was within normal limits.

CASE 2

History. This 23-year old white, Marine combat man was admitted to the hospital on July 5,

there was no evidence of marked emotional disturbance.

The family history was essentially negative.

The physical examination revealed the following significant findings. There was a 40 percent hearing loss in the left ear and Shrapnell's membrane was red on the left side.

Eye findings. Vision was: O.D., 20/20; O.S., 20/25, and the amplitude of accommodation was 2.4 diopters (42.3 cm.) in the right eye and 2.3 diopters (44 cm.) in the left eye.

The cycloplegic (homatropine hydrobromide) refraction was: O.D., +0.75D. sph. ⊃ +0.25D. cyl. ax. 95° = 20/20; O.S., +0.5D. sph. ⊃ +0.37D. cyl. ax. 80° = 20/20. Versions and phorias were within normal limits. His PcB. was 25.5 cm. Perimetric studies were normal. The external ocular examination was essentially normal and slitlamp findings were within normal limits.

The fundi revealed the media to be clear, the discs were round, flat, and had distinct margins. There was increased visibility of the fine vessels. The appearance of the retinas, as a whole, was

that of semitranslucence from edema. In the equatorial regions and periphery, the edema increased in degree to produce moth-eatenlike areas of graywhite retinitis, irregular in shape and size, which were deep in the retina as determined by parallax. Diffuse, small, retinal pigment clumps were present. In the choroid, evidence of mild healed choroiditis was present and, in the left eye, a disc-sized hemorrhage was present in the peripheral choroid below. The maculas appeared to be normal.

The laboratory findings were essentially negative.

The neuropsychiatric consultation revealed no

of a mortar-shell explosion 10 feet from him. The patient stated that he was unconscious for 12 hours following the trauma. There had been gradual improvement in his condition since then.

The authenticated past history revealed that the patient was first admitted to the sick list with the diagnosis of "blast concussion, atmospheric," on February 19, 1945, with the symptoms as he described. He continued as a patient in the naval medical facilities until May 23, 1945, at which time he was discharged to limited duty. The family history was essentially normal, as was the general physical examination.
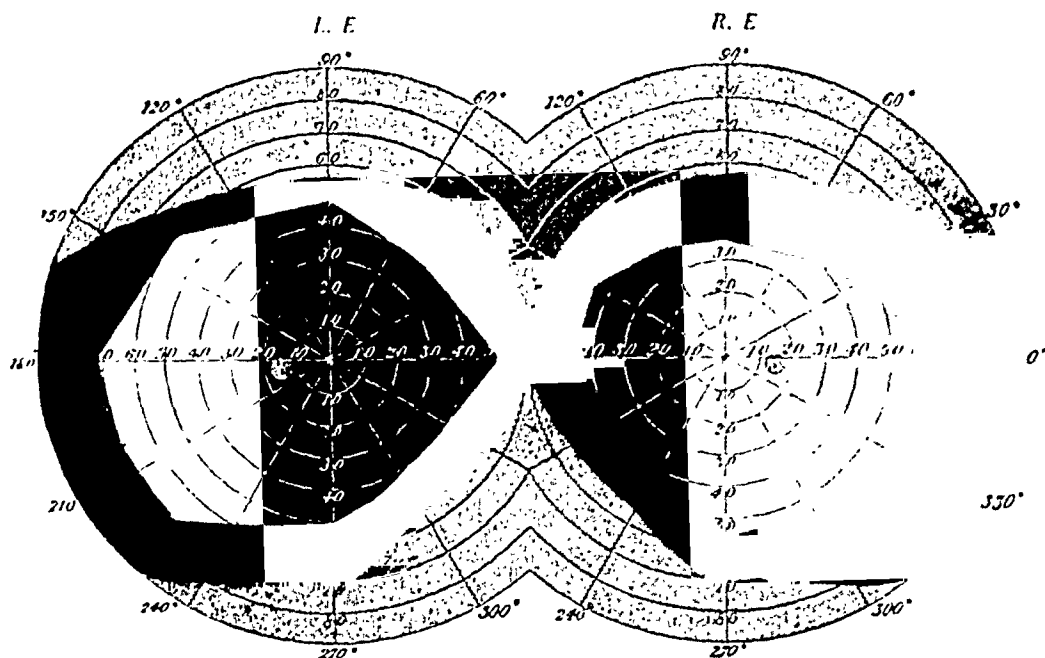
Fig. 2 (Smith). *Case 3.* Visual fields, taken on September 19, 1945, showed a 15-degree constriction to 3/330 white.

neurologic disturbance. The psychiatric evaluation revealed, "a coöperative but tense individual with normal speech. Combat rumination is interfering with thought processes. Affect is appropriate and grasp good. Service history confirms a severe blast concussion syndrome in February, 1945, on Iwo Jima with neuropsychiatric disability at that time. His present eye and somatic pain plus thought irregularity, are considered due, in the main, to his recent organic brain injury. Unfit for service of indefinite duration and recommend that he be discharged from the U.S. Naval Service."

CASE 3

History. The patient, a white man, aged 20 years, was a private first class in the U.S. Marine Corps, who was admitted to the hospital on September 17, 1945, with the complaints of a shaky feeling, headaches, rapid ocular fatigue when reading, general fatigability, and restlessness during sleep. These symptoms had begun 7 months previously, following exposure to the concussion

Eye findings. Vision was: O.D., 20/20; O.S., 20/20. Cycloplegic (homatropine hydrobromide) refraction revealed: O.D., +0.75D. sph. ⊃ +0.25D. cyl. ax. 100° = 20/20; O.S., +0.75D. sph. ⊃ +0.37D. cyl. ax. 80° = 20/20. The amplitude of accommodation was: R.E., 7.7 diopters (13 cm.); L.E., 6.9 diopters (14.5 cm.).

The fundi presented a slight but definite appearance of retinal edema in the periphery with the findings in the right eye being the most marked. Fine pigment changes were present in the pigment epithelium. Versions and phorias were within normal limits. Peripheral field (fig. 2) studies with a 3-mm. white target revealed a 15-degree constriction from normal.

The neurologic examination was negative and the psychiatric examination revealed mild mental tension, anxiety, and sleep disturbance. The patient was continued on limited active duty.

CASE 4

History. This 24-year-old Marine corps ser-

geant (white) was admitted to the hospital on November 5, 1945, for reëvaluation of his symptoms of restlessness, irritability, and nightmares.

His authenticated past history revealed that on November 15, 1944, he suffered trauma to both eyes and head from "blast concussion, atmospheric," as a result of a hand grenade exploding directly in front of him. This incident was followed by tinnitus, ocular pain, and headache. In January, 1945, the patient began to show mental symptoms of nervousness, restlessness, irritability, and sleeplessness. In February, 1945, he was admitted to the sick list because of accentuation of these symptoms

The neuropsychiatric examination revealed residual evidence of his occupational fatigue and it was felt that he was not qualified for full duty (fig. 4).

DISCUSSION

The major damage sustained by the eyes as a result of exposure to atmospheric concussion has been elaborated upon in the past; however, the effect upon the ocular tissues of relatively minor degrees of atmospheric
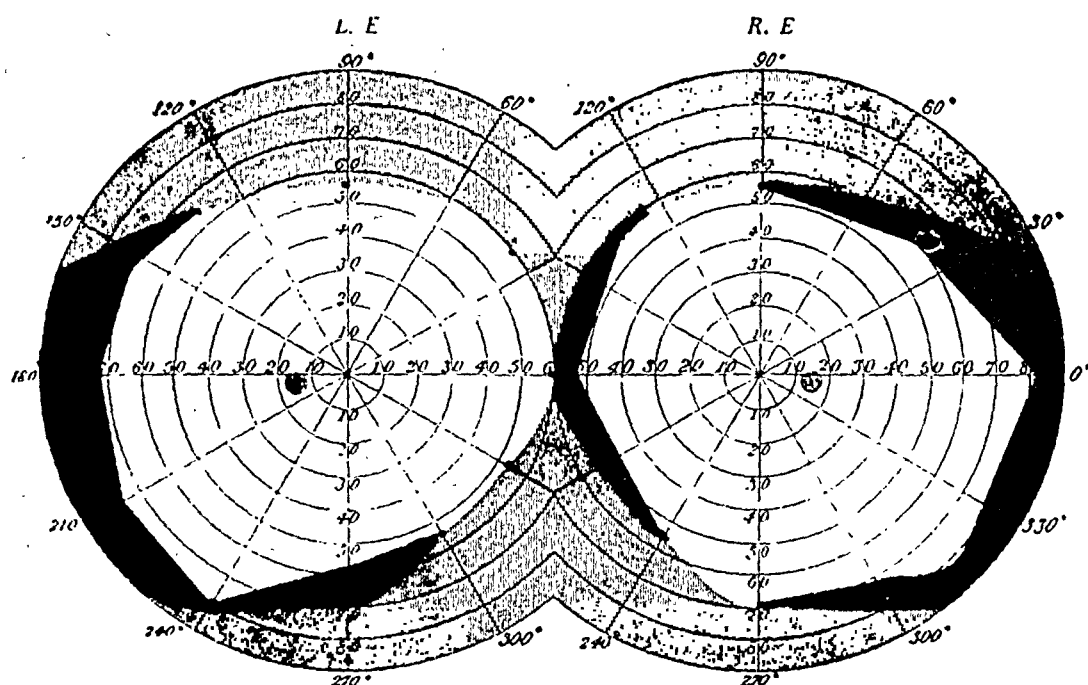
Fig. 3 (Smith). *Case 4.* Visual fields, taken on March 22, 1946, showed a slight peripheral constriction to 2/330 white.

and was ultimately placed on limited active duty in the United States on April 18, 1945, with a diagnosis of "fatigue, operational." The physical examination at this time was essentially normal.

Eye findings. Vision was: O.D., 20/20; O.S., 20/20. Cycloplegic (homatropine hydrobromide) refraction showed: O.D., +0.75D. sph. = 20/20; O.S., +0.75D. sph. ⊃ +0.12D. cyl. ax. 90° = 20/20. The amplitude of accommodation was: R.E., 7.4 diopters (13.5 cm.); L.E., 7.2 diopters (13.8 cm.). The PcB. was 8.5 cm.

The external ocular examination and pupillary findings were within normal limits. The fundi revealed a diffuse pre-equatorial irregularity in the pigment epithelium. There was a translucent appearance to the retina in the periphery with areas of cystic degeneration. Occasional areas of increased and dispersed choroidal pigment were seen between the choroidal vessels which were interpreted as residue of previous choroiditis. The field studies with a 2-mm. white target showed a slight peripheral field constriction (fig. 3).

concussion producing lesser damage has been infrequently mentioned. From the cases cited above, it appears as if comparatively minor but important changes may occur in the tissues of the eye as a result of exposure to atmospheric concussion.

The changes seen in the fundi and the deficiency manifested by the accommodative apparatus were rather constant, and the latter was the apparent source of a constant symptom on the part of these patients—that is, fatigability upon reading or with close detailed work. These ocular lesions aided the neuropsychiatric department in evaluating the concussion trauma background which contributed to the psychiatric complaints of

patients who had been exposed to atmospheric concussion.

Westcott[46] and Groves[47] differ somewhat in their opinoin as to the disturbance to the

to the defect in the accommodative apparatus. The pathologic defect in the accommodative mechanism is apparently in the ciliary body, which is consistent with the fundus
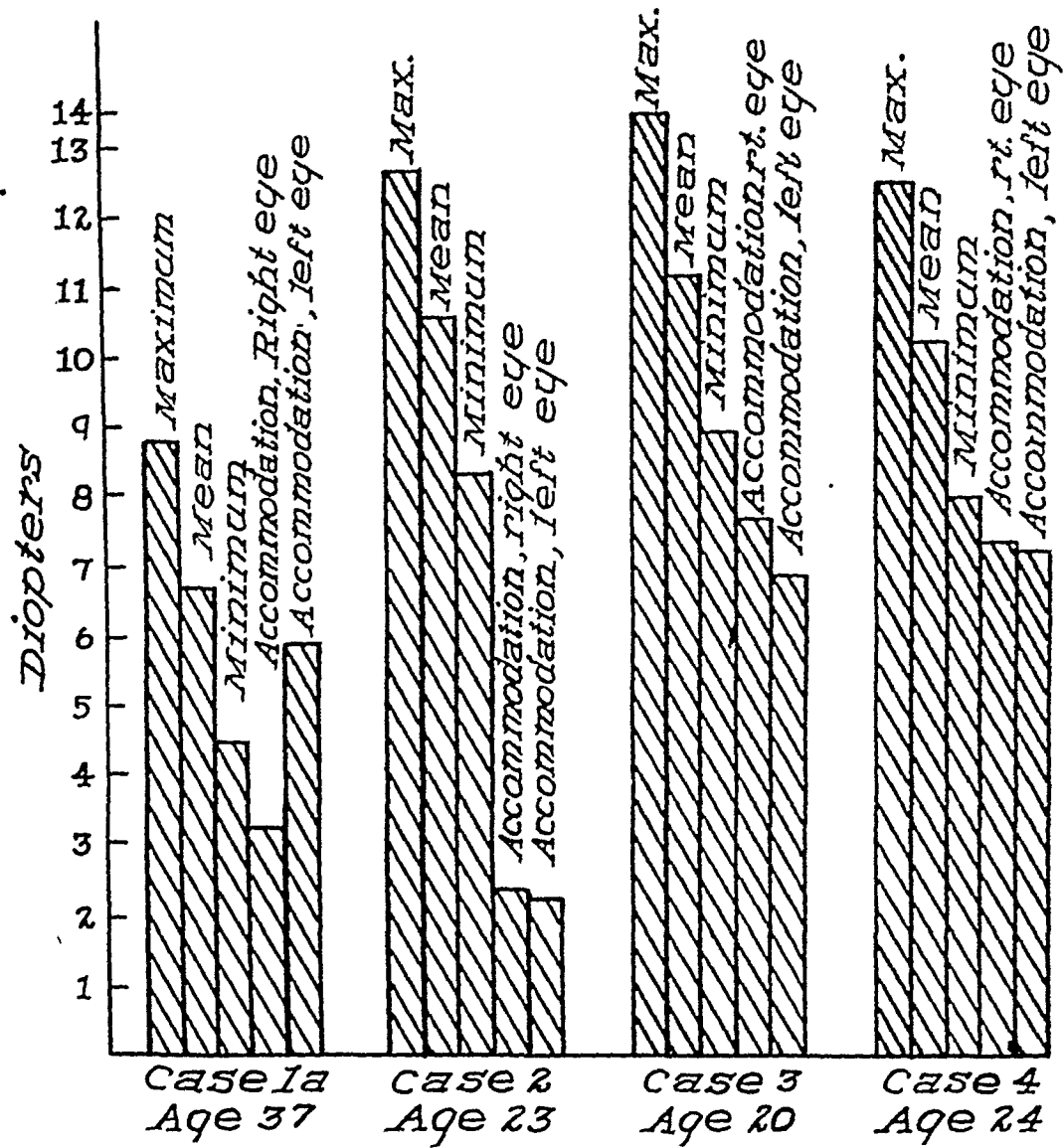
Fig. 4 (Smith). Accepted limits of accommodative values for patient's age (see reference 48) compared with the accommodative findings exhibited by the patients in this study.

accommodative power of the eye resulting from blunt traumatic concussion. The more extensive work of Wescott indicates that there is no significant posttraumatic change in the accommodative amplitude; rather, the reading discomfort experienced by these patients is due to a disturbance in the higher cortical centers.

In our cases the inability to read with comfort seemed to be directly attributable

changes increasing in degree and extent as the ora serrata is approached.

SUMMARY

Four cases with authenticated histories of exposure to atmospheric concussion of undetermined degree have been presented. They had been examined at posttraumatic intervals which varied in time from 10 days

to 12 months. In one case follow-up study was made after 20 months. All cases were seen as consultations for the neuropsychiatric service for evaluation of their ocular complaints.

The cases presented the following fundamental pathologic features:

1. Symptoms of headache, irritability, inability to concentrate, restlessness, fatigability, ocular fatigue and pain upon reading.

2. Deficiency in the amplitude of accommodation.

3. Retinal edema which was more marked in the equatorial and pre-equatorial regions of the fundus.

4. Mild peripheral choroiditis lesions.

5. Cystic degeneration of the periphery of the retina.

6. Constriction of the peripheral visual fields.

CONCLUSION

Atmospheric concussion may affect the ocular structures to a variable degree. In minor degrees, there appear disturbances in the ocular structure and function which are uniformly constant. These are of aid to the ophthalmologist in evaluating the ocular complaints, and help the psychiatrist in his evaluation of the part played by the trauma in patients who manifest the symptoms of the "postconcussion syndrome."

Furthermore, there appears to be no correlation between the eye findings in the atmospheric and blunt traumatic postconcussion cases.

Atmospheric concussion may produce an ocular syndrome characterized by deficiency of accommodation, retinal edema, mild choroiditis, and peripheral field constriction.

1005 Medical Arts Building (1).

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OPHTHALMIC MINIATURE

The examination of eyes affected with fungus haematodes, in its early period, has led to the conclusion that the disease consists in organic change of the retina, or in a growth from the retinal extremity of the optic nerve. This would account satisfactorily for the appearance, exhibited in the commencement, of an adventitious growth in the fundus of the eye.

Sir William Lawrence, *A Treatise on the Diseases of the Eye*, 1833.

VERTICAL NYSTAGMUS ON DIRECT FORWARD GAZE WITH VERTICAL OSCILLOPSIA*

MORRIS B. BENDER, M.D., AND WARREN F. GORMAN, M.D.

New York

Vertical nystagmus may be present either on upward gaze or on direct forward gaze. Vertical nystagmus on upward gaze is not uncommon. As a rule, it is indicative of acquired disease of the brain stem.[1] Vertical nystagmus on direct forward gaze, however, is rare and is usually found in a patient with "congenital" nystagmus.[†]

On rare occasions, vertical nystagmus on direct forward gaze may be seen in patients with acquired disease of the nervous system. In these cases of vertical nystagmus it is necessary to distinguish the congenital from the acquired type. Although the differential diagnosis depends on a consideration of all the factors in each case, the presence of oscillopsia is frequently a deciding feature.

Oscillopsia is a visual experience in which the patient sees a stationary object as moving from side to side (horizontal oscillopsia) or up and down (vertical oscillospia). The oscillopsia is concomitant with the rhythmic movements (nystagmus) of the eyes and it is usually indicative of an acquired nystagmus. The following two case reports are studies of patients with acquired upward nystagmus on direct forward gaze.

REPORT OF CASES

CASE 1

History. E. M., a 55-year-old man, was admitted on January 2, 1948, to the Bellevue Psychiatric Hospital. For two days before

admission he felt weak and had the sensation of "falling backwards." The past medical history disclosed that in 1945 he was rendered momentarily unconscious by a blow on the head. In 1942, he had a discharge from the right ear, with subsequent tinnitus and poor hearing. He later admitted to consuming a quart of sherry wine daily.

On examination he was found to be emaciated, with dry peeling skin, fissures at the corner of the mouth, and injection of the conjunctivas with vascularization about the limbus of both eyes. There was frequent blinking, avoidance of light, and other signs of photophobia. (The patient claimed that he had always been sensitive to light.)

There was a constant tremor of the entire body, and a coarser tremor of the right lower extremity. He walked slowly on a broad base, falling to the left or backward. Both ankle jerks were diminished. There was plantar hyperesthesia and calf tenderness. Vibratory sense was diminished in both lower extremities. All laboratory studies, including spinal fluid examination, X-ray studies of the skull and chest, gastro-intestinal series, liver chemistries, blood bromides, and blood Wassermann tests, were negative.

Ocular status. There was photophobia with frequent blinking and narrowing of the palpebral fissures. Eye movements were performed well in all directions of gaze. However, when he looked directly forward, there was a very rapid nystagmus in the vertical plane. The nystagmus took place entirely above the horizontal meridian and the fast component was in an upward direction.

As the patient looked to each side, the spontaneous vertical nystagmus became oblique, inclining about 45 degrees to either side. When the patient lay on his side or

† In the congenital form, vertical nystagmus on forward gaze is not the only ocular finding. It is frequently associated with a nystagmus on lateral, upward, and downward gaze. Often in these cases there is a history that the patient has had "dancing eyes" for many years.

back, the nystagmus continued unchanged relative to the long axis of the body. Closing one eye or both eyes did not alter the nystagmus. On extreme upward gaze, however, the nystagmus increased. On downward gaze the nystagmus diminished. The nystagmus fluctuated in rate and amplitude. In time, it gradually diminished.

Subjectively, the patient reported that objects "moved up and down"—vertical oscillopsia. He said that near objects oscillated less than far objects and not as rapidly.

Special Studies

A. Vestibular Tests

1. Turning tests. The patient was placed in a Bárány chair in a sitting position, with his head inclined 30 degrees forward. With his eyes closed, he was rotated 10 times in 20 seconds to either side. In a normal individual this procedure produces horizontal nystagmus in a direction opposite to that of rotation. In this patient the Bárány test modified the spontaneous upward nystagmus, resulting in an oblique (up and out) nystagmus.

The patient's head was then inclined 90 degrees toward the right shoulder and he was again rotated to the right and left. With the head in this position, rotation of normal people to the right (clockwise) produces downward nystagmus, and rotation to the left (counter-clockwise) produces upward nystagmus. On rotating the patient in this manner to the right, it was found that the expected downward nystagmus was not present. Instead, his spontaneous upward nystagmus ceased for 15 seconds, then slowly reappeared. On rotation to the left, the preexistent upward nystagmus was increased in amplitude for 24 seconds, after which time the resting upward nystagmus became apparent at its usual amplitude.

2. Caloric tests. Aural examination revealed that there was no significant hearing loss. Each ear was irrigated for 60 seconds with ice water while the patient was sitting erect and his eyes fixating forward. Such

irrigation of the right ear produced nystagmus to the left and irrigation of the left ear produced nystagmus to the right. There were no abnormal changes on the past pointing. Vertigo was present.

B. Optokinetic Nystagmus

A drum, 9 inches in diameter, papered with one-half inch alternate black and white vertical stripes, was rotated in front of the patient's eyes at a speed of 2 revolutions per second. In normal individuals, rotation of the drum with the axis in the vertical plane results in horizontal nystagmus. In our patient such rotation produced oblique nystagmus. With the axis of the drum in the horizontal plane, downward rotation accentuated, while upward rotation diminished the spontaneous upward nystagmus.

C. Effects of Drugs.

It is known that barbiturates influence nystagmus and other ocular movements.[2] Latent nystagmus or any other type of nystagmus which is present on forward gaze is abolished by intravenous injections of sodium amytal. In a previous communication[3] it was also reported that an ocular squint disappeared whenever that patient was intoxicated with alcohol. Evidently alcohol had the same effect as barbiturates. Consequently we tried the effect of the drugs (amytal and alcohol) in our two cases of vertical nystagmus on forward gaze.

1. Sodium amytal. Sodium amytal (0.2 gm.) was injected intravenously over a period of two minutes. Within two minutes the spontaneous upward nystagmus on forward gaze stopped and the oscillopsia disappeared. Deviation of the eyes in the vertical or horizontal plane resulted in nystagmoid movements but on many occasions the nystagmoid movements were fine and rapid.[4] During the period when the nystagmus on forward gaze was abolished by amytal, there was likewise no response to the optokinetic drum on forward fixation. We did not carry out Bárány-turning or caloric-stimulation

tests while the patient was under the influence of amytal. After 11 minutes, the spontaneous upward nystagmus on forward gaze and the concomitant oscillopsia began to return.

2. *Alcohol.* The patient was given 1,000 cc. of medicinal sherry in 10 minutes by stomach tube, after a gastric analysis. He became intoxicated and showed slurred speech, cheerful affect, and an increase in staggering. His body and extremity tremor diminished. The nystagmus on forward gaze ceased completely, as did the oscillopsia. However, as in amytal narcosis, nystagmus on lateral or vertical gaze persisted.

3. *Hyoscine.* It was suggested that the spontaneous nystagmus on forward gaze might be an extrapyramidal disorder. For that reason the effect of hyoscine on ocular movements was tried. Hyoscine (1/100 gr.) was injected subcutaneously. After 35 minutes, the patient complained of a dry mouth, and showed dilated pupils and a diminution of the tremor of the extremities. However, there was no effect on the nystagmus.

Course. The patient was given large doses of water-soluble vitamins orally and liver extract intramuscularly. The nystagmus fluctuated in rate and amplitude from day to day, but gradually subsided. Although, originally, lateral deviation of the eyes had resulted in oblique nystagmus, after 9 weeks lateral gaze produced largely horizontal nystagmus. The spontaneous vertical nystagmus above the horizontal meridian on forward gaze gradually diminished in rate and amplitude, being almost imperceptible 13 weeks after admission to the hospital. The peripheral neuropathy improved gradually.

Comment. This patient, a known alcoholic, showed vertical nystagmus and vertical oscillopsia on forward gaze. Under observation the nystagmus and the oscillopsia subsided, thus suggesting that the ocular signs and symptoms were of the acquired type. Of interest is that amytal given intravenously and alcohol by mouth temporarily abolished the vertical nystagmus on forward gaze and the associated oscillopsia.

CASE 2

History. W. T. M., a 48-year-old white carnival operator, was admitted on October 8, 1947, to the Bellevue Psychiatric Hospital with early delirium tremens. On October 2, 1947, he noted that objects "jumped up and down"—(oscillospia)—"that the room seemed to turn around" and that he "saw double both to one side or above." He complained of dizziness and blurred vision. He also volunteered that "when one doctor examined me down here I couldn't turn my eyes to the left at all," thus suggesting a paralysis of conjugate gaze to the left.

Routine examination revealed signs of diffuse involvement of the entire nervous system. Defects in recent memory were present. There was a coarse irregular jerky tremor of all extremities. There were signs of peripheral neuropathy with absent knee and ankle jerks, diminished vibration sense below the knees, hyperesthesia to pin prick in the glove and stocking areas, calf tenderness and hyperpathia on stroking of the plantar surface of the feet.

All laboratory examinations, including spinal fluid studies, X-ray studies of the chest and skull, electroencephalogram, blood count, urinalysis, blood bromides, blood and spinal fluid Wassermann tests, and liver chemistry tests, were within normal limits. Gastric analysis showed that there was no free acid. It should be noted that the patient had had a subtotal gastrectomy for peptic ulcer three months before the present admission.

Ocular status. The patient was transferred to the neurologic service on October 10, 1947. He was observed daily during his hospital stay and at frequent intervals thereafter for a total of 9 months. Special eye examinations were periodically performed. It was noted that when the patient looked straight ahead the eyes moved rhythmically up and down (vertical nystagmus). The excursions

occurred entirely above the horizontal meridian and the quick component was in an upward direction. The eyelids moved in synchrony with the upward nystagmus. Position of the head did not alter this nystagmus. Subsequent examinations showed that with the head erect, lateral deviation of the eyes was also accompanied by an upward nystagmus but frequently there were rotary components.

On forward gaze there was also spontaneous zig-zag rotary movement of each eye, more so on the left. These zig-zag movements in one eye were neither coördinated nor associated with the movements in the other. Similar, almost myoclonic, movements were noted in various muscles throughout the body, especially in the tremulous upper extremities. On extreme downward gaze, the vertical nystagmus stopped. On moderate elevation of gaze, the vertical nystagmus became more conspicuous but, on extreme upward gaze, the nystagmus disappeared.

Fixation of near and far objects did not alter the nystagmus on forward gaze but the oscillopsia was much more apparent to the patient when he fixed objects at a distance. There was a latent weakness of both external rectus muscles. On occasions, when he attempted to look to the left, the right eye rotated to the left, but the left eye turned inward toward the nose. The mirror image of that pattern of movement took place on his attempt at right lateral gaze.

Convergence was good. The visual acuity on admission to the neurologic service was 20/100 and within a few weeks improved to 20/30 in each eye. Examinations of the central and peripheral fields of vision for form and color were normal.

Special Studies

A. Vestibular Tests

As already noted, the patient reported that the vertical oscillation of objects diminished as they approached him. Tests with targets at near and distant points revealed that the vertical oscillopsia disappeared when he fixed

a target within one meter of his eyes. Beyond this point the vertical oscillopsia was pronounced. Bárány turning tests induced no significant abnormalities. Caloric tests, using cold-water irrigation of the ears, also yielded apparently normal reactions.

B. Optokinetic Nystagmus

On rotating a striped drum before the patient's eyes, the spontaneous nystagmus was altered. When the axis of the drum was horizontal and the rotation toward the patient,* the amplitude of the upward nystagmus was increased. When the direction of rotation of the drum was reversed, the eyes dipped below the horizontal axis and the upward nystagmus diminished in amplitude. On rotation of the drum in the vertical axis before the patient's eyes, clockwise or counter-clockwise rotation produced oblique (up and out) modification of the spontaneous vertical nystagmus.

C. Effect of Drugs

1. Sodium amytal. About two minutes after intravenous injection of 0.25 gm. of sodium amytal, the nystagmus on forward gaze began to decrease in amplitude. The vertical nystagmus on direct forward gaze disappeared completely 12 minutes after the injection was begun and remained absent for a period of 13 minutes. The oscillopsia likewise disappeared during this period. The zig-zag and completely dissociated eye movements were also abolished by amytal.

2. Alcohol. Intravenous injection of 80 cc. of ethyl alcohol, equivalent to 5 ounces of whiskey, caused the vertical nystagmus on forward gaze to disappear. The nystagmus on upward and lateral gaze, however, became more marked in amplitude. There were oblique components on lateral gaze. By the time tests with alcohol were made, the zig-zag eye movements were no longer present.

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*In the normal individual such rotation of the drum produces slow deviation of the eyes above the horizontal axis with upward nystagmus.

Therefore, we have no information as to the effect of alcohol on these movements.

Course. Under observation the vertical nystagmus on forward gaze subsided and ultimately disappeared after 8 weeks. There was a concomitant disappearance of the vertical oscillopsia on forward gaze. Vertical nystagmus on forward gaze persisted for 12 weeks. Horizontal nystagmus on lateral gaze was still present after 5 months. Seven months after admission, there was slight rotatory nystagmus on left lateral gaze.

The peripheral neuropathy improved gradually. The knee jerks reappeared in 16 days, while the ankle jerks could be elicited again after 3 weeks. Calf tenderness disappeared after 9 weeks of hospitalization and vibration sense returned at that time.

Comment. This was a case of upward nystagmus on forward gaze in an alcoholic individual. The vertical nystagmus was accompanied by vertical oscillopsia. Since the patient became aware of oscillopsia and since nystagmus and oscillopsia disappeared simultaneously, it may be safely assumed that these symptoms were acquired and not of the congenital type. The patient showed another rare disorder in eye movements: spontaneous zig-zag or dissociated eye movements, which are sometimes seen in subacute encephalitis and often associated with marked, almost myoclonic, tremors throughout the body. It is remarkable that amytal and even alcohol, when given intravenously, abolished the upward nystagmus on forward gaze. The spontaneous, dissociated, almost choreiform, eye movements were also abolished by amytal.   •

DISCUSSION

There are three points worthy of comment: (1) Nystagmus, (2) oscillopsia, and (3) effect of drugs on nystagmus and oscillopsia.

1. Nystagmus. Distinction must be made between vertical nystagmus on upward gaze and vertical nystagmus on direct forward gaze. Spontaneous vertical nystagmus on di-

rect forward gaze is seen almost solely in cases of congenital nystagmus. The spontaneous vertical nystagmus on forward gaze found in our two cases, however, is of the acquired type. In each, the oscillopsia appeared shortly before admission to the hospital and both the oscillopsia and nystagmus on direct forward gaze subsided concomitantly with treatment.

Both of the patients were chronic, severe alcoholics who exhibited signs of encephalopathy and peripheral neuropathy. It is known that such patients have diffuse lesions throughout the entire nervous system and that the brain stem is one region which is frequently involved in cases of severe alcoholism. One of the symptoms of disease of the brain stem is vertical nystagmus on upward gaze. Clinicopathologically, cases of vertical nystagmus on upward gaze have been reported in patients with verified lesions of the colliculi, of the caudal part of the pons and the medulla at the level of the inferior olivary bodies, and, in fact, with lesions of the brain stem at almost any level.[1]

There have been few, if any, reports of clinicopathologic studies of cases of vertical nystagmus on direct forward gaze. To date, therefore, it is not possible to localize the lesion in these cases of vertical nystagmus on direct forward gaze with any degree of accuracy. One can only suspect that the pathologic condition is somewhere in the brain stem.

On the other hand, judging from animal experiments, it would appear that the lesion might be in the vermis of the cerebellum. Lesions in the posterior part of the cerebellar vermis in the experimental animal have resulted in spontaneous vertical nystagmus.[5]

Using cats, Spiegel and Scala electrocauterized the vermis to obtain "positional nystagmus." They also recorded that the animal exhibited vertical nystagmus on being observed in its "normal position" which is analogous to forward gaze in the erect human subject.[5]

This vertical nystagmus in the normal

position of the operated cats consisted of very slow oscillations—five jerks in 30 seconds in one instance. The fast component was generally upward, but in one experiment in which both globose nuclei, the pyramis and uvula, were destroyed, it was downward.

2. *Oscillopsia.* Oscillopsia is a symptom caused by movements of the eyeballs. It is usually apparent in the vertical plane. Vertical oscillopsia has been reported in cases of multiple sclerosis,[6] encephalitis, brain tumors, and vascular disease of the brain and brain stem.

Oscillopsia can be produced by vestibular stimulation. Vertical oscillopsia is frequently found when vertical nystagmus is induced by the Bárány chair or caloric tests. However, when horizontal nystagmus is induced, it is interesting to note that individuals tend to report their sensations as "dizziness" and omit the phenomenon of horizontal oscillopsia.

Horizontal oscillopsia is often seen in cases of congenital latent nystagmus. It becomes apparent when there is interference with binocular vision. Thus, when one eye is covered or a piece of cardboard is placed on the bridge of the nose so as to interfere with binocular vision, a marked horizontal nystagmus becomes manifest. With this horizontal nystagmus, the patient complains that the observed object shimmers or moves back and forth in the horizontal plane.

3. *Effect of drugs.* Despite the presence of gross nystagmoid movements of the eyes, oscillopsia is not found in cases of congenital horizontal nystagmus on forward gaze. There is, instead, a marked impairment of visual acuity. Under the influence of intravenous sodium amytal, the ever present congenital nystagmus can be arrested. This is followed by an improvement in the visual acuity.[2]

As the effect of the amytal wears off and the congenital nystagmus reappears, the patient complains of foggy vision. Interestingly enough, there is no oscillopsia at this latter time but instead the visual images may appear elongated in the plane of the nystagmus, or may appear multiple.[7]

In our cases, intravenous sodium amytal or alcohol by mouth temporarily abolished both the acquired vertical nystagmus on direct forward gaze, and the concomitant vertical oscillopsia.

SUMMARY

Two cases of vertical nystagmus on direct forward gaze are described. Both of the patients complained of images bobbing up and down—vertical oscillopsia. When the nystagmus ultimately subsided the oscillopsia disappeared. Intravenous sodium amytal or alcohol temporarily abolished the vertical nystagmus and the concomitant vertical oscillopsia. Differentiation has been made between the acquired and the congenital types of vertical nystagmus on direct forward gaze.

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TEMPORAL SUBCONJUNCTIVAL HEMORRHAGES AS A COMPLICATION OF RHINOPLASTIC PROCEDURES

WAYNE W. WONG, M.D.
Honolulu, Hawaii

AND

W. B. SLAUGHTER, M.D.
Chicago, Illinois

The occurrence of subconjunctival hemorrhages in one or both eyes as a minor complication of a rhinoplastic surgical operation is so consistent that this study was undertaken in an attempt possibly to explain some of the factors which cause these hemorrhages to be located in the temporal sector of the globe. It was thought that this study of 55 consecutive cases of rhinoplastic patients might also help to explain the frequent temporal location of the common spontaneous innocuous subconjunctival hemorrhages.

Only those cases that required a complete operation were selected. All operations were performed under local infiltrative anesthesia. The operating conditions and technique were essentially the same in the entire series.

In this series of 55 cases, subconjunctival hemorrhages were observed in 32 cases in one or both eyes. In 31 of these, the subconjunctival hemorrhages occurred only in the temporal sector of the bulb. Only in one patient were the hemorrhages other than temporal, this solitary case being circumlimbal in one of the eyes only. Even in this case, however, the hemorrhages were more intense in the temporal sector.

Table 1 shows the age, sex, degree of ecchymosis, and presence or absence of subconjunctival hemorrhages in these patients. The blood pressure was normal in all cases. No general systemic disease was found in the entire group. No local ocular inflammation was observed before, during, or after surgery. These cases were entirely elective and were done for corrective purposes.

From Table 1, it can be readily seen that the occurrence of subconjunctival hemorrhages is directly dependent on the degree of ecchymosis that is evident following surgery.

The degree of ecchymosis as listed in Table 1 was divided roughly into three groups. It was considered minimal when there was a slight puffiness of the lower lid with only a faint discoloration which disappeared in a few days; moderate, when both lids were swollen and discolored to a greater degree; and pronounced, when both lids were swollen shut and the discoloration of the lids was violescent (fig. 1).

When subconjunctival hemorrhages com-

Fig. 1 (Wong and Slaughter). (A) Bilateral ecchymosis and bilateral temporal subconjunctival hemorrhages are present on the third postoperative day. (B) Close-up view of a typical subconjunctival hemorrhage.

plicate a rhinoplastic procedure, these factors are noted. Immediately postoperatively, the bulbar conjunctiva is not injected nor congested. There is no chemosis. The edema of the lids, in those cases that do have some reaction, is noted within 6 to 8 hours postoperatively. This is accompanied by a slight glassiness of the conjunctiva, with or without a slight congestion of the conjunctival vessels. This is due in part to the decreased sensitivity of the blinking reflex following the preoperative medication and the postoperative mental relaxation. No evidence of any subconjunctival hemorrhages is noted at this time.

TABLE 1

Occurrence of Subconjunctival Hemorrhages in Rhinoplastic Patients

No.	Sex	Age	Ecchymosis	Subcon-junctival Hemorrhages	Remarks
1	F	25	L.E. 3+	L.E.	Duration 3 weeks
2	F	18	B.E. minimal	None	
3	F	21	B.E. 2+	None	
4	F	27	B.E. 3+	B.E.	Duration 25 days
5	M	35	B.E. minimal	None	
6	F	18	Minimal	None	
7	M	18	B.E. 3+	B.E.	Duration 3½ weeks
8	F	21	R.E. 2+, L.E. 4+	L.E.	Duration 26 days
9	M	22	B.E. 4+	B.E.	Duration 4 weeks
10	F	26	B.E. 2+	L.E.	Punctate temporal
11	F	22	None	None	
12	F	23	Minimal	None	
13	F	23	R.E. 2+, L.E. 3+	B.E.	L.E. worse; duration 4 weeks
14	F	23	B.E. 3+	L.E.	Duration 20 days
15	F	15	B.E. 3+	B.E.	Duration 3 weeks
16	M	25	B.E. 3+	B.E.	Duration 3½ weeks
17	F	20	B.E. 2+	B.E.	Duration 4 weeks
18	M	28	Minimal	None	
19	F	23	B.E. 2+	R.E.	3 small postop. hem., L.E.
20	F	32	B.E. 3+	None	
21	F	30	R.E. 4+, L.E. 2+	R.E.	Duration 3 weeks
22	F	38	R.E. 4+, L.E. 3+	B.E.	R.E. more; and in nasal
23	F	32	R.E. 3+, L.E. 4+	L.E.	Duration 15 days
24	F	24	R.E. 2+, L.E. 4+	L.E.	Duration 15 days
25	F	26	R.E. 3+, L.E. 2+	B.E.	L.E. minimal
26	F	28	Minimal	None	
27	F	37	Minimal	None	
28	F	18	R.E. 4+	B.E.	Marked
29	F	25	Minimal	None	
30	M	25	Minimal	None	
31	F	45	Minimal	None	
32	F	42	B.E. 3+	None	
33	F	35	Minimal	None	
34	M	16	B.E. 3+	B.E.	
35	M	38	L.E. 2+	None	
36	F	24	B.E. 4+	B.E.	
37	M	30	L.E. 2+	None	
38	M	22	B.E. 3+	B.E.	Marked
39	F	26	R.E. 2+	R.E.	
40	F	30	Minimal	None	
41	F	26	Minimal	None	
42	F	20	R.E. 3+	B.E.	
43	F	25	Minimal	L.E.	Fractured right side
44	F	25	B.E. 2+	B.E.	Postop. epistaxis
45	F	30	B.E. 4+	B.E.	R.E. greater than L.E.
46	F	25	Minimal	B.E.	Very small
47	M	26	B.E. 3+	B.E.	
48	M	30	Minimal	None	
49	M	22	B.E. 2+	B.E.	Very small
50	F	24	B.E. 2+	B.E.	Small
51	F	18	Minimal	None	
52	F	28	Minimal	B.E.	Small
53	M	21	B.E. 2+	B.E.	
54	M	30	Minimal	None	
55	F	38	Minimal	None	

About 12 to 24 hours postoperatively, ecchymosis develops in one or both eyelids. The bulbar conjunctiva is not changed remarkably during this period. Immediate and constant use of ice compresses postoperatively does not appear to influence the de velopment nor the degree of ecchymosis in those cases that subsequently develop ecchymosis of the lids.

At the 24-hour postoperative period, sub

conjunctival hemorrhages have not yet appeared in all the cases that will eventually develop them. It is more common for the subconjunctival hemorrhages to appear between the 24th to 36th postoperative hour than between the 36th to the 48th hour. The general appearance of these subconjunctival hemorrhages when they first appear easily separates them into two distinct varieties.

In one group of patients, they form an intensely red triangular-shaped patch in the exposed temporal sector of the bulbar conjunctiva—the area delineated by the upper and lower lids as it meets the temporal limbus at about the 1:30 to the 4:15-o'clock positions. This area may or may not extend to the limbus, since there may be a bridge of clear conjunctiva between the limbus and the patch of hemorrhage. The hemorrhage may show some variation in intensity of color, but this is due mainly to the degree of oxygenation by the lacrimal secretion.[1]

On the second day of its appearance, there is a variable tendency for the hemorrhage to extend into the inferior fornix so that by the 72-hour period, the triangular patch may reach the limbus at the 6-o'clock position and may extend down into the inferior fornix, stopping at the inferior attachment of the palprebral conjunctiva. This downward extension is due to the massaging effect of the upper lid, as well as to gravity.

In a second group of patients, a less extensive type of hemorrhage is found. These occur as an irregular, horizontal, linear type of low-intensity hemorrhage and lie definitely in the 3- to 9-o'clock meridian. Composed of a small amount of blood, they are faint in comparison to the first type and their dense portion is usually closer to the limbus. The lateral extensions usually fade gradually into the normal surrounding conjunctiva. In width these hemorrhages are usually about 3 to 5 mm. at their widest portions. Such hemorrhages do not appear to be affected by the massaging effect of the lids nor by gravity.

The difference between these two types of hemorrhages is one of degree, although the causative factor and the location of the pathologic vessels are also different. In the first type, there appears to be a leakage from the deeper subconjunctival vessels; while in the second, there appears to be a diapedesis of the superficial conjunctival vessels. Ruedemann[2] describes these two types as (1) hemorrhages of obstruction and (2) hemorrhages of diapedesis.

The duration varies according to the amount of blood found subconjunctivally and the rate of absorption. Thus, some of these hemorrhages may be absorbed in 7 days while others may last as long as 4 weeks. The macroscopic rate of disappearance is unpredictable. A dense patch of subconjunctival hemorrhage may seem to remain stationary for many days but, in an equal number of days, the size of the hemorrhage may be rapidly reduced.

The direction of absorption is not always centripetal. In many cases, a clear patch of normal conjunctiva separates temporal patches of hemorrhage from the limbus, and this separation is maintained until the hemorrhages finally disappear. In other cases, the larger patches of hemorrhage are broken down into several smaller ones before they are finally absorbed. In most cases, however, the hemorrhage recedes slowly until there is only a small dot remaining at the 3-o'clock limbus. Massage does not appear to influence the rate of disappearance.

Studies[1] in the same patients of the resorption of subconjunctivally injected blood showed about the same rate of disappearance as spontaneously produced subconjunctival hemorrhages. However, these studies cannot be compared with the hemorrhages observed in our series since there were no disturbances of local circulation by adjacent surgical trauma.

Under the slitlamp one can readily see that the bulbar conjunctiva contains two layers of blood vessels.[2] The deeper layers of larger vessels are part of the branches of the anterior ciliary arteries and form a

part of the episcleral and scleral tissues. They anastomose rather freely with the superficial conjunctival vessels and penetrate the sclera about 3 to 4 mm. from the limbus. The superficial vessels are small and are located just beneath the conjunctival mucosa. There are approximately 2 to 3 times as many veins as arteries.

The difference in the size of the blood vessels between the deeper and superficial layers of conjunctival vessels forms the basis of the two types of hemorrhages. The large dense hemorrhage is from the deep vessels which are actually small arteries; whereas, the smaller, sketchy type of hemorrhage is from the superficial vessels which are arterioles and venules and are comparatively small. These hemorrhages are definitely venous in character. The greater number of veins in proportion to arteries in this region would leave the veins, according to the law of chance, more vulnerable to the forces of stress and strain.

If the superficial conjunctiva is touched with a moist cotton applicator or by the moving lids, it will move very freely over the deeper episcleral tissues. This freedom of movement appears to give the subconjunctival tissues an almost fluid appearance. It is in this rather loose areolar tissue that the subconjunctival hemorrhage occurs.

The dense type of hemorrhage, being from the deeper vessels, pours the blood from the bottom of this loose layer, therefore, making it impossible to locate the involved vessels. The thin sketchy type of hemorrhage empties the blood into this layer from the top of the areolar tissue. Here one can see small, faint patches of hemorrhage which appear as pinkish tufts located at the visible termination of the vascular tree. The confluence of these small areas of diapedesis produces a visible patch of subconjunctival hemorrhage.

The blood from the conjunctival vessels can be readily seen flowing toward the limbus in the normal conjunctiva. As these vessels are followed through an area of hemorrhage, their course stands out rather

clearly because there are clear areas paralleling them. The older the hemorrhage, the easier it is to see these perivascular channels, which are areas of absorption and digestion of the subconjunctival hemorrhage.

DISCUSSION

CIRCULATION OF CONJUNCTIVA

The circulation of the conjunctiva forms a part of the general circulation and is dependent on the general arterial pressure and on the general venous return flow. The arteries, capillaries, and veins, which form the circulatory units, are under the control of the vasomotor system that regulates the degree of constriction and dilatation of the vessels.

The local circulatory units can be subjected, therefore, to several kinds of disturbances.[3] (1) Vasomotor, which results from the change in neural control; (2) mechanical, such as those produced by mechanical obstruction of the lumen of the vessel either by a thrombus or an embolus within the lumen, by changes in the wall of the vessel, or by compression from without; and (3) biochemical, such as the action of split proteins from surgical trauma acting on the capillary wall or the action of surgical trauma depleting certain constituents from the body whose lack would in turn weaken the capillary wall.

The vasomotor disturbances have been shown by Ricker[4] to act in various degrees, depending on the strength of the stimuli. A weak stimuli affects the dilator fibers only and causes a dilatation of the vessels with an increase in the blood flow. A slightly stronger stimuli affects the constrictor fibers and causes a constriction of the arteries with a slowing of the circulation in the capillaries and veins. A stronger stimuli causes paralysis of the constrictor fibers and stimulation of the dilator fibers. At first this produces a dilatation of the vessels with an increase in the blood flow, but the dilator fibers soon become paralyzed and, above the dilated vessels, the artery is constricted. This results in

a slowing of the blood stream to complete cessation or stasis.

Depending on the action of the agents on the vasomotor system, three states of the local tissues can be distinguished. These are (1) active hyperemia with an increase in the blood flow, (2) passive hyperemia with a slowing of the blood flow, and (3) stasis or cessation of the blood flow.

Active hyperemia is produced by stimulation of the dilator fibers, the constrictor fibers remaining unaffected. Arteries, capillaries, and veins are dilated, and the blood flow is increased. There is, also, an enormous increase in the number of open capillaries with only a slight loss of fluid through the capillary wall.

Passive hyperemia with the slowing of blood flow occurs with the stimulation of the dilator fibers and a change in the constrictor fibers, which may either show a diminished activity or become completely inactive. In the region of the inactive constrictor fibers, the arteries, capillaries, and veins are dilated, and the circulation is slow and irregular. This form of hyperemia is characterized by an increased passage of fluid through the capillary walls and its accumulation in the surrounding tissues.

Stasis. When the central artery of the affected area becomes more constricted, there is still a greater dilatation of the vessels in the affected area and a still greater slowing of the blood stream results. Circulation is present but slowed. This form of vasomotor activity is characterized by the passage of red blood corpuscles through the capillary walls. They may pass through the capillary wall singly at one point, or hemorrhages may occur at a number of points. If the artery central to this area is markedly narrowed or completely occluded, the activity of the vasomotor fibers in the area is completely lost and, as a result, the vessels are relaxed and circulation is slowed to such a degree that stasis ensues. This latter state does not occur as a result of surgical trauma following rhinoplastic operations.

Obstruction to blood flow. The circulation of the conjunctiva can be disturbed mechanically by an obstruction to the flow of blood in the arteries or veins supplying it. When the obstruction is not complete and varying degrees of reflex constriction below the point of obstruction occur, there is a corresponding dilatation of the arterioles, capillaries, and venules distal to the point of constriction. The resulting condition produces a transudation of fluid and hemorrhages to a varying degree.

Mechanical obstruction of a vein is followed by a cessation of circulation in the vein and accompanied by a corresponding reflex constriction of the artery supplying the region. This occurs only in complete obstruction. Before circulation stops, however, there is first a slowing of the blood flow which produces a state of prestasis with its attendant hemorrhages. The immediate results of local circulatory disturbances are, therefore, a transudation of plasma into the tissues and attendant hemorrhages.

According to Landis,[5] the capillary blood pressure is capable of rising conspicuously during hyperemia (from 14 cm. of water to 23 cm. of water) and returns toward the lower resting level as hyperemia recedes. By the use of the micropipette introduced into the venous limb of a capillary at the base of the human fingernail, it was noted that, on cooling the skin at the base of the nail, a vasoconstriction resulted with a distinct drop in the capillary blood pressure. This, however, is followed in a few minutes by a secondary rise associated with a reactive hyperemia which has been studied so thoroughly by Lewis and his co-workers.[6] This mechanism may explain the nonbeneficial results of the ecchymosis reducing factor of ice compresses applied immediately postoperatively in our cases.

Another contributing factor in the production of these subconjunctival hemorrhages is suggested by an observation made by Hueck[7] that the protoplasm of the endothelial cells of the capillaries and the base-

ment membrane is capable of undergoing a transitory liquefaction to such a degree that it causes numerous openings to form and thus allows plasma and, in the case of larger openings, red blood corpuscles to pass through. This condition is produced in the state of prestasis, when the slowing of the circulation in the capillaries causes a diminution in the supply of oxygen and of nutrition to the walls of the capillaries. This same observation was also noted by Landis[5] in the capillary of the frog.

PHYSIOLOGY OF CAPILLARIES

Most of the studies on the physiology of the capillaries have been made on the vessels themselves with little regard of the action of the contents of the vessels. The observations of Knisely and his co-workers[8] on the action of traumatized capillaries on the blood corpuscles and their subsequent effect on the capillaries themselves throw new light on the basic pathologic physiology of the blood vessels.

Briefly stated, Knisely discovered that, in injured tissue and blood vessels and in certain diseased states, the individual blood corpuscles become agglutinated and form clumps of cells. This mass of cells or "sludge" resists its own passage through the small vessels and consequently the rate of flow in these vessels becomes progressively slower. The "sludge initiating factor" at the site of injury continues to form more "sludge blood" which reduces the rate of flow through the capillary bed and slowly leads to various degrees of stagnant anoxia all over the body.

When this happens the walls of the postcapillary venules and small venules lose their ability to retain blood colloids. Anoxia of the endothelium is alone sufficient to cause this and severe anoxia always causes endothelium to leak rapidly.

One of the key facts in Knisely's observation is that blood coming through the arterioles of any organ may be studied as a valid sample of all flowing arterial blood in the body. He has used the uninjured bulbar conjunctiva of human beings in the study of "sludge blood" in various diseases.

It appears that one of the important factors in the production of subconjunctival hemorrhages is a local weakening of the capillary wall to any increase in intravascular pressure. The strength of the capillary wall is actually a measure of the intracellular adhesive power of the endothelial cells which make up the capillary wall.

This is, in turn, affected by such substances as rutin, vitamin P, citrin, and so forth, which are flavone glucosides in various degrees of purification, and factors causing endothelial anoxia. There is some question as to the mode of action of these substances and as to whether the tourniquet test which measures capillary fragility has any bearing on capillary hemorrhages.[9]

Wolffe and Danish[10] reported two cases in which subconjunctival hemorrhages occurred during the administration of rutin. In one case, the hemorrhage occurred about four weeks after continuous rutin therapy. In the second case, the hemorrhage occurred 24 hours after the starting of rutin therapy. In both of these cases capillary fragility tests, as measured by the Gothlin method, were normal.

The possibility that other causes may be concerned in the integrity of the normal cells must also be considered.[11, 12] It is highly improbable that the explanation can be found in a single agent or a group of similar agents but rather in a complex biologic reaction of which the flavone glucosides form only a part.

STRUCTURE OF TEMPORAL CONJUNCTIVA

The almost constant location of these subconjunctival hemorrhages in the temporal sector of the bulb can be explained on an anatomic and functional basis. It is a well-known surgical fact that the structure of the temporal conjunctiva is much thinner than that of the nasal sector. The ocular movement of convergence, being a positive

function, places a stretching force on the conjunctiva of the temporal sector while that of the nasal sector is compressed into folds.

In addition, the anterior ciliary arteries that travel around the eyeball on the recti muscles are usually paired on all the recti muscles, except for the lateral rectus which usually carries one and occasionally no visible artery.[13, 14] The stretching force of ocular convergence on the temporal conjunctiva plus the strain of any venous obstruction would weaken this sector more than the others.

Biochemic Effects of Trauma

The biochemic effects of trauma have been studied in severe injuries, such as burns and fractures.[15] It seems probable that the formation of "sludge blood" is directly or indirectly concerned with the biochemic effects of trauma. Andreae and Browne[15] observed a rapid and marked destruction or utilization of ascorbic acid during the period immediately following injury.

Levenson and others[16] state that the stresses associated with severe injury are followed by a markedly increased turnover of protein and carbohydrate metabolism. Since it is known that the vitamins of the B group are intimately concerned with the metabolism of these substances, it is likely that the demand for and the utilization of them is likewise increased.

However, the trauma associated with the surgical procedure of rhinoplasty cannot be compared with cases of severe injury whose measurable demands on the body physiology are definite. Nevertheless, one may expect some of the physiologic forces to come into play, even though to a much lesser degree, in less severe injuries.

With all these factors contributing to the development of the temporally located subconjunctival hemorrhages in postrhinoplastic cases, it appears that the variable factor is the patient's reaction quotient to trauma. This particular aspect of the problem has been studied in the lower animals.[17, 18] The degree of postoperative edema in our cases would be a rough measure of the individual patient's reaction to trauma. When we consider this variable individual factor, the formation of these subconjunctival hemorrhages is the end result of a multitude of physiologic conditions.

Synopsis

The chain of events may be hypothesized in the following manner. The operative trauma causes an increase in the protein concentration of the lymph.[19] The formation of "sludge blood" now becomes a factor. This increase in protein concentration may not, in itself, change the permeability of the capillary walls[20] but, with a given capillary pressure, the colloidal osmotic pressure may vary to such an extent so as to influence capillary permeability.[5] Whether the permeability of the capillaries is changed reflexly or by the slowing of the blood stream by sludging, the total tissue anoxia and subsequent edema are increased. This postoperative edema causes a congestion of the angular veins and of the internal pterygoid plexuses so that the drainage from the external eye is affected directly and, possibly, reflexly.

The operative trauma may further deplete or utilize more rapidly certain substances which may have to do with capillary fragility. The subconjunctival hemorrhage is, therefore, a result of a disturbance in venous circulation when the postoperative congestion exceeds the intracellular adhesive power of the capillary wall. This congestion requires about 24 to 48 hours to create enough obstruction so that any sudden further increase in venous pressure, such as might be caused by coughing, laughing, or straining, plus the factor of ocular convergence, would be enough to put a strain on the weakest spot of the conjunctival vascular tree.

The single lateral rectus ciliary artery would have to carry a pressure load which in the other recti muscles is divided between two vessels. Moreover, the rare occurrence

of a spontaneous subconjunctival hemorrhage over the superior or inferior recti muscles is partly due to the compression and support afforded these areas by the upper and lower lids. The nasal and temporal 'sectors are subjected to an increase in the local vascular pressure. The structural weakness of the temporal conjunctival vascular tree is thus made evident by the typical temporally located subconjunctival hemorrhage.

Trauma per se is definitely not related to these hemorrhages. In a case in which a 12-mm. dermoid cyst was excised from the left supraorbital region under local infiltration anesthesia, a very large temporal patch of subconjunctival hemorrhage was noted within 24 hours postoperatively. There was a moderate amount of edema of the upper lid in this case, but the trauma incident to the removal of the cyst was certainly minimal.

In Case 43, in which it was necessary to fracture only one maxillary process, the subconjunctival hemorrhage occurred in the temporal sector of the opposite eye. The factor of a contrecoup force must be considered in this case, but it does not account for the absence of subconjunctival hemorrhages in those cases in which the apparent hardiness of the maxillary process required an excessive amount of trauma and yet no hemorrhages appeared. These observations seem to suggest that trauma in itself is not a sufficient cause but rather that the response of these patients to surgical trauma is the important factor.

SUMMARY

1. In a series of 55 consecutive cases of rhinoplastic patients, 32 cases, or 58 percent, developed temporally located subconjunctival hemorrhages as a complication of the surgical procedure.

2. These subconjunctival hemorrhages were of two varieties, an intensely red triangular type and a streaky horizontally linear type.

3. Both of these types of hemorrhage appeared to be definitely related to the degree of postoperative ecchymosis and not to the degree of surgical trauma.

4. These hemorrhages always appeared from 24 to 36 hours following surgical trauma.

5. They were definitely venous in nature.

6. A discussion of the possible mode of formation and an explanation of their temporal location has been given.

1221 Victoria Street (34).
55 East Washington Street (2).

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OPHTHALMIC MINIATURE

To Mrs. Jane Mecom

London, July 17, 1771

Dear Sister,

. . . I thought you had mentioned in one of your letters a desire to have spectacles of some sort sent you; but I cannot now find such a letter. However I send you a pair of every size of glasses from 1 to 13. To suit yourself, take out a pair at a time, and hold one of the glasses first against one eye, and then against the other, looking on some small print.—If the first suits neither eye, put them up again before you open a second. Thus you will keep them from mixing. By trying and comparing at your leisure, you may find those that are best for you, which you cannot well do in a shop, where for want of time and care, people often take such as strain their eyes and hurt them. I advise your trying each of your eyes separately, because few peoples eyes are fellows, and almost every body in reading or working uses one eye principally, the other being dimmer or perhaps fitter for distant objects; and thence it happens that the spectacles whose glasses are fellows suit sometimes that eye which before was not used tho' they do not suit the other.— When you have suited your self, keep the higher numbers for future use as your eyes may grow older; and oblige your friends with the others. . . .

Your affectionate brother,

B. FRANKLIN.

NOTES, CASES, INSTRUMENTS

CILIA IN THE ANTERIOR CHAMBER*

WITH A REPORT OF A CASE

OLGA SITCHEVSKA, M.D., AND
BRITTAIN F. PAYNE, M.D.
New York

Cilia may enter the anterior chamber in perforating injuries of the eyeball, when they are cut or torn off from the lid margin and are carried into the anterior chamber either through the corneal or limbal wound. Occasionally the cilia may be implanted into the anterior chamber during surgical intervention for a cataract extraction.

The cilia sometimes are found lying free in the anterior chamber, but more frequently one end of the cilium is embedded in the iris. If the lens is injured one end of the cilium is stuck in the lens or lens capsule. In some cases the cilium is adherent to the corneal scar. Cilia are observed less frequently in the posterior chamber.

If cilia remain in the anterior chamber for a length of time, they may undergo certain changes, like splitting of the hair or separation of the cuticle. Blanching or depigmentation of the cilia may occur under the influence of the alkaline reaction of the aqueous. Wagenmann[1] stated that cilia may be occasionally absorbed by giant-cell formation.

Considering the frequency of perforating eye injuries, it is remarkable that cilia are not found more often in the anterior chamber. Sherman[2] gives an interesting explanation of this phenomenon. He believes that the reflex closure of the lid is usually delayed until the injury of the eyeball has occurred, so that the traumatizing object misses the contact with the lid margin. On rare occasions the closure of the lids occurs simultaneously with the impact of the injuring object which cuts the cilia and carries them into the anterior chamber. The injuring object in such cases frequently does not enter the eyeball as its force of motion is diminished by its friction against the lid margin.

FREQUENCY OF INFECTION

Since cilia usually enter the eye in industrial accidents, in workers whose faces and eyelashes are soiled during the work, one could expect that the eyelashes would be a source of infection. This, however, does not occur frequently. It would seem that the rapid filtration of the aqueous from the anterior chamber allows little opportunity for bacterial growth there.

Lauber[3] believes that when an infection occurs in perforating injuries, it may have been brought about by the perforating object rather than by the cilia themselves. Müller[4] in culturing cilia of a number of working persons found no pathogenic microörganisms.

On the other hand, in a case described by Wagenmann[1] a cilium implanted in the anterior chamber caused a purulent iritis with a hypopyon 2.5 mm. high. After the removal of the cilium, the inflammation subsided promptly. Sympathetic inflammation was observed by Gunier[5] six months and by von Graefe[6] two weeks after the perforating injury with cilia implantation had occurred. Extraction of the cilia resulted in healing of the eyes.

COMPLICATIONS FROM RETAINED CILIA

While cilia may remain in the anterior chamber for a long time without giving rise to disturbing symptoms, they may sooner or later cause complications, such as epithelial tumors. The epithelium of the root sheath may become implanted, forming a cyst.

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* From the New York Eye and Ear Infirmary.

"The implantation cysts thus formed may be of two distinctive types: solid looking, round or oval tumors, so-called pearl cysts, or translucent cysts with thin walls" (Duke Elder[7]).

Implantation cysts of the iris associated with the intrusion of an eyelash into the interior of the eye were reported by Bonnet and Paufique,[8] and Roth and Geiger[9] in whose case the injury was caused by a lead pencil, by Krachmalnikov,[10] Moore,[11] and by Horay.[12]

CILIA IN ANTERIOR CHAMBER

Cilia in the anterior chamber are not common. Popov[13] states that only two such cases have been seen among 80,000 eye patients in the Rostov Clinic and only one case in three years was found among 43,471 patients in the Astrakhan Clinic. Müller[4] reported that only five cases of cilia were observed in Fuchs's clinic in Vienna among 30,000 new patients. Sharpe[14] in his review of the literature, in 1925, stated that 75 similar cases were reported within the last 100 years.

At the New York Eye and Ear Infirmary, out of a total number of 374,721 eye patients examined during 15 years (1932 to 1947), only two such cases (including ours) have been recorded. These data confirm the infrequency of penetration of cilia into the interior of the eye.

Reports in the literature indicate that cilia may remain in the anterior chamber for a number of years without causing inflammation. Gradle[15] examined a 24-year-old man for blepharoconjunctivitis. There was a history of an injury to the right eye with scissors at the age of five years. The slit-lamp examination showed the presence of a depigmented cilium in the anterior chamber. The cilium has been there for 19 years without evidence of inflammation.

Hughes,[16] while refracting a naval officer, discovered an eyelash in the anterior chamber. A history was obtained from the patient that he was injured in the eye with a fountain pen when he was a child.

Roll[17] reported a case of a cilium being adherent to the opaque lens for a period of 19 years. Koenigstein[18] and Guzman[19] observed a cilium in the anterior chamber for 20 years. Henneberg[20] reported that inflammatory symptoms appeared 15 years after a perforating injury of an eye with the implantation of a cilium. Sharpe[14] reported a case of a cilium in the anterior chamber for 33 years. Schwartz[21] and Müller[4] each described a case of eyelash in the anterior chamber for 34 years. The eyes remained quiet all that time.

CASES OF MORE THAN ONE CILIUM

It is evident from literature that cases of cilia in the anterior chamber are rare, and cases in which more than one cilium is observed are still rarer. Shagov[22] discovered two cilia in the anterior chamber after a magnet extraction of a piece of steel from the eye. An attempt to remove the cilia was unsuccessful as they moved to the posterior chamber. They remained there for a two-year period of observation.

Lichtner[23] and Payne[24] removed two cilia from the anterior chamber after a perforating injury of the eye. Franklin and Cordes[25] found three cilia and Sharpe[14] and Begle[26] have observed four eyelashes in the anterior chamber.

Bulson[27] and Valude[28] each reported a case of five cilia entering the interior of the eyeball after a perforating injury with a piece of wire. Mikhailov[29] reported a case of six cilia in a young woman's eye which was hit with a piece of wood; they were embedded in the iris. Three cilia were removed with an iris forceps with ease through an incision at the limbus, while the other three were removed with great difficulty and a cataract formed a week later.

REMOVAL OF CILIA

The removal of the cilia from the anterior chamber is by no means a simple procedure, particularly when more than one

cilium is implanted. A number of complications may occur: the collapse of the anterior chamber because of the rapid outflow of the aqueous, the tendency of the iris to prolapse, or a hemorrhage from the iris which obscures the operating field. The most serious danger is the injury to the lens. Paderstein[30] reported a case in which he

in the left eye by a fine piece of wire from another toy a nearby worker was handling. She experienced a sharp pain in the eye and the vision became blurred at once.

Eye examination. There was marked photophobia and ciliary injection of the left eyeball and a gaping wound of the cornea at the 12-o'clock position, 4 mm. below the
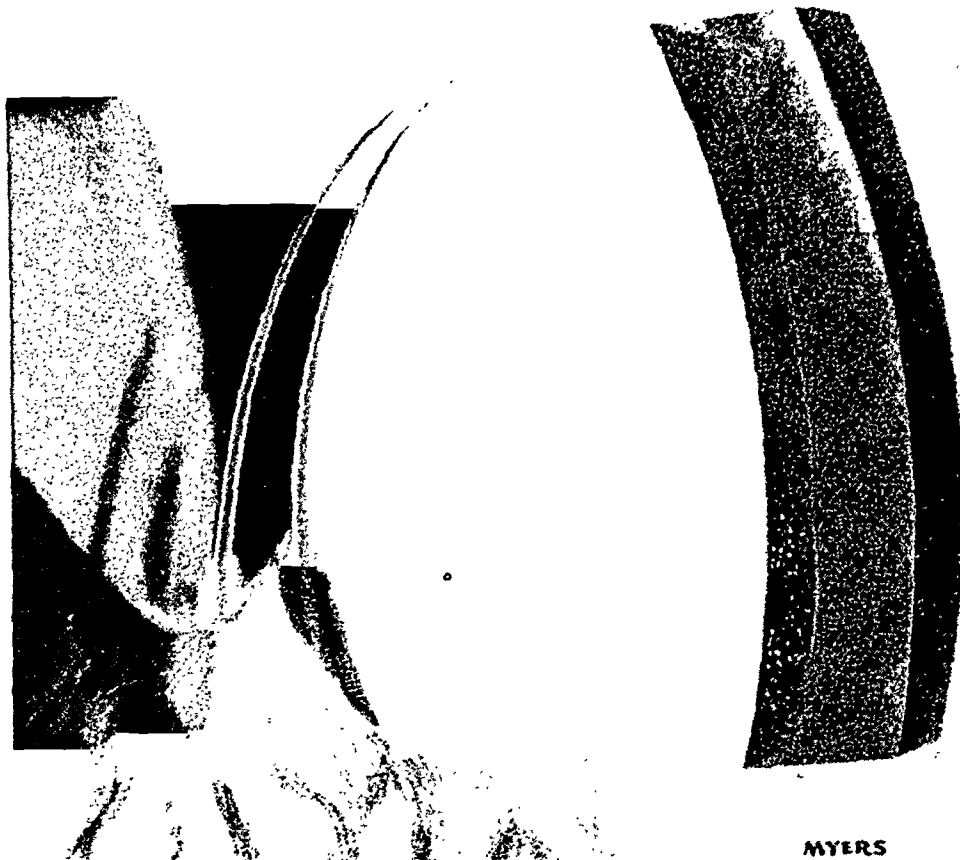
Fig. 1 (Sitchevska and Payne). Photograph of slitlamp drawing of two cilia implanted in the anterior chamber following a perforating injury of the left eye. The cilia, embedded in the iris, are enveloped by an exudate.

removed a cilium 5 weeks after a penetrating wound of the eyeball; 8 weeks later another cilium was seen and the attempt to remove it was frustrated by a hemorrhage from the iris with the lens becoming cataractous a week following the operation.

REPORT OF A CASE

History. - E. J., a Negro girl, aged 19 years, was first seen on March 4, 1948, one-half hour after an injury to the left eye. While working on a toy, she was struck

limbus. The anterior chamber was filled with clotted blood, mixed with grayish shreads of the turbid aqueous; the fundus could not be seen. Vision was reduced to hand movements. The right eye was normal and the visual acuity was 20/15.

The patient was hospitalized at the New York Eye and Ear Infirmary. She was given cold compresses, drops of a solution of atropine sulphate, and intravenous injections of triple typhoid vaccine. Three days later the hyphemia was absorbed.

The slitlamp examination showed that the corneal wound was sealed and the anterior chamber was restored. The aqueous was still somewhat cloudy. A square corneal opacity was forming at the site of the injury and there was another deep-seated opacity in the cornea at the 6-o'clock position, 3 to 4 mm. above the limbus, which extended toward the temporal side of the cornea.

The striking feature of the slitlamp examination was the presence of two thin, long foreign bodies in the anterior chamber which were recognized by one of us (B. F. P.) as cilia. The cilia were embedded in the pupillary margin of the iris at the 7-o'clock position. One cilium was located at the anterior border of the iris; while the second seemed to be behind in the posterior chamber. They were surrounded with a newly formed grayish exudate.

The free ends of the cilia were extending obliquely across the dilated pupil at about axis 70°. A small opacity in the lens capsule near the embedded cilia was observed. A posterior synechia had formed, and the pupil was of irregular shape at this site (fig. 1).

The roentgenogram showed no intraocular foreign body. The eye quieted down; vision improved to 20/50; and the patient was discharged from the hospital three weeks after admission.

Course. Four weeks following the injury, the patient complained of pain in the eye. Photophobia and ciliary injection were present and a flare in the anterior chamber was observed on slitlamp examination. She was re-admitted to the hospital and was operated on April 6, 1948 (5 weeks after injury), under local anesthesia for the removal of the cilia.

Operation. A keratome incision was made at the 9-o'clock position at the limbus and the incision was enlarged with scissors on either side. A Hunt capsular forceps was used to enter the anterior chamber, and one cilium was removed with ease. It was dif-

ficult to remove the second cilium, however, and several attempts were made before it was finally grasped and removed. A small peripheral iridectomy was done in order to prevent prolapse of the iris.

At the conclusion of the operation a pigmented, filmlike emulsion filled the anterior chamber, which had to be irrigated. This probably was free pigment from the pigment layer of the iris. Postoperatively, the patient was put on intramuscular injections of penicillin. Recovery was uneventful.

At examination, five months after the injury, the eye was quiet, an opacity of the cornea was seen below the limbus at the site of the entrance wound and another one was present at the 9-o'clock position, the field of the operation. A third pigmented corneal opacity was deeply seated about 4 mm. above the limbus at the 5-o'clock position. The opacity of the lens capsule remained unchanged. The vision of the eye was 20/50, unimproved.

CONCLUSION

A case of two cilia in the anterior chamber following a perforating injury of the eye and their successful removal is described. The fine piece of wire must have hit the eye and lid with sufficient force to cut off the cilia and carry them into the anterior chamber, injuring the cornea below from the endothelial side and causing no injury to the lens itself, which is rather remarkable in a penetrating injury of this type.

The frequency of occurrence, the number of eyelashes in the interior of the eye, complications encountered during the operation for their removal are discussed.

Although the cilia may be retained for a number of years in the anterior chamber without giving rise to symptoms, it is our belief that an attempt should always be made at the earliest possible moment to remove them because of various threatening complications, chiefly that of the formation of epithelial cysts.

30 Fifth Avenue (11).
17 East 72nd Street (21).

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POSTOPERATIVE WOUND INFECTION CURED BY PENICILLIN*

BEULAH CUSHMAN, M.D.
Chicago, Illinois

History. Mr. H. J. H., aged 38 years, came to the late Dr. G. F. Suker in September, 1931, with the history of attacks of blurred vision in the right eye, lasting for 10 minutes to one hour, for three years. Vision in the left eye had become blurred for the first time a few days earlier.

A diagnosis of chronic glaucoma was made, and deep root iridectomies were done on both eyes in October, 1931. Miotics were necessary in the right eye after a few weeks and in the left eye after a few months.

Tension in the right eye gradually increased and remained around 35 mm. Hg (Schiøtz), with a total loss of vision in 1937. The tension in the left eye was irregular at intervals, but it always responded satisfactorily to the use of various miotics. Prostigmin solution and tablets by mouth were found to be the most satisfactory treatment when the patient became sensitive to pilocarpine after 1940.

Course. In 1944, the refraction gradually changed to a compound myopic astigmatism and there was a mild iridocyclitis of the right eye. An incipient cataract was present in the left eye. In April, 1946, the diagnosis of diabetes mellitus was made. This condition was controlled with diet.

Operation. On August 14, 1946, Dr. Der-

Fig. 1 (Cushman). Visual field studies before and after cyclodialysis and intracapsular lens extraction in the left eye.

rick Vail did a cyclodialysis of the left eye preliminary to an intracapsular lens extraction in this eye. The lens extraction was done the following week.

On the day following the operation, pain was complained of during the early morning, but no pain was present at the time of rounds, and the dressing was not changed. On August 16th, when the dressing was changed, an exudate was present along the corneal wound and in the anterior chamber. The conjunctiva was swollen and the upper lid edematous. Scattered, superficial abscesses were present in the skin of the upper lid.

Infection and treatment. A smear was positive for Staphylococcus hemolyticus, and later the culture was reported positive. Penicillin (1,000 units) was dropped into the eye immediately, and 10,000 units were given intravenously every three hours. Typhoid vaccine (15,000,000) was given.

The following day, penicillin was instilled into the anterior chamber after removal of 0.1 cc. of aqueous by means of a fine needle introduced through the recent incision. Sulfadiazine and soda bicarbonate (10 gr. every 4 hours) were given.

Improvement of the eye was immediate following the instillation of penicillin into the anterior chamber, and healing proceeded most satisfactorily.

Outcome. Vision in the left eye was: October 21, 1946—fingers at three feet; left pupil drawn up; April 14, 1947—iridotomy; June 24, 1947—20/16 with a +11.0D. sph. +4.0D. cyl. ax. 160°; with a +4.0D. addition, 4-point type.

The visual field of the left eye was contracted to 20 degrees with a 3/1,000 test object. There was complete cupping of the left disc. Tension in the left eye was 19 mm. Hg (Schiøtz).

25 East Washington Street (2).

SOME OCULAR EFFECTS OF THE SYSTEMIC ADMINISTRATION OF ANTIHISTAMINICS

Joseph V. M. Ross, M.D.
Berwick, Pennsylvania

The use of antihistaminics is becoming an increasingly popular procedure in everyday medicine and a rather complete knowledge of the side-effects of such drugs seems to be desired. Ocular side-effects have been recorded often in the literature and in a review of 12 articles[1-12] I found them men-

tioned in 6. Some of the authors feel that most antihistaminics possess an atropinelike or vagal-paralyzant effect. There seems to be some disagreement as to whether or not oral administration might give pupillary dilatation and reduce the capacity for accommodation as does topical application. Blurred or dim vision is the ocular complaint mentioned. In one report in which a shocklike effect followed the oral administration of an antihistaminic, it was not clear if the origin of the blurred vision was cerebral or not.

During the past two years I have seen four cases in which the use of an antihistaminic resulted in ocular complaints, and which bring up some problems that warrant reporting.

CASE REPORTS

Case 1. A. G., a woman, aged 38 years, was receiving therapy for a limbal type of vernal conjunctivitis. Before medication was given, vision was normal for near and far with or without the correction (determined by cycloplegia): O.D., +0.5D. sph. $\bigcirc$ −0.5D. cyl. ax. 175°; O.S., +0.25D. sph. $\bigcirc$ −0.25D. cyl. ax. 170°. The patient received 100 mg. pyribenzamine daily for 13 days, at the end of which time she complained of blurred vision for far and near with difficulty in reading. Vision was 20/30, O.U., at far and 8-point type was read at 14 inches, O.U. Refraction revealed the following: O.D., +0.25D. sph. $\bigcirc$ −1.0D. cyl. ax. 175° = 20/20; O.S., −1.5D. cyl. ax. 170° = 20/20. An addition of +1.5D. sph., O.U., was necessary to give normal near vision.

With a contact lens in place, the following was found: O.D., +0.25D. sph. $\bigcirc$ −0.5D. cyl. ax. 175°; O.S., −1.0D. cyl. ax. 170°.

The amplitude and range of accommodation were diminished and the refractive changes noted, but all other ocular findings were normal. With cessation of the medication all symptoms disappeared and the findings at a later date were the same as at the early visits.

Case 2. J. M., a man, aged 65 years, had relative visual acuity of 20/50, O.U., and 0 at 14 inches, O.U., corrected to normal at near and far. The patient had chronic asthma and, after having taken 100 mg. of pyribenzamine daily for one month, complained of blurred vision for near and far.

Ophthalmic survey was normal except for vision of 20/40, O.U., at 6 meters with corresponding near vision, not correctible. There was a diffuse corneal edema similar to that seen following the ingestion of atabrine and an increased corneal relucency. The refraction (which was done with difficulty) was the same as found previously. All symptoms cleared when the drug was stopped; all findings were normal in one week.

Case 3. W. F., a man, aged 55 years, presented a bilateral contact dermatitis of the lids. Both near and far vision were easily corrected to normal. Eight days after taking 75 mg. of pyribenzamine daily he complained of blurred vision, especially for near. The patient saw 20/20 O.U., however, but only read 8-point type at 14 inches instead of 4-point, but with a +3.25D. addition, O.U., instead of the +2.25D. he was wearing, read normally at near.

All other findings were normal except for the finding of a few vitreous opacities which were not noted previously. Refraction for distance was the same as previously. In one week after cessation of the drug, the patient had no complaints and the findings were as they had been at the first visits. The vitreous opacities persisted, however, and the patient was now conscious of them.

Case 4. G. H., a boy, aged 11 years, presented a limbal type of vernal conjunctivitis for which pyribenzamine was given (100 mg.) for two days. Relative visual acuity was 20/25, O.U. Cycloplegic refraction then revealed the following: O.D., +0.5D. sph. $\bigcirc$ −2.75D. cyl. ax. 7° = 20/20; O.S., +0.5D. sph. $\bigcirc$ −2.5D. cyl. ax. 175° = 20/20. The postcycloplegic findings two weeks later were the same, but the patient

complained of a mist before the eyes. Now, only 20/25, O.U., vision could be attained. The pyribenzamine was discontinued and two weeks later the refraction with cycloplegia was: O.D., +0.25D. sph. $\subset$ −0.5D. cyl. ax. 18° = 20/20; O.S., +0.5D. sph. $\subset$ −0.5D. cyl. ax. 172° = 20/20. All other findings were normal throughout.

SUMMARY

Four cases are presented in which there were ocular side-effects from the systemic administration of antihistaminics. The condition for which the drug was originally administered was not benefited in any case. The complaint in all these cases was blurred vision for far and near. The mechanisms involved were varied and all the reasons are not clear at this writing. In no case were the pupillary reflexes disturbed.

In Case 1, there was a depression of accommodation as well as refractive changes. Use of the contact lens suggested that these changes were due, at least in part, to factors other than corneal. The refractive changes were similar to those in Case 4.

In Case 2, that of a patient who had been asthmatic for years, there was seen a diffuse corneal edema with an increase in corneal relucency and no other significant changes.

In Case 3, a depression of accommodation only was noted. The question of the vitreous opacities is not settled.

In Case 4, an extreme refractive change occurred and the patient needed high minus cylinders at an axis of nearly 180°.

All changes abated with discontinuance of the drug, and the drug was not readministered to test specificity of action. The exact incidence of ocular side-effects was not determined.

DISCUSSION

The ophthalmologist should certainly include in his history a question as to whether the patient is taking antihistaminics. In some cases, these drugs can cause blurred vision for near and far. The factors as determined in these cases were corneal edema, refractive changes, and depression of accommodation. Apparently factors other than corneal are involved in the refractive changes although corneal changes might likewise occur. The depression of accommodation might well be explained by the atropinelike action of the drug. The presence of vitreous opacities in one case brings up the possibility of vitreous changes.

321 East Front Street.

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A NEW ORBITAL IMPLANT

ORWYN H. ELLIS, M.D.
Los Angeles, California

Many new orbital implants for use following enucleation have been developed during and since World War II and much of the credit for stimulating interest in this work must go to Cutler.[1,2] A new type of completely covered implant, which embodies a combination of sound surgical and prosthetic principles, is presented in this report. The indications for enucleation and evisceration will not be discussed, and only minor points in the enucleation procedure, as they affect the orbital implant, will be presented.

SURGICAL ANATOMY

As is well known, Tenon's capsule and the conjunctiva are fused with the sclera for a distance of 1 to 2 mm. about the limbus. The normal cornea has an average diameter of between 11 and 12 mm. Thus in doing an enucleation, approximately 16 mm. of circumference are lost.

The exact size of a sphere which can be inserted into the reduced space of Tenon following an enucleation can therefore be computed by subtracting the lost circumference from the circumference of the eyeball. In an adult a round implant of more than 18 mm. in diameter will stretch Tenon's capsule, and I agree with Fralich[3] that those surgeons recommending an implant of 20 to 21 mm. in diameter are forgetting the size of Tenon's space after enucleation.

When Cutler basket implants were used, I found that they were frequently extruded and that, when retained, considerable atrophy developed above and behind the implants. It was also noted, especially in children, that the conjunctiva pulled into the

cavity was at the expense of the conjunctiva of the cul-de-sacs, especially the superior. A prosthesis that could be inserted had, therefore, to be narrow with very little motion. It is a well-established fact that the prosthesis will move in direct proportion to the movement of the cul-de-sacs, provided transfer of motion from the implant stump to the prosthesis is successful. If atrophy or reduction in size of the cul-de-sacs takes place, motion of the prosthesis is correspondingly reduced.

NEW IMPLANT

When Cutler's basket implants were placed in orbits, I noted that the prosthesis made after the socket-mold technique moved about the same whether or not the peg or stud was added to the prosthesis. A plastic basket was then made increasing the depth with plastic, with the idea that the muscles could be attached to the rim or tied through the holes and that the rim and sides of the implant would transfer motion to the prosthesis.

Later it was found that, by increasing the amount of plastic posteriorly so that the implant was essentially a plastic sphere with a rim, the prosthesis could be fitted to the sides where the covered implant transfers motion most readily to the prosthesis (fig. 1) and that, by so doing, motion could be increased.

PROCEDURE

The procedure of choice as it evolved is: The conjunctiva is incised as close to the limbus as possible. The conjunctiva and Tenon's capsule are then freed from the globe by blunt dissection. One rectus muscle is isolated and Tenon's capsule is stripped well back. A double-armed chromic catgut

suture is placed in the tendon, adding a cinch suture in the lateral band of the tendon, similar to the muscle stitch of Wiener.[4] The tendon is then cut from the globe. In succession the tendons of the other three recti muscles are similarly sutured and cut. The enucleation is completed and the hemorrhage controlled.

Next, the ends of each suture are passed through the corresponding holes under the rim of the implant and the tendons are tied together, medial to lateral and superior to inferior. If desired, the tendons may be attached to the rim in the manner described by Cutler.[2] However, to date and in my hands, Cutler's technique has seemed to prolong the procedure unnecessarily.

A running purse-string suture of white silk is then placed in Tenon's capsule and pulled tight, completely covering the implant. It was found that Tenon's capsule must be separated well back from each muscle before cutting it loose from the globe, otherwise the operator will be unable to close the capsule completely over the implant. A simple running black silk, or interrupted sutures, are used to close the conjunctiva in a horizontal line.

When the optic nerve is cut, a perforation of the capsule is made posteriorly through which an implant could be forced if one too large were inserted. Irvine[5] recommends suturing this posterior hole. He finds that this gives good support, since it brings the implant well forward. However, this method results in a considerable reduction in the size of the remaining Tenon's space, and it is therefore necessary to use an implant of smaller size.

Postoperatively, with the new implant, there has been surprisingly little edema, no more than with the routine enucleation using a glass-ball implant without muscle sutures. The original pressure dressing should be left in place 5 to 7 days, if possible. By this means postoperative edema is kept to a minimum. In no case has the conjunctiva bulged out between the lids. These patients are usually ready for a temporary prosthesis before two weeks.

DISCUSSION

When a glass-ball implant was used, the implant stump usually moved well in all directions, but the stump did not transfer its
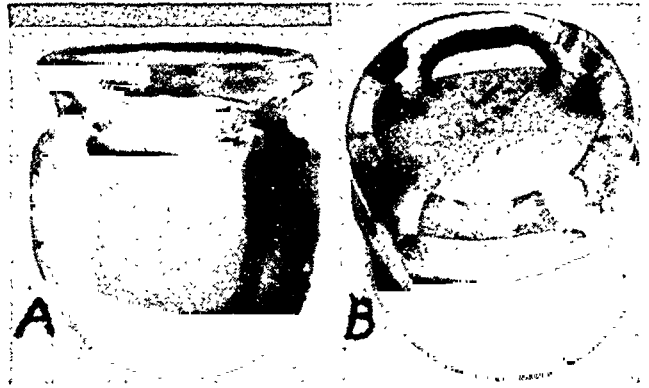
Fig. 1 (Ellis). A new orbital implant. (A) Side view. (B) Top view.

motion to the prosthesis. With this new implant, the movement of the ring is transferred directly to the prosthesis, and the lag of motion frequently seen in covered implants has not been noted.

The implant is made in varying sizes. In most adult orbits the large (18 mm.) size fills Tenon's space nicely but does not distend it. The implant is of the proper depth so that the covered rim protrudes 2 to 4 mm. which is adequate to provide flat sides for the proper fitting of the prosthesis. The inner surface of the prosthesis is molded to fit as snugly as possible around the outside of the projecting rim and sides of the implant. In this manner it is possible to avoid pressure on the conjunctiva, the weight is distributed evenly and, since the prosthesis does not rest on the lower lid, sagging is eliminated. After the prosthesis is fitted a wide excursion is present, but movements in the extremes of rotation are not necessary.

The status of implants that are not completely covered with conjunctiva has not been fully settled. A number, even under the most favorable conditions, are not re-

tained. Frequently, the muscles pull loose from the implant. When the implant herein reported is used, the muscles are attached with ease, and they aid in maintaining the implant in its proper position in the orbit.

Sensitivity to acrylic has occurred following use of implants not completely covered by conjunctiva. In some instances, apparently, a foreign-body reaction has taken place. No case of sensitivity to this new implant has come to my attention. The fact that it has been made only from Lucite may account for the lack of reaction.

To date a total of about 80 of these implants have been used by a number of ophthalmologists besides me, all of whom are enthusiastic about the ease of insertion, the normal appearance of the prosthesis, and the extensive excursion usually present when this implant has been used in conjunction with a prosthesis expertly made by the socket-mold technique. In only one case has there been extrusion or migration of the implant. A number have now been in place for two years. In no case has the implant changed position, orbital atrophy has not occurred as yet, and complications concerning the prosthesis have been few and of minor importance.

Since the introduction of this implant, quite a number of modifications have appeared. In some instances, the rim has been omitted; in others, the rim has been flattened. These changes, in my opinion, are steps backward. The Cutler basket implant taught us one thing—that the rim will transfer movement from the implant to the stump which, except in rare instances, the round implant will fail to do. The implant herein presented is certainly not perfect. It is in a stage of development from which, it is hoped, an implant that will satisfy all specifications may be evolved.

When the procedure as presented is used with the new implant, uniformly good results will be obtained. The method is not technically difficult and requires little additional time to that of routine enucleation with implant. One of the most important factors in orbital implants is permanency, and to date the completely covered implant herein described gives every promise of fulfilling this requirement.

523 West Sixth Street (14).

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HISTORICAL MINIATURE

Egyptian Ophthalmology

The "rising of water in the eye" was treated with a preparation of lapis lazuli, verdigris, balsam, milk, and crocodile earth. Ebers interprets the name of the disease as cataract, but Hirschberg agrees with Lüring that intractable epiphora is meant.

Hirschberg, *Graefe-Saemisch Handbuch.*

SOCIETY PROCEEDINGS

Edited by Donald J. Lyle, M.D.

WASHINGTON (D.C.) OPHTHALMOLOGICAL SOCIETY

January 3, 1949

Dr. Jerome A. Sansoucy, *president*

ABNORMALITIES OF THE OPTIC DISC

Dr. Frank B. Walsh, Baltimore, Maryland (by invitation) spoke on "Abnormalities of the optic disc; their importance in diagnosis," and illustrated his very interesting talk with numerous slides. Among others, the conditions that excited most interest were pseudoneuritis, aplasia of the optic nerve, hyaline bodies of the disc, holes in the disc, and the ophthalmoscopic differentiation of papilledema and optic neuritis.

Dr. Walsh described some of the abnormalities of the optic disc which cause confusion in diagnosis. Most of the anomalies selected for consideration have been confused from time to time with papilledema associated with increased intracranial pressure.

His criteria for the diagnosis of papilledema associated with increased intracranial pressure were: (1) Absence of pulsations of the vein on the disc, (2) measurable amount of papilledema, (3) the presence of exudates or hemorrhages, (4) presence of pallor of the swollen disc, (5) marked narrowing of retinal vessels, and (6) transient blurring of vision.

The ophthalmologist should be the examiner, Dr. Walsh stated, who briefly refutes the diagnosis of papilledema, and explains the presence of the apparent choking in conditions like persistent Bergmeister's papilla, hyaloid cyst, hyaline bodies, high hyperopia, and tilting of optic discs. He placed particular emphasis on the subject of hyaline bodies in the discs, their appearance, and the field defects with which they are sometimes associated. Costen was quoted as saying that there seems no question regarding progress of the field defects.

Dr. Walsh's paper was discussed by Dr. Benjamin Rones, and questions were proposed from the floor by Mrs. Helenor Wilder, Dr. Sterling Bockoven, Dr. David Cogan, Dr. Edward Cummings, Dr. O. H. Fulcher, Dr. Joseph Kemler, Dr. H. V. Rizzoli, Dr. Ernest Sheppard, Dr. G. Victor Simpson, Dr. Harold Stevens, and Dr. Jonathan M. Williams.

Thomas A. Egan,
Secretary-Treasurer.

COLORADO OPHTHALMOLOGICAL SOCIETY

September 18, 1948

Dr. Ralph Danielson, *presiding*

PERSISTENT HYALOID ARTERY

Dr. William Kuhlman presented M. V., a girl, aged 10 years. She had been an eighth month premature, weighing 3½ pounds at birth. At 3 months she had an obstructive jaundice. At present she is well, but has spastic movements and is mentally subnormal. Vision in the left eye is 20/100. The left lens is clear. Extending from the disc to the lens is an entire central hyaloid artery in a thin membrane. The artery breaks up into branches as it nears the lens.

KERATITIS WITH IRIDOCYCLITIS

Dr. von Haller Brobeck and Dr. Sam Brown presented Mr. N. C. R., aged 57 years. On December 9, 1946, he was seen with a corneal ulcer with keratitis. The ulcer was cauterized with iodine and the eye kept atropinized. The ulcer healed, leaving two scars in the center of the cornea.

On May 11, 1948, he returned, again complaining of pain in the right eye. Vision in the right eye was 20/40. A central keratitis was present. No history of tuberculosis was elicited. Physical examination was negative. Reaction to tuberculin was markedly positive. The pupil was dilated with atropine and typhoid-H antigen was given intravenously. In June, since no improvement had taken place, a course of penicillin treatment was given, and whole blood was instilled into the eye. An iridocyclitis developed. Salicylates were given orally. The vision decreased to perception of large objects only. The thermophore was used on the cornea. In August, an abscess developed in the anterior chamber. A keratotomy was performed and culture of the pus showed Staphylococcus albus. Since then there has been no pain but the eye continues very red. Vision is reduced to seeing large objects.

Discussion. Dr. William Kuhlman said that he had had this patient in the hospital for 10 days under streptomycin therapy. The eye cleared while under treatment. Perhaps, if it had been continued, there would have been more clearing.

Colonel Martin said that, in his experience, while streptomycin is being given, the eye clears but, when it is stopped, the infection starts up again. He considers that the bacterial invasion has been stopped but no immunity built up. He uses 1 gm. a day in divided doses for 30 days, than 0.5 gm. a day for 90 days.

Dr. George Brown suggested X-ray treatment. Dr. James Rigg said that carbuncles clear when penicillin is injected in the tissue around. He suggested retrobulbar and circumcorneal injection of streptomycin or penicillin.

Dr. George Stine saw the patient in consultation two years ago. It was a compensation case, the cornea having been scratched by a box while the patient was at work. At that time he had a small, irritable, sharply delimited opacity. It is a bizarre keratitis, probably a tuberculous process.

Dr. Morris Kaplan had tried injecting penicillin into the anterior chamber but a severe reaction had taken place. Colonel Martin suggested that it might be possible to introduce penicillin into the anterior chamber by iontophoresis. This treatment has produced a reasonable clearing of a sclerosing keratitis of 11 years' duration. It is useful in corneal and iritic lesions.

BAND-SHAPED KERATITIS

DR. VON HALLER BROBECK and DR. SAM BROWN presented Mr. J. S., aged 36 years. The right eye has had an opacity since childhood. About eight years ago a similar opacity began to appear in the left eye. It had become much more dense in the past year. Vision is: R.E., 20/60; L.E., 20/50, with or without glasses. Each cornea has a dense horizontal band across the center with clear cornea above and below. Each iris is markedly atrophic. On June 25, 1948, the scar was resected. During the operation, the cornea was perforated and a conjunctival flap was drawn over it. When the flap retracted, a pseudopterygium remained. On August 9, 1948, this was removed. Following this, a good cosmetic result was obtained. On September 3rd, nutrient vessels leading into the scar were cauterized with trichloracetic acid. At this time a descemetocele was beginning to form in the upper outer area of the cornea.

CENTRAL CHOROIDITIS

DR. F. NELSON presented Mr. R. H., a Negro aged 46 years. One year ago he was seen by several other oculists over a period of several months because vision in the right eye had started to blur. No objective pathologic condition was found at that time. When the patient was seen on June 17, 1948, vision of the right eye was reduced to 5/18, partly. A central scotoma was present. Ophthalmoscopically an extensive destructive process was found in the right macula which appeared to be punched out. A sausagelike hemorrhage surrounded the macular region below and nasally. This hemorrhage was

subretinal and the vessels could be seen climbing over it. An incomplete white star figure was between disc and macula and below the macula. The left eye was normal.

Physical examination revealed several dental abscesses, the largest one, located above the upper right molars, measured 2.5 by 1.5 cm. All pus cysts were removed from the patient's jaw and the retinal process then cleared up gradually. On August 20th, vision was 5/15, partly.

In cases of central scotoma with deterioration of vision and no evidence of retrobulbar neuritis the macular region of the affected eyes must be checked over a long period of time. A search for focal infections is especially indicated in such cases.

CENTRAL CHORIORETINITIS

DR. GEORGE H. STINE and DR. KATHARINE H. CHAPMAN presented two cases of old healed central chorioretinitis in which the patients were not conscious of having any trouble. K. K., a boy, aged 15 years, first noticed last summer that his right vision was blurred. He had never had any discomfort in his eyes. He has always shot with the gun at his left shoulder. He writes with his left hand. At about three years of age he had a severe pneumonia. Vision is: R.E., 20/200; L.E., 20/12. The right macula has an area of choroidal atrophy, 1 p. d. in diameter, with irregular pigmented margins.

Mrs. C. G., aged 31 years, a housewife, had noticed some dimness of vision with pain in the left eye for a few days about 10 years ago. No oculist was consulted at that time, and only recently had she noticed that she could not see to read with the left eye. Vision is: R.E., 20/25.; L.E., 4/300. The left eye has a large chorioretinitic scar in the macula. The right eye has a small area of choroidal atrophy with pigment, nasal to the disc.

Katharine H. Chapman,
Secretary.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

June 8, 1948

LEUKEMIC INFILTRATION OF ORBIT

DR. J. WESLEY McKINNEY reported the case of J. H., aged 5 months, who was referred for removal of a tumor of the right lower lid. The parents first noticed a redness and then a lump in the right lower lid which had progressively enlarged for one month. The child was otherwise apparently well. There was a firm mass involving most of the floor of the right orbit. The mass was not attached to the skin but attached to the periosteum. The lower lid was bulged outward and the eyeball displaced upward slightly. The globe was internally and externally normal. The other eye and orbit were normal. The baby was sent to a local pediatrician for general physical examination. He reported a white blood count of 105,000, with 98-percent lymphocytes, and severe anemia. He made the diagnosis of acute lymphatic leukemia. The child died within two weeks.

ECZEMATOUS KERATITIS

DR. J. WESLEY McKINNEY reported the case of Dr. M. C., aged 32 years. She gave the history of having repeated ulcers of the left cornea for the past four years. For the past six months the eye had been slightly injected and irritated to such an extent that she was able to carry on her work with difficulty. She was a resident physician at the Cleveland Clinic and had had many examinations and had tried many forms of treatment. Physical examinations were negative except for a low basal metabolism rate for which she was taking 3 gr. of thyroid daily. She was allergic and had been found sensitive to many things. Desensitization with various allergens gave no relief. Among the medications tried were vitamins generally and locally, riboflavin injections intrave-

.nously, adrenalin drops, holocaine and sulfathiazole ointments. She was finally advised to leave Cleveland.

When first seen here, the right eye was entirely normal. The epithelium of the left cornea showed widespread stippling of the cornea. Almost the entire corneal surface stained with fluorescein. There was only slight pericorneal injection and moderate blepharospasm. Corneal sensitivity was slightly reduced. With the use of a protective goggle, which allowed a minimum of air to reach the cornea, the condition cleared to some extent and the staining areas fluctuated in size from time to time. During this time all medication was stopped. The patient, however, was never free from discomfort.

It was finally decided to try X-ray therapy on the basis of the good results often obtained in eczema of lids. A total of 600 r. was given in 6 equal doses at 4-day intervals. There was a moderately severe conjunctival reaction to the X rays which lasted about four weeks. During this time the stippling of the corneal epithelium could still be seen but there was no staining. The patient reported being entirely comfortable. One month later the corneal epithelium was entirely clear and there was no discmofort. Two months later or four months after the X-ray therapy, there had been no return of symptoms and the cornea was entirely clear.

CENTRAL SCOTOMA DUE TO PITUITARY TUMOR

DR. RALPH O. RYCHENER presented R. P. S., a man, aged 25 years, who, two months previously, had discovered a loss of central vision in the left eye. Various examinations were done in his own city and he was seen at the Veterans Bureau at Jackson, Mississippi, where removal of the left eye was advised because of intraocular sarcoma. Examination disclosed normal vision, visual field, and normal eye grounds in the right eye. Vision in the left eye was reduced to moving objects and the field was inconclusive, although central vision was definitely lost. The fundus of the eye was heavily tessellated and, at the periphery far above, there was a dense accumulation of choroidal pigment which was interpreted as a benign melanoma.

The patient was returned to his referring physician, Dr. J. C. Pegues of Greenwood, Mississippi, and was advised to have a course of treatment consisting of foreign protein and vasodilators, since the condition seemed to be a retrobulbar neuritis. At the completion of this treatment, there was no visual change and he was seen again in Jackson, Mississippi, where the advice of the removal of the eye was reiterated.

Upon the patient's return to Memphis the same diagnosis was made as on the previous visit and he was admitted to the Eye, Ear, Nose, and Throat Hospital for further foreign protein and vasodilator therapy. At the conclusion of this treatment, vision in the left eye returned to 6/60, J12. At this time the form and color fields disclosed a temporal hemianopia in the left eye and a relative hemianopia in the right eye. Diagnosis was then changed to that of a pituitary lesion. X-ray films disclosed an eroding pituitary tumor and on May 11th, Dr. Nick Gotten removed a chromophobic adenoma of this gland.

Visual improvement was almost immediate and, within two weeks, it had returned to 6/6, J1 in the left eye, with slight improvement in the visual field and a residual pallor of the temporal portion of the optic disc. X-ray therapy through four portals is completing the treatment.

PROGRESSIVE ENLARGEMENT OF FILTRATION BLEB FOLLOWING IRIDENCLEISIS

DR. PHILIP MERIWETHER LEWIS presented a white woman, aged 52 years, with an increasingly large corneal bleb following operation for glaucoma.

On August 16, 1945, the right eye began to pain and, when seen the following day, was stony hard with vision reduced to hand movements. Treatment with eserine, pro-

stigmin, and mecholyl failed to lower the pressure. Iridencleisis was performed, the scleral incision being made ab externo, approximately 1.5 mm. from the limbus. The iris prolapsed, was split meridionally, and both pillars incarcerated into the angles of the wound. Convalescence was uneventful, the pressure remaining around 20 mm. Hg (Schiøtz) for about a month. Vision returned only to 20/70, which was partially due to some early lens opacities. Six weeks after operation the tension was only 12 mm. Hg and the filtration bleb was quite prominent, but did not extend forward past the limbus. Vision was 20/70. The left eye was normal.

The patient was not seen for seven months (April, 1946) at which time vision and tension were the same, but the bleb was uncommonly large and extended slightly into the cornea. She was asked to return every few months, but did not come back for over a year (July, 1947). She then had an acute attack of glaucoma in her left eye. Reduction of pressure could not be obtained by strong miotics, so an iridencleisis was performed. The anterior chamber did not restore for 10 days and has remained shallow ever since. Vision could not be improved to better than 20/100 after operation and the gradual development of a cataract reduced it to 15/200.

The bleb of the left eye was larger than average, but small in comparison to that of the right. The bleb of the left eye now extended 1 mm. over the limbus into the cornea; that of the right extended 4.5 mm. downward toward the pupil—from the 10- to 2-o'clock positions on the limbus, a distance of 13 mm.—and it was more than 2 mm. thick. It formed a mass that was uncomfortable to the patient and disfiguring. The tension could not be measured due to the bleb covering more than one third of the cornea. Tension of the left eye was 8 mm. Hg and that of the right eye seemed about the same to palpation. The patient was reluctant to undergo further surgery, but it

was felt to be necessary, as the bleb was destroying the cornea, dissecting it somewhat in the manner of an aneurysm. Removal of the corneal portion of the bleb, curettage of the upper part of the cornea, and the drawing down of a conjunctival flap have been contemplated. Possibly cauterization of the upper cornea should be done to try to secure a firm cicatrix and to prevent a recurrence of the enormous corneal bleb.

Daniel F. Fisher,
Recorder for Eye Section.

OPHTHALMOLOGICAL SOCIETY OF MADRID

April 16, 1948

FATTY DEGENERATION OF CORNEA

DR. MARIN AMAT read a paper on two cases of fatty degeneration of the cornea following herpes corneae, one traumatic, the other spontaneous.

In both cases there was a rapid infiltration of fat in the whole cornea, during a period of two to three weeks, with complete loss of vision. It thus appears that herpes corneae predisposes the eye to such fatty infiltration. The fact that one case was due to an accident while the patient was at work gives it great importance from a legal standpoint.

In connection with these cases, Dr. Marin Amat discussed the presence of fatty substances in the cornea as possibly being caused either by a simple accumulation of fat occurring normally in the circulation, or by the production in situ of lipoids caused by foreign substances stimulating the tissues. In exceptional cases it may be due to an excessive quantity of fat in the circulating blood.

The fatty substance is found in a very fine emulsion in the blood stream and in the cells, constituting an integral part of the protoplasm and participating in its activities, though to a minor extent, since it is continually destroyed by the intracellular

oxidase. But if the oxidation is deficient, the fine emulsion of neutral fat and of cholesterol condenses and gives the typical picture of fatty degeneration.

Thus this process can be caused by local, insufficient oxidation, by excessive cholesterol in the diet, or by a disturbance of lipoid metabolism. In accordance with these concepts, Dr. Marin Amat suggested applying locally substances which provide abundant oxygen to the corneal tissues.

Discussion. Dr. Mario Esteban said that Dr. Marin Amat's paper touched on a topic of great practical interest since little is known of the intimate mechanism of local and general metabolic disturbances which lead to the fatty degeneration of the cornea. The therapeutic suggestions are scientifically sound and should be investigated, especially as we are now powerless to stop these processes.

Dr. Marin Amat agreed with Dr. Mario Esteban that secondary fatty degeneration of the cornea is a relatively frequent complication, but he does not know of any published case of its following herpes corneae. In addition, herpes corneae is considered an occupational disease when it accompanies or follows ocular trauma. Moreover, it seems that the herpes virus tends to dispose the corneal tissue to fatty degeneration.

RETINAL DETACHMENT DIAGNOSED AS RETROBULBAR NEURITIS

DR. CARRERAS-MATAS described a case of a woman patient whose only symptom was a central scotoma. The ophthalmoscope showed no alteration at the posterior pole of the fundus which could explain the scotoma, and it was diagnosed as retrobulbar neuritis.

Several days later, the scotoma became denser and spread to the periphery. The ophthalmoscope showed a retinal detachment with a very minute tear in the centrocecal region.

Dr. Marin Amat said that a small retinal detachment may be confused in the beginning, because of the central scotoma, with retrobulbar optic neuritis, since the papillomacular bundle is involved in the neuritis. In the case described the papillomacular bundle was also involved by the slight edema and the subsequent detachment of the retina, which in the beginning could not have been detected.

The only difference which may be mentioned is that, in optic neuritis, the papillomacular bundle is affected in its course in the optic nerve and, in this case, in its course between the fovea and the papilla.

It is evident that the blue blindness which the detached zones of the retina show, which in turn is a form of hemeralopia, can also be explored by perimetry.

In the days when there was no operation for retinal detachment and the detachments became larger and more fixed, it was common observation that the patients would tell us when the retina became adherent. Although they could not see the color of the sky during the day, in the morning on opening the window they were enthused on seeing the beautiful, intense blue color of the sky. What happened was that, during the night, with the absorption of the subretinal edema, the retina became attached, although only for a transitory period.

John I. Pascal,
Translator.

THE JUNE MEETINGS

The American Ophthalmological Society held its 85th annual meeting at Hot Springs, Virginia, on June 2nd to 4th. The weather was perfect, the surroundings beautiful, comradeship evident, and the program highly satisfactory and instructive. There were 120 members and 29 guests in attendance, and 21 scientific papers were read and discussed. Most of these were meritorious and several were particularly noteworthy.

To mention briefly a few, Dunnington discussed late fistulization of operative wounds and described an operation by suture to close the fistula. Cordes described bilateral malignant ocular melanoma. Joy's paper on nevus flammeus associated with glaucoma added further evidence that increased capillary permeability may occur in the condition.

Scheie presented further evidence that goniotomy is efficient in congenital glaucoma. Reese contributed valuable material to the subject of spontaneous cysts of the ciliary body simulating neoplasms. Prof. G. B. Bietti, of Pavia, and Gundersen's paper on the use of para-amino-salicylic acid and streptomycin was well received.

One of the most interesting papers was

that by Dunphy on ocular conditions associated with idiopathic hyperlipemia. Dr. Bedell had some beautiful retinal Kodachromes, as usual, to illustrate his discussion of retinitis punctata albescens. Fink's contribution on the anatomic approach to surgery of the oblique muscles was convincing and valuable.

These papers and others similarly important produced lively discussions which often developed points of interest and instruction that were as significant, or at times more so, as many presented by the essayists.

The Howe Medal, which hereafter will be known as the Distinguished Service Medal of the society, was granted to Phillips Thygeson of California for his outstanding contributions to the field of ophthalmic bacteriology and virus diseases.

Parker Heath of Boston was elected the president, and John H. Dunnington of New York, the vice-president. The retiring president, Bernard Samuels, presented a beautiful chain and badge of office to the society, and graciously hung it about the neck of the incoming president.

The members of the society unanimously adopted a by-law to the constitution whereby a member found guilty of accepting rebates would forfeit his membership in the society. This is the first national ophthalmic organization to take this important and long-delayed stand.

Most of the members moved on to Philadelphia to attend the 18th scientific meeting of the Association for Research in Ophthalmology which was held on June 6th and 7th. At this meeting, 18 splendid papers of strictly research interest were given. Of these, the papers by Collins on "Experimental studies on sympathetic ophthalmia," and Smelser and von Sallmann on the "Correlation of microscopic and slitlamp examination of developing hereditary cataracts in mice," von Sallmann and Dillon on "Studies of the eye with radioiodine autographs," Kinsey on "A study of the possible conversion of dehydroascorbic acid to ascorbic acid in the aqueous

humor," Koelle and Friedenwald on "The histochemical localization of cholinesterase," and Day on "Polysaccharides in ocular tissue," were particularly outstanding.

Wilson evaluated a radium-D applicator that has been widely sold and leased to ophthalmologists and pointed out that it has a low output and superficial penetration. An increase in the dosage of radium D to obtain adequate irradiation of deeper tissues would produce more damage superficially than radon or radium.

William F. Hughes, Jr., was elected the new trustee. Most of the 150 members registered stayed throughout the entire meeting, and one could not help but be impressed by the growth, enthusiasm, and great significance of this organization. There is no question that outstanding work in experimental ophthalmology is being accomplished by an increasing number of investigators who are native born and trained. The best of the new work appears to be done in the few "institute" type of organizations that are available in this country.

The Section on Ophthalmology of the American Medical Association held its annual session on June 8th to 10th at Atlantic City. There were 450 members of the section registered, although the audience at times was greater than this number.

M. Hayward Post, Jr., the chairman, in his address discussed the functions of the various national organizations in this country with particular reference to that of the section. He pointed out the key position in American ophthalmology occupied by the section and its importance to ophthalmologists.

A symposium on ocular injuries, put on the program at the request of the Surgeon General of the Army, followed Dr. Post's address. It was well received, and should be useful to the armed forces and to the general practitioners for future reference.

Ten scientific papers of excellent merit were given during the rest of the session. These were well discussed not only by the

official discussors but by members from the floor, as well. The subject of retrolental fibroplasia was reviewed by King and also by Heath who spoke on its pathologic aspects.

Among other noteworthy papers were those by Cowan and Klauder on "The frequency of the occurrence of cataract in atopic dermatitis," Bietti on "New trends in ciliary body surgery for the relief of glaucoma," and Sanders and Cutler on "General anesthesia for cataract surgery."

Ray A. Irvine of Los Angeles and Albert LeMoine, Sr., of Kansas City were elected chairman and vice chairman, respectively. Dr. Conrad Berens of New York was awarded the Scientific Medal of the section for his many important contributions to ophthalmology.

The section was represented by eight exhibits, all excellent, in the Scientific Exhibition of the parent organization. Of these, the exhibit by A. L. Kornzweig, of New York, on the pathology of the eye in old age received the Silver Medal of the association for Group II, and that of Peter Kronfeld, Roy Riser, and John Parker of Chicago, on glaucomatous excavations, a Certificate of Merit, Group II.

In making the busy round of these meetings, one is convinced that our science in this country is growing by leaps and bounds. Earnest and eager workers are increasing in numbers. The scientific and literary merit of their contributions is on a very high level of integrity and truth. The stimulation of hearing them is almost overwhelming and mildly depressing, especially to those of a slightly lazy nature. However, those who attended the meetings will, no doubt, return to their work determined to improve the quality of their activities and refreshed by their experience.   Derrick Vail.

WILMER RESIDENT'S MEETING

The Wilmer Resident's Association held its eighth clinical meeting at The Johns Hopkins Hospital and University on April 6,

7, and 8, 1949. The association is composed of former senior residents of the Wilmer Ophthalmological Institute. Their annual clinical meeting provides an opportunity to review the work done in the institute during the past year, and to follow the activities of the former residents.

The program indicated the scope of the research which is in progress at the institute and was organized to present subjects of interest to the clinician and to the investigator as well. The influence of Dr. Alan C. Woods, the director, and of Dr. Jonas S. Friedenwald pervaded the meeting. Dr. Frederick Verhoeff was in constant attendance and took every available opportunity to present the "Boston" point of view in his inimitable discussion which delighted the group.

Dr. Woods presented what was in substance a symposium on uveitis. His three papers were entitled: "Classification and special symptomatology of uveitis," "The etiological diagnosis of uveitis," and "Treatment of uveitis." The granulomatous and nongranulomatous types of uveitis were clearly differentiated. Repeated attacks of nongranulomatous uveitis can produce vascular damage, thrombosis, and necrosis and, with subsequent repair, give a picture of plastic iritis which may superficially resemble granulomatous uveitis. Dr. Woods interprets this vascular damage as a manifestation of the Arthus phenomenon.

Granulomatous uveitis usually can be diagnosed and the etiology presumptively determined. An exception is in the case of chronic brucellosis. During the past year the armamentarium for indicating toxoplasmosis has been enhanced. The skin test of Frenkel, indicating sensitivity, and the methylene-blue dye test of Sabin show good correlation in evidence of the presence of neutralizing antibodies in the patient's blood. Sabin prefers the dye test to the rabbit test he formerly employed.

New possibilities for the treatment of uveitis are accumulating. Streptomycin,

promin and promizole in tuberculosis, aureomycin in brucellosis, penicillin in syphilis, and desensitization to bacteria causing the nongranulomatous type of the disease, are the outstanding examples. There is no question about the miraculous effect of penicillin on syphilitic uveitis. In other instances of the disease, penicillin is of no value and the promiscuous use of this antibiotic in cases not due to syphilis was censured. The final evaluations of streptomycin, promizole, and aureomycin await further clinical trial. The use of these and other new drugs and antibiotics was further discussed by Dr. Perrin Long in "Modern status of antibiotics."

In nongranulomatous uveitis due to sensitivity to streptococci, gonococci, and staphylococci, treatment by desensitization, particularly to specific strains of streptococci, is an approach to the problem that is being re-emphasized. In some cases desensitization to specific organisms found in foci of infection is being carried on with encouraging results.

Putting time and effort into the study of each uveitis case, tracking down the etiology before instituting treatment, according to a rigid and carefully planned attack, as is done at the Wilmer Institute, is the only way the problems of this disease can ever be solved or judicious treatment be prescribed.

A fascinating paper by Dr. Malcolm W. Bick and Dr. Ronald Wood on "Heparin and ocular sensitivity" may prove to have a bearing on the problem of uveitis. They showed that heparinizing animals minimized or overcame induced states of hypersensitivity. Additional work along the lines of this investigation would seem to have great potentialities of application.

The perplexing and disheartening problems of uveitis are gradually being reduced, by such investigation as is being carried on at Wilmer, to more basic factors of tissue and humoral reactivity, and therapeutic measures are becoming accordingly more specific. The organization of uveitis services throughout the country, along the lines prescribed by Dr. Woods, would inestimably facilitate the care and cure of patients afflicted with this disabling disease. The goal is far from sight, but I predict that the tenacious and Herculean efforts of Alan C. Woods are setting the course and pattern for its realization.

"Sympathetic ophthalmia following intraocular surgery" was the subject of Dr. Howard A. Naquin of the resident staff. He analyzed 35 cases proved by pathologic examination. Many of these were operated on elsewhere than at Wilmer. In all cases there was evidence of incarceration of uveal pigment in the wound. The impression was that early enucleation of the activating eye has a favorable effect on the course of the disease. This is contrary to several previously reported investigations, particularly one which the author conducted in 1937. Further observations are warranted, as analyzing all cases in the literature where sympathetic ophthalmia is reported to have become apparent only after the exciting eye had been removed, and this eye revealing evidence of the specific infiltrate.

Dr. Jack S. Guyton, assistant director of the Wilmer Institute and associate professor of ophthalmology, read two papers on strabismus. The first, entitled "Surgical correction of horizontal strabismus: A new concept of the mechanics involved," emphasized the varying effect of the vertical muscles, particularly the obliques, on horizontal rotation as the eye is rotated laterally different degrees. The concept is based on mathematical formulas which heretofore have not been applied to the mechanics of ocular rotation. Application of Guyton's idea may lead to a more accurate estimation of the effects one may expect from recession, resection, and advancements. A simple mathematical formula to be used in surgery combined with a proper understanding of innervational factors is sorely needed if the results of strabismus surgery are ever to be uniformly predictable. His second paper, "Surgery of the horizontal recti: approach through a concealed conjunctival incision," demon-

strated a simple way to avoid unsightly scars without unnecessarily complicating the surgery.

Four papers dealt with the subject of glaucoma. The first of these was "Some ocular effects of a new anticholinesterase agent, tetraethyl pyrophosphate (T.E.P.P.)." Dr. William G. Marr, the present senior resident, presented evidence that this drug may cause detachment of the retina through extreme contraction of the ciliary muscle, and also that sensitivity reactions to this drug are so excessive as to preclude its clinical use at present.

Dr. Angus L. MacLean presented a method of "Corneoscleral trephine and intracapsular extraction in one procedure for primary glaucoma combined with cataract." Motion pictures were used to illustrate the procedure. The use of a Berens's punch in place of a trephine might possibly simplify the technique.

"The results of surgery in acute glaucoma" were analyzed by Dr. Herman K. Goldberg. Simple iridectomy was a satisfactory operation if the patient was being treated for a first attack of glaucoma. After a second attack, some type of iris-inclusion operation combined with separation of the iris at its base gave the best results. The last paper on glaucoma was "Changes in intraocular pressure following miotics," by Dr. Rufus C. Goodwin.

Two outstanding papers undoubtedly were inspired by the research of Friedenwald utilizing histochemical techniques for the study of physiology of the eye. The first, by Dr. Robert Day, "Polysaccharides in ocular tissue" dealt primarily with the distribution of polysaccharides and the effect of the enzymes, hyaluronidase and amylase, in depolymerizing these polysaccharides in the eye. The second, by Dr. George B. Koelle, was "Histochemical localization of choline esterase in ocular tissue."

Dr. Jonas Friedenwald's significant contribution was entitled "Inhibition of mitosis in the corneal epithelium by ionizing radiation."

His experiments suggest that X rays inhibit cell division through chemical changes produced in the cells rather than through direct ionization of some component of the mitotic mechanism.

Dr. Roy O. Scholz concluded from his data on "Use of radioactive indicators for study of aqueous humor" that the aqueous is a secretion. He determined the concentration of radioactive sodium in the serum and the aqueous with the lids open and then with the lids closed.

Dr. Robert C. Laughlin, now associate professor of ophthalmology at the new medical school of the University of Washington, reported his interesting observation on "A new variety of corneal pigmentation" in workers in factories making poisonous gas. Approximately 50 percent of the employees in these factories showed what appeared as a Stahli's line in the cornea.

"New radon and radium-D applicators" were discussed by Dr. William F. Hughes, Jr. He has devised one in which small glass vials of radon gas are imbedded in beeswax in the tip of the applicator. The dosage can be varied by varying the number of vials used. Beta radiation, so applied, can obliterate vessels deep in the cornea, and the radiation is sufficiently strong so that it need be applied only for a very brief duration. Dr. Hughes explained that the radon-D applicators on the market give off a soft Beta radiation that can be used for surface-fire effect, but not effectively for destroying vessels deep in the cornea. The new applicator he described can be used for deep or superficial effect, and the time of application can be very short.

In "Cataract section following filtering operations," Dr. Russell T. Snip reviewed the results of such operations performed at the institute to determine which type of section affected the drainage least and produced fewest corneal changes. A corneal section away from the filtration bleb, rather than through it, was least detrimental to subsequent drainage in the eye. Sections above or

to one side, or below, in the cornea showed no appreciable difference in the incidence of subsequent dystrophic changes in the cornea.

Dr. Frank B. Walsh presented a masterful treatise on "The anatomy of neurologic defects in pituitary tumor." Diagrams and illustrations depicted clearly the anatomic basis for various signs and symptoms of pituitary disorders.

A thorough study of "The effect of retrobulbar alcohol injection on the eyes of experimental animals" was made by Dr. Walter Kornblueth, who was formerly at Wilmer and is now working at Stanford under the direction of Dr. Alfred E. Maumenee, the former Wilmer resident who is now professor of ophthalmology at Stanford Medical School. In the experimental animals, repair processes in the cornea were definitely inhibited by the retrobulbar injection of alcohol. The significance of this finding may not be as ominous as one might suppose, for clinical reports on patients reveal no alarming complications following such injections. However, this new experimental evidence should put the clinician on guard.

It was interesting to hear Dr. Walter H. Benedict discuss "Prognosis for vision in anoxia," because of the content of the paper and the manner of presentation, and, in addition, because of his resemblance to a certain well-known ophthalmologist from the Middle West who was an attentive listener.

From the department of physiological optics, Dr. Louise L. Sloan and Miss Lorraine Wollach reported on "Total color blindness."

In the field of electrophysiology Dr. Carlton C. Hunt, Dr. Stephen W. Kuffler, and Dr. Samuel Talbot demonstrated "New retinal recording methods from the intact eye." Action currents were recorded from single nerve elements.

A collection of fundus and external eye pictures were exhibited in the institute during the meetings. These drawings were made by Annette S. Burgess and represent the finest collection of fundus drawings in the country. Many hours could be profitably spent studying these pictures.

The outstanding single presentation at this meeting was that of Dr. William C. Owens and Dr. Ella Uhler Owens. The title was "Vitamin-E studies in relation to retrolental fibroplasia." These workers have already proved that retrolental fibroplasia is an acquired condition, first manifesting itself about two months after birth as dilatation of the retinal vessels with subsequent edema and exudate of the retina, then separation of the retina into peripheral folds that become organized behind the lens, finally forming a gray membrane. Because the condition is acquired, some factor in the care of prematures was suspected in the etiology. Because of the presumed poor assimilation of fats by the premature infant and because of the anemia and growth requirements, the accepted treatment in recent years has included high protein diet with high vitamin-A and iron intake. It has been shown that in some animals, particularly in chicks, high doses of vitamin A and iron inhibit the availability of vitamin E, resulting in a relative deficiency of E, leading to nutritional encephalomalacia.

No such clinical entity as vitamin-E deficiency has been recognized in humans, but the facts in experiments with chicks led the Drs. Owens to believe that deficiency in available vitamin E might be a factor in the development of retrolental fibroplasia.

Three groups of prematures were observed. The first group were treated in the usual way and the incidence of retrolental fibroplasia was the usual figure of 12 to 25 percent. A second group were given a new water-miscible vitamin-E preparation and less vitamin A and less iron than the first group. No instance of development of the condition was seen in this group. A third group, in whom the disease was just becoming apparent, were treated with addition of vitamin E and reduction in vitamin A and iron intake

and regression or cure of the disease resulted.

In discussing this paper Dr. Kinsey of the Howe Laboratory paid tribute to the accomplishments of the Drs. Owens as showing perspicacity of the highest order in the plan of investigation and the analysis of results, and he said that, in his opinion, those privileged to be present had witnessed an epochal contribution. It remains a mystery why the incidence of the condition is much higher in Boston, Baltimore, and Chicago than in some other cities, as for instance, Los Angeles, when the accepted modern treatment of prematures includes correspondingly high doses of vitamin A and of iron in all localities.

It is to be hoped that many of these fine papers will soon be published, for they are worthy of a nationwide audience.

S. Rodman Irvine.

BIFOCALS FOR JUVENILES

Not infrequent are misconceptions as to the care and significance of presbyopia and as to the prescription of bifocals. In infancy the healthy crystalline lens is so nearly fluid that its consistency presents no appreciable obstacle to the changes necessary in accommodation. If the eye is approximately emmetropic, all that is necessary for accurate vision of near objects is such an amount of activity of the ciliary muscle as will produce the proper increase of convexity of the crystalline lens. If the eye is made emmetropic by proper correction of hyperopia, myopia, or astigmatism, the same sort of physiologic need is satisfied by the same sort of action on the part of the ciliary muscle. Apart from uncorrected refractive error, this physiologic effort of accommodation normally causes no symptoms and is not harmful to the patient.

There used to be a rather general notion that the hyperopic patient possessed more, and the myopic patient less, than the normal capacity for accommodation. More exact study has shown this not to be the case. The myopic patient's accommodation, in the presence of an accurate distance correction, is normally as ample as that of the emmetropic or hyperopic patient under similar conditions of age and general vitality. Thus it is a mistake to assume that the properly corrected myopic child or adult is less equal to the task of reading, writing, or drawing than other properly corrected children.

Exact measurement and recording of the patient's accommodation is too generally neglected or carelessly undertaken. It should preferably be indicated in diopters on the basis of the least distance at which the patient can still see sharply (even with effort if necessary) the smallest detail of type or other fine test object which can be made out at such distance; the test being made either without or with correction, or with a presbyopic addition, according to the circumstances of the case.

Statements have been made as to the influence of convergence in relation to the myopic eye, but there is no adequate evidence as to the significance of any such relationship. Nor is there, in spite of all that has been said as to the effect of near work in the production of myopia, any proof that the mere exercise of accommodation, apart from the bearing of posture and other conditions upon the general health, is capable of damage to the young eye.

In the normal course of life the crystalline lens steadily becomes less fluid or elastic, and the near point of accommodation gradually recedes from the eye, until at last the eye is no longer capable of sufficient adjustment to provide for the ordinary range of close work, especially reading or sewing. In most eyes with proper distance correction this stage is reached somewhere around the age of 45 years.

It used to be rather customary to lay down a "rule of thumb" that the patient should be given (over and above his distance correction) about one diopter of plus spherical

addition at the age of 45 years, two diopters at 50, two and a half diopters at 55, and three diopters at 60 years. These figures are more or less excessive for most people, and were quite certainly dependent upon the fact that it was formerly much less usual to give patients adequate basic correction for hyperopia, so that they were regarded as being more presbyopic than they actually were. With proper distance correction, most people can manage very well with a 2.25 diopter near addition until well beyond the age of 60 years.

Every accurate ophthalmologist encounters from time to time a patient who has been given a bifocal addition unnecessarily. In the experience of the present writer, such cases have usually been those in which the basic hyperopia was inadequately corrected. More rare, to most of us, is the experience of seeing bifocals placed on young children. Now and then we have to do with an optician's or optometrist's prescription for a case of strabismus in which the distant correction has been grossly underestimated.

According to an ophthalmologist correspondent in the Middle West of the United States, there is in his vicinity a sort of "epidemic" of the furnishing of bifocals to cases of high myopia, or even sometimes to cases of only moderate myopia. This practice is seen, according to our correspondent's experience, among the respectable type of optometrist, and is explained as due to lectures given under a so-called "optometric extension program."

As examples of the practice are listed patients of ages ranging from 10 to 20 years, and with myopic errors running from minus 0.25 sphere through minus 1 or 2 diopters and up to 4 or 5 diopters. All the patients listed had excellent visual acuity, accommodation, and convergence. They were always grateful for withdrawal of the bifocal addition.

In defense of such a practice, the optometrist responsible was disposed to urge the frequent suggestion in older textbooks that the myopic correction prescribed for distance should be reduced for near work. It may be added that this older advise is more or less vaguely excused in some more recent publications.

The cause of marked differences in refraction, in families in which the hereditary factor is not clearly responsible, is far from being definitely understood, but there is good reason to suppose that it has something to do with an increased hereditary capacity for variation in the family or individual, especially in the period of active growth. It is now general practice to prescribe a full correction for this refractive anomaly, although of course with precise attention to astigmatic errors and inequality of the two eyes, as well as extreme accuracy in the placing of the lenses. The present writer has followed this procedure in very many cases of high or moderate myopia, in children usually healthy and physically vigorous, and has never seen cause to regret doing so. Nor, in adopting such a course, is it necessary to take the patient out of school. The rapid progression in amount of myopia frequently seen is almost certain to become much less marked at the close of the period of active growth.

One rather important point commonly overlooked is that the patient with an uncorrected low amount of myopia may suffer from eyestrain caused by habitual cramping of the lid muscles in the instinctive effort to sharpen vision.

Although, let us hope, usually done with a clear professional conscience, the ordering of bifocal glasses for myopic children is not only unnecessary but objectionable, and suggests in the prescriber a lack of scientific understanding of ocular physiology. The satisfaction subsequently created by withdrawal of the presbyopic element at the hands of an enlightened ophthalmologist must be somewhat disturbing to the reputation of the optometrist concerned.

W. H. Crisp.

OBITUARIES
ARTHUR N. ALLING
(1862-1949)

Dr. Arthur Nathaniel Alling was born in New Haven, Connecticut, July 1, 1862, of an old New England family. He prepared for college at the Hopkins Grammar School and received his B.A. degree from Yale in 1886, remaining for an extra year in the Sheffield Scientific School. In 1891, Dr. Alling was graduated from the College of Physicians and Surgeons, Columbia University. Having become interested in ophthalmology, he remained in New York for a year to work under the late Dr. Herman Knapp and began practice in New Haven, in 1893. In 1896, Dr. Alling became lecturer in ophthalmology at the Yale School of Medicine and, in 1902, was made clinical professor, which position he held until 1938.

A man of sterling character, keen mind, and ready wit, Dr. Alling was a skillful operator, a stimulating teacher, and enjoyed a large practice. He was a member of the New York Ophthalmological Society, the American Ophthalmological Society, and a Fellow of the New York Academy of Medicine.

Eugene M. Blake.

WARREN DOUGLAS HORNER
(1890-1948)

Dr. Warren Douglas Horner died on the night of October 22, 1948, in his home following a lingering illness. He was born September 11, 1890, at Klamath Falls, Oregon. After obtaining his preliminary education in Chico, California, he attended the University of California, where he was graduated in 1913. Three years later he received his M.D. degree from the university's medical school. Following this he served his internship at the San Francisco Hospital.

During the first world war, Dr. Horner served as a Navy lieutenant at base hospitals in Scotland and France. Upon discharge from the Navy he devoted one year to special study of the diseases of the eye, ear, nose, and throat at the University of Vienna, following which he entered private practice in 1923. From 1929 on, Dr. Horner limited his practice to the diseases of the eye and was appointed associate clinical professor of ophthalmology of the University of California and chief of ophthalmology of the University of California's Section of Ophthalmology at San Francisco Hospital.

Immediately after the attack on Pearl Harbor, Dr. Horner was recalled to active duty in the Navy with the rank of captain and was finally stationed at Oak Knoll Hospital, where he was retired in 1945.

He contributed numerous important articles to the ophthalmic literature, the most outstanding one being his thesis for the American Ophthalmological Society entitled, "A study of dinitrophenol and its relation to cataract formation."

Dr. Horner was honored by his colleagues on numerous occasions serving as chairman of the eye sections of the county and state societies. He was the first president of the San Francisco Ophthalmological Round Table, and was vice chairman of the Section on Ophthalmology of the American Medical Association at its centennial celebration in Atlantic City in 1947.

In addition to his appointment to various San Francisco hospitals, he was ophthalmic surgeon and consultant at the United States Marine Hospital of San Francisco.

Dr. Horner was a member of the San Francisco County Medical Society, the California Medical Association, the American Medical Association, the American Academy of Ophthalmology and Otolaryngology, the American Ophthalmological Society, the Association for Research in Ophthalmology, the San Francisco Round Table, and the Pacific Coast Oto-Ophthalmological Society.

On June 28, 1919, he was married to Madge Clendenin. To this happy marriage with its beautiful home life were born a

daughter, Mrs. Harold A. Hyde, and a son, Douglas C. Horner.

Aside from his practice, Dr. Horner's chief interest was in his work with the students and residents. Persistence and attention to detail were primary virtues that he tried to instill in his associates. He was a good teacher, and gave freely of his time in this field. He was devoted to his work, and was an intelligent observer and a skillful operator.

Dr. Horner was tall, handsome, friendly, with a modest personality and a keen sense of humor, and was always ready with a clever story. His charm, graciousness, and love of people gained for him a host of friends within and outside his profession. To his friends he was known as "Bud," and because he was so real and so gracious he is remembered by thousands of friends, patients, and students.

Frederick C. Cordes.

BOOK REVIEWS

CORNEAL GRAFTS (keratoplasties) (Les Greffes de la Cornée). By L. Paufique, G. P. Sourdille, and G. Offret. Published under the auspices of the French Society of Ophthalmology. Paris, Masson et Cie, 1948. 359 pages, 135 figures, 20 plates, 4 of which are in color, bibliography. Price, not listed.

The authors have succeeded in giving us a well-illustrated, factual description of corneal grafting in all of its manifestations from history, instrumentation, and the various techniques to a discussion of the healing and its complications. The indications and contraindications for the operation are clearly set forth. It is gratifying to note the prominence given to American authors in the contributions to this field of ocular surgery.

An analysis of the results of the authors' partial nonperforating keratoplasty operations showed 71 anatomically favorable results out of 90 cases (75 percent) according to the criterion of Filatov, that is, the graft remained transparent, permitting one to see the details of the anterior chamber and the ocular fundus. There were eight poor results. These results are a little better than those obtained from keratectomies.

The book is well printed and is a worthy companion of those hitherto published by the same firm under the auspices of the French Society of Ophthalmology. Ophthalmologists who read French will get much out of it. It is hoped that an English edition may become available.

Derrick Vail.

DA BIOMICROSCOPIA ESTÉROSCÓPICA DO FUNDO DO ÔLHO DO CÃO NA VIGÊNCIA DA HIPERTENSÃO (Experimental stereoscopic Biomicroscopy of the Ocular Fundus of the Dog in the Course of Experimental Hypertension). By Cyro de Barros Rezende. Independently printed monograph, São Paulo, Brazil, 1948. Stiff paper covers, 167 pages, 28 plates, 21 in color, 7 in black and white.

This is the author's thesis presented to the Faculty of Medicine of the University of São Paulo in competition for the chair of professorship of clinical ophthalmology, "approved with distinction." Following to some extent the lines of Goldblatt's work on the same general topic, the author describes (in Portuguese) his modified method of slitlamp study of the ocular fundus of the experimental animals, with ample illustrations of the special apparatus employed, as well as description and illustration of the supplemental apparatus for measuring the arterial pressure of the dogs. Goldmann's contact lens was successfully applied to this study.

The beautiful color drawings, under the slitlamp, of the tapetum lucidum and nigrum in normal animals and in the course of the hypertensive studies were made by Professor Rezende's São Paulo colleague, Dr. A. G. Silva. There are also five excellent photomicrographs of retinal changes.

Interference with the circulation of the

kidney in the 24 experimental dogs was accomplished by clamping the retinal artery with Goldblatt's silver forceps.

The author states the following conclusions: Of all the ocular changes in benign experimental hypertension of the dog, the first and most constant is superficial edema of the retina. This is chiefly located in the tapetum nigrum and was most frequently evident in those retinal areas traversed by the large vessels. Even in the incipient edemas, the light bundle of the slitlamp showed slight elevation of the internal limiting membrane of the retina. As the edema became more intense, the retina lost its transparency and became grayish white. These appearances were confirmed in microscopic sections. In the benign experimental stage there was also accentuation of the median reflexes of the retinal arteries, with sheathing of the vessels and compression at the arteriovenous crossings. Changes encountered in malignant experimental hypertension included one instance of intense intraocular hemorrhage, white patches with fluffy margins, papillary edema, and marked lateral tortuosity of the retinal arteries. (List of 72 references.)

W. H. Crisp.

RÉPERCUSSIONS SUR L'ENFANT DES MALADIES INFECTIEUSES DE LA MÈRE PENDANT LA GROSSESSE. By F. Bamatter. Basel and New York. S. Karger, 1949. 60 pages, 24 figures. Price, 7.50 francs.

In this excellent monograph the author discusses, in general, the exogenous factor in the fetal dysgeneses and the placental transmission of maternal infections. A full-page table lists the bacteria, viruses, protozoans, and helminthes, the placental transmission of which has been demonstrated in man and in animals.

After a very brief statement of the known facts of the transmission of syphilis, tuberculosis, infectious icterus, paratyphus, and malaria, monographic treatment is accorded

toxoplasmosis and the embryopathy of rubella.

A tabulation makes all the important clinical and pathologic data perspicuous. Excellent halftones illustrate the monograph, two of which are particularly illuminating. In one, the sites of localization of toxoplasmosis are indicated on a drawing of a fetus together with brief statements on mode of infection. In the other the tissues which may be injured by maternal rubella are indicated on a model of a 4-mm. (one-month) human fetus.

F. H. Haessler.

BULLETIN SOCIÉTÉ BELGE D'OPHTALMOLOGIE. Number 89, 1948.

In the minutes of the meeting of June 20, 1948, is a discussion of the eye signs preceding death. In speaking of retrobulbar injection, one author says that he uses a 5-cm. needle and injects 1.5 cc. of novocain-adrenalin (4 percent) solution.

Van Lint discusses the role of pressure on the globe in intracapsular cataract extraction and explains his technique which includes a conjunctival flap, keratome and scissors section, total iridectomy, and removal of the lens by suction, coupled with pressure from below toward the center of the globe with an Arruga expressor.

A case of total ossification of the choroid following an injury 60 years before is presented.

Of the two instruments discussed, one is for the removal of foreign bodies from the cornea and the other is a shadow-casting device to be used with the biomicroscope.

Among the case reports are a case of parenchymatous keratitis with keratoplasty resulting in a final vision of 0.1; two cases of Groenouw's disease of the cornea; and one of hypercalcemia and corneal calcifications.

Ophthalmoscopic manifestations of myasthenia gravis are discussed, and photographs

are shown of the patient before and after the injection of prostigmin.

Three cases of gargoylism are presented. Three cases of keratoconjunctivitis sicca are mentioned, with various treatments, including closure of the tear points, section of the sympathetic nerves, irradiation of the lacrimal gland, injections of pilocarpine and prostigmin, installation of gelatin drops of Gifford, vitamin-B_2 therapy, and male-hormone therapy.

There is a gonioscopic picture of a case of acute iridocyclitis. Two cases of acute glaucoma which followed the subconjunctival injection of adrenalin for the treatment of iritis are described. Treatment of four cases of optic neuritis are discussed. Intraarachnoid injections of penicillin were given.

There is a discussion of therapeutic tissue implants in the treatment of retinitis pigmentosa. Among the ocular manifestations in one case of this disease were irregular distribution of the cutaneous pigment, light perception only, convergent strabismus, nystagmus, atrophic globes, seclusion of the pupil, miosis, and hypotony of each eye. It is stated that only 11 comparable cases have been reported in the literature. It is a congenital syndrome.

Two cases of retinal tears without detachment are discussed.

Bennett W. Muir.

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TRANSACTIONS OF THE OPHTHALMOLOGICAL SOCIETY OF PARIS (and of the Ophthalmological Societies of the East, of Lyon, and of the West). Meeting of June, 1948, pp. 242-328; meeting of July, 1948, pp. 334-401.

Mme. Nada Matavulj reported her observations on the tissue therapy of Filatov. In spite of the short time of this study (3 years), it seems to be clear that the biogenic stimulation in the form of placenta, placental extract, aloes, and cod-liver oil gave unexpected improvement in otherwise hopeless cases.

François Pierre reported on three children with retrolental fibroplasia. He describes the clinical appearance and differential diagnosis and stresses the fact that this anomaly was described in France in 1883 by Vassaux.

Delthil, Halbron, and Navdin describe two cases of postsurgical aniridia which they do not consider to be as critical an accident as is generally believed.

Thurel doubts the importance of opticochiasmal arachnoiditis but considers the blocking of the pericerebral arachnoidal spaces of influence because it causes the resorption of air over the hemispheres and accumulation of cerebrospinal fluid and, with it, distention of the cisterna basalis.

Bonnet found that the fundus pictures of amaurotic idiocy in a child with craniofacial dysostosis suggested that this latter condition might be not only a malformation and premature closure of the facial sutures but also a degeneration of the cerebrum and the retina.

In the July issue is an interesting and concise paper on the heterophorias, as delivered by Suzanne Braun-Vallon at the November, 1948, meeting of the French Society of Ophthalmology. The fundamental principles and clinical applications are adequately presented in six chapters, with 11 figures, charts, and a bibliography.

Alice R. Deutsch.

ABSTRACT DEPARTMENT

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Bodian, M. An aid in detecting trachoma-like inclusion bodies in the conjunctiva. Arch. Ophth. 40:147-151, Aug., 1948.

The inclusion bodies are observed in the conjunctival scrapings in cases of trachoma, inclusion conjunctivitis, psittacosis and lymphogranuloma venereum. A red light obtained by using the E light red photographic filter (Wratten), series 23A, over the light source, increases the visibility of the bodies in slides stained by the Giemsa method. John C. Long.

Samuels, B. Necrosis of intraocular tissues. Arch. Ophth. 40:101-120, Aug., 1948.

Noninflammatory necrosis is caused by circulatory disturbances and may follow iridodialysis, cyclodialysis and glaucoma. Inflammatory necrosis may be caused by pyogenic bacteria in the cornea, anterior chamber or vitreous. Necrosis caused by trauma and by neuropathy and degeneration of malignant melanomas is described in detail. Artificially induced necrosis may follow radiation therapy for retinoblastomas and diathermy treatment of retinal detachment. (10 figures.) John C. Long.

Weiss, C., Shevky, M. C., and Perry, I. H. Experimental investigation of the pathogenicity of diphtheroids isolated from the human conjunctiva. Arch. Ophth. 40:23-38, July, 1948.

The first attempt to establish an etiologic relation between a diphtheroid and a disease of the eye occurred in 1879, when Italian investigators isolated Corynebacterium xerose during the course of an institutional epidemic of xerophthalmia. Later, in 1883, German workers demonstrated the presence of diphtheroids on the conjunctiva of patients with a nutritional deficiency but it was soon realized that these bacteria are usually present on normal and inflamed conjunctivas and other surfaces of the body. In general, corynebacteria are non-motile, grampositive, aerobic, nonsporulating rods, which resemble Corynebacterium diphtheriae, and usually show uneven staining and variable morphologic changes during growth. When mucin, which occurs in the conjunctiva and other mucous membranes, is used as a vehicle in which to suspend certain bacteria, the

organisms may acquire an increase in virulence for experimental animals. Mucin functions as a protective capsule for the micro-organisms, decreases phagocytosis and intracellular digestion of bacteria and reduces the bacteriolytic power of serums.

Diphtheroids, resembling C. xerose, which were isolated from the human conjunctiva, grew well in a menstruum of mucin. When suspended in this medium and inoculated into the anterior chamber of the eyes of albino rabbits, cultures retained their viability in vivo for several days, while in suspensions in saline solution they were rapidly destroyed. Intraocular injection of diphtheroids suspended in saline solution produced moderate inflammation of the ciliary process in albino rabbits. When suspended in mucin, the reaction lasted longer, was much severer and was associated with acute keratitis.

It may be concluded that diphtheroids, which are almost constantly present on the normal and inflamed human conjunctiva, may be potential pathogens.

Ralph W. Danielson.

3

VEGETATIVE PHYSIOLOGY, BIO-CHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Bonavolontà, G. **Microspectroscopic observations on the living eye.** Ann. di ottal. e clin. ocul. 74:339-349, May, 1948.

In making his microspectroscopic observations Bonavolontà used a Gullstrand slitlamp fitted with Abbe's spectral eyepiece and with an arc light in place of the usual Nitra lamp. Conjunctiva, cornea, aqueous, and vitreous have a uniform continuous chromatic spectrum, without distinguishing peculiarities, but may present the characteristic spectrum of oxyhemoglobin in the presence of circulating or extravasated blood. The spectrum of the normal crystalline lens is shortened toward the red end (it does not extend

beyond 620 to 630 μμ., whereas the spectrum of the conjunctiva extends to 660 or 670 μμ.) and is relatively dim toward the violet end. These characteristics of the lenticular spectrum disappear as the lens becomes cataractous, so that the spectrum of a mature cataract is normal as regards extension and brightness. Spectroscopy affords a means of differentiating between hemorrhagic and inflammatory exudates in the vitreous.   Harry K. Messenger.

Brolin, S. E. **Spectrometric, photoelectric determination of the fluorescence of the eye lens. A quantitative and objective method for experimental investigations.** Acta ophth. 26:395-411, 1948.

During certain pathologic conditions of the lens fluorescence undergoes significant changes, and it is possible that fluorescence may be a sensitive indicator of metabolic changes in the lens. The author describes a method of spectrometric determination of the intensity of lens fluorescence, which is accurate enough for experimental investigation. The fluorescent light from a lens preparation in a quartz tube is analyzed with a spectrograph and an electron multiplicator photocell. The data can be recorded objectively, and small changes in the fluorescence of the lens can be recognized spectrometrically. There is a difference in the intensity and spectral localization between the cortex and the nucleus.

Ray K. Daily.

Davson, H. **Some considerations on the salt content of fresh and old ox corneae.** Brit. J. Ophth. 33:175-182, March, 1949.

The eyes from freshly killed oxen were examined, immediately and after 24 hours of ice storage, for sodium, potassium, chloride and water content of the cornea and of the aqueous humor. After 24 hours the cornea had an increase of water content, a slight decrease in sodium and a slight increase of potassium and chloride.

There was a corresponding decrease in the concentration of ions in the aqueous which suggests that the increased hydration represents a migration of aqueous into the cornea and not a mere osmotic drainage of water from this fluid.

Morris Kaplan.

Feldman, J. B. **Mydriatics.** Arch. Ophth. 41:42-49, Jan., 1949.

This paper evaluates the clinical merit of the commonly available mydriatics as to such factors as safety, speed of action and return to normal pupillary size. In this study 12 mydriatics were checked. Ordinarily, they worked more efficiently on cloudy days and on patients with blue eyes. Homatropine hydrobromide, 1 percent, atropine methylnitrate, 1 percent, and dibutoline sulfate, 5 percent, dilated the pupil in the greatest number of patients. Dibutoline sulfate, 5 percent, gave definite cycloplegia in association with mydriasis in the greatest number of patients.

Paredrine hydrobromide was less potent but was quite satisfactory as a mydriatic in a number of cases. Glaucoma is indeed a rare complication of mydriasis. Even when a mydriatic has been mistakenly used in "pre-glaucoma" one will obviate disaster by keeping the patient until the pupil has contracted particularly since much more powerful miotics than 1-percent pilocarpine hydrochloride are available. Ralph W. Danielson.

Jaffe, N. S. **Cholinesterase in the aqueous of the eye.** Arch. Ophth. 40:273-278, Sept., 1948.

Theoretically, there can be only faint traces of cholinesterase in the normal aqueous, since the enzyme is a protein. Aqueous from the eyes of 10 normal cats showed no cholinesterase, or insignificant traces of it. The first and second aqueous after paracentesis showed marked cholinesterase activity; the amount is pro-

portionate to the plasma protein in the aqueous. Ralph W. Danielson.

Jaffe, N. S. **Practical application of the denervated iris.** Arch. Ophth. 40:317-325, Sept., 1948.

The denervated iris, of the cat is too sensitive an indicator of the epinephrine content of foreign solutions, but may be used as a very sensitive indicator of the increase in the epinephrine level of the blood. In the stage of excitement of ether anesthesia the output of the epinephrine in eight cats was so great that it remained for an hour. Ether is sympathomimetic. Barbiturates inhibit the production of epinephrine due to ether anesthesia. Ralph W. Danielson.

Lehrfeld, L., and Donnelly, E. J. **Contaminated ophthalmic ointments.** Arch. Ophth. 40:39-45, July, 1948.

The unused tube of ointment was in most instances sterile, whereas the used tubes were frequently contaminated. The observations in this study call for a revaluation of the use of ophthalmic ointments in the eye after operation and of the use of ointments for ophthalmic conditions in general. The authors have no proof that infections actually occur from the use of contaminated ointments, nor that the organisms found in the contamination were pathogenic bacteria but even sulfathiazole ointment and penicillin ointment may become contaminated before the contents of the tube are exhausted.

Ralph W. Danielson.

von Sallmann, L. **Controversial points in penicillin therapy of ocular diseases.** Arch. Ophth. 39:752-804, June, 1948.

This is a comprehensive report based largely on detailed experimental studies of the use of penicillin in the eye. The parenteral us of the drug is investigated from the standpoint of the passage of penicillin across blood aqueous barrier,

penicillin levels in ocular fluids after ligation of the renal vessels and the passage of penicillin into the ocular fluids in ocular inflammation. The surface application of penicillin by means of solutions, ointments, and iontophoresis is studied. Studies are described of the injection of the drug into the conjunctiva, anterior chamber, lens, and the vitreous.

The best results from the systemic administration of penicillin in severe ocular infections are obtained by the administration of massive doses in the acute phase, aided by the simultaneous local instillation of vasodilators in less violent inflammations. The continuance of penicillin activity was usually observed in the tears for eight hours after one instillation of drops or ointment. The rather involved factors concerned in iontophoresis are discussed. With observance of specifically outlined requirements, direct injection of penicillin into the vitreous can be considered at present the most reasonable treatment of infections of the posterior segment. The many points revealed by this searching investigation should be of great value in the practical application of penicillin therapy in eye infections.

John C. Long.

von Sallmann, L., and Moore, D. H. Electrophoretic patterns of concentrated aqueous humor of rabbit, cattle and horse. Arch. Ophth. 40:279-284, Sept., 1948.

Information about the effects on the eye of the drugs, which are usually administered locally, when they are administered systemically in their usual dosage, is limited.

In experiments the authors found that morphine sulfate administered intramuscularly in doses ranging from 8 to 18 mg. produced pupillary constriction, increase in accommodative power and decrease in ocular tension in normal eyes. Morphine produced similar effects in glaucomatous eyes; in none of the 14 eyes studied did

its use lead to an increase in intraocular pressure. In equivalent doses, atropine, given intramuscularly, produced much less pupillary dilation and weakening of accommodation than did scopolamine. Neostigmine, in a dose which produced definite increase in intestinal peristalsis, had no consistent ocular effects.

Ralph W. Danielson.

Schlosshardt, H., and Adam, W. The penicillin content of the aqueous after intramuscular, intravenous and local penicillin. Klin. Monatsbl. f. Augenh. 113:333-342, 1948.

The results, which were all obtained in animal experiments, correspond to those found in the American literature. (References.) Max Hirschfelder.

Theodore, F. H. Use of propionates in ophthalmology. Arch. Ophth. 41:83-94, Jan., 1949.

The purpose of this paper is to acquaint ophthalmologists with a group of physiologic antibiotics, which have hitherto not been used in treatment of ocular infections, and which have certain advantages over medicaments now in general use. The group consists of the lower fatty acids which occur in the human body. In this preliminary report the sodium salt of one of these fatty acids, sodium propionate, was selected for study. The lower fatty acids are nontoxic, physiologic antibiotics and fungicides. Sodium propionate, a fatty acid derivative, was used clinically in about 400 cases of conjunctivitis, blepharitis, and keratitis. It has proved efficacious and nonirritating, especially in treatment of chronic conditions. Ralph W. Danielson.

Woods, A. C., and Burky, E. L. Studies in experimental ocular tuberculosis. Arch. Ophth. 39:471-490, April, 1948.

The authors report on the experimental

results in the therapy of ocular tuberculosis in immune-allergic rabbits using two sulphones, "promin" and "promizone," as the therapeutic agents. Both of these agents exert a deterrent action on the course of the ocular tuberculosis. The action becomes evident after the third week of treatment. The action of the two drugs is about the same.

Histologic evidences of tuberculous disease persist in the majority of the eyes of the treated animals. The lesions, however, are fewer and are less severe than in the control eyes. In transfer experiments with the extract of the uveal tract from the eyes of the seven treated animals only one positive result was obtained. All of the control eyes gave positive transfers. These results may be due either to a degradation of the virulence of the organisms, allowing the resistance of the host to become effective, or to a direct bactericidal action.　　John C. Long.

Woods, A. C., and Burky, E. L. **Studies in experimental ocular tuberculosis.** Arch. Ophth. 40:1-13, July, 1948.

In a previous study of the effect of treatment with two sulfone compounds, "promin" and "promizole," on experimental ocular tuberculosis in the immune-allergic rabbit, it was not clear whether the deterrent action of the sulfone compounds noted was due to a bactericidal action or to degradation or attenuation of the virulence of the organisms, thus allowing the resistance of the host to become more effective. The experiments here reported were undertaken to clarify this point. "Promin" and "promizole" used in the same dose as that which had a pronounced deterrent effect on ocular tuberculosis in the immune-allergic rabbit were only slightly deterrent on ocular tuberculosis in animals that had not been sensitized. These drugs probably have a limited bactericidal effect on the tubercle bacillus.　　Ralph W. Danielson.

Woods, A. C., and Wood, R. M. **Studies in experimental ocular tuberculosis: XII. Effect of streptomycin and "promizole" on experimental ocular tuberculosis in the immune-allergic rabbit.** Arch. Ophth. 40: 413-432, Oct., 1948.

Streptomycin exerted a deterrent action on the course of ocular tuberculosis produced by inoculation of the eyes of immune-allergic rabbits. Despite the absence of clinical evidence of activity, histologic examination of the eyes showed minimal to moderate activity and transmission experiments and cultures showed that the tubercle bacillus was still alive in some of the eyes. A combination of streptomycin and "promizole" produced a more dramatic response. After four weeks of combined treatment, the diseased eyes were clinically and histologically inactive and transmission experiments were negative in more of the animals. Streptomycin has a definite bacteriostatic and a partial bactericidal action on the tubercle bacillus in ocular tuberculosis. The combination of streptomycin and "promizole" is somewhat greater than would be expected from a summation of their individual actions.　　John C. Long.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Auerswald, W. **The area effect in scotopic vision.** Ophthalmologica 117:104-109, Feb., 1949.

For threshold stimuli there is a fairly simple mathematical relationship between intensity and duration of the stimulus as long as the portion of stimulated retina is kept small. Stimulation of larger retinal areas introduces a new factor, the so-called area effect. The occurrence or non-occurrence of the area effect seems to depend more upon the location than upon the total number of the stimulated retinal elements.　　Peter C. Kronfeld.

Balcet, A. **Myopia from the manufacture of woolen goods.** Rassegna ital. d'ottal., 17:379-383, Nov.-Dec., 1948.

In a group of forty-two women workers, ranging from 16 to 19 years of age, only nine were emmetropic. The others had two to five diopters of myopia. The writer ascribes the myopia to the nature and conditions of their work, which is very exacting, is done at close range and in poor light.   E. M. Blake.

Berger, Curt. **Some experiments on the width of symbols as determinant of legibility.** Acta ophth. 26:517-569, 1948.

The purpose of this study was to determine the effect of a change in the width of symbols on their legibility. An important interaction takes place between all factors affecting legibility, such as form, width and height. This study is a part of a long-range statistical program which will emphasize the effect of interaction between the factors.

The graphic data show that the increased width of the letters results in an increased legibility which is explained as a purely retinal function, namely the resolution threshold of the fovea centralis. (19 graphs.)   Ray K. Daily.

Best, F. **Embryologic considerations in the origin of the lateral inversion of the optic pathways in the brain.** Klin. Monatsbl. f. Augenh. 113:234-246, 1948.

Best provides a critical review and an extension of the theories of Cajal.
                Max Hirschfelder.

Bottoni, Angelo. **The light sense, and the various methods of measuring it in clinical practice.** Ann. di ottal. e clin. ocul. 74:396-420, June, 1948.

This article is a monograph on the light sense and its measurement and is illustrated with diagrams of various adaptometers and other devices. Bottoni finds adaptometry clinically useful in the detection and measurement of vitamin A deficiency, in studying the role of vitamin A in community and racial health, and in the detection and treatment of night blindness in night workers.
                Harry K. Messenger.

Casanovas, José. **Chalazion and astigmatism.** Arch. Soc. oftal. hispano-am. 9: 23-27, Jan., 1949.

Transient astigmatism may be caused by a chalazion, and glasses prescribed before its extirpation may be unsuitable afterwards.   Ray K. Daily.

ten Doesschate, J. **The relationship between the extrafoveal scotopic threshold and the distribution of retinal rods.** Ophthalmologica 117:110-115, Feb., 1949.

This is another quantitative study of the relationship between visual function and the number of visual elements per mm.^{2} of stimulated retina. The histologic basis for most of the recent work in this field was furnished by Østerberg who reported the results of careful visual cell counts in the eye of a 16-year-old boy. Crozier and Holway compared these results with their own determinations of the extrafoveal absolute scotopic threshold of the light sense and found no simple relation between the two sets of data. Now ten Doesschate compares Østerberg's rod counts in the horizontal retinal meridian with the scotopic light threshold determinations of Stiles and Crawford and finds *good agreement between the histologic and the visual data. The existing minor discrepancies can easily be explained by individual variations and other causes.* These results strongly support the theory —already firmly established—that the cones and rods form the anatomical substrata of the photopic and scotopic mechanism, respectively. Peter C. Kronfeld.

Hardy, L. H., Rand, G., and Rittler, M. C. **Incidence of defective color vision among psychotic patients.** Arch. Ophth. 40:121-133, Aug., 1948.

A high incidence of defective color vision in psychotic patients has been reported but the authors found that the incidence of color blindness in the 235 psychotic patients tested with pseudo-isochromatic plates was not significantly higher than that in the normal population.

John C. Long.

Henderson, J. W. **Cotton sutures in ophthalmic surgery.** Arch. Ophth. 39:545-548, April, 1948.

Cotton fiber is an inert material with a natural twist which can be tied into small, stabile knots with a high tensile strength. It incites early healing with little undesirable tissue response. These characteristics are features that might be considered in the possible use of cotton as a suture material in ophthalmic surgery. The author illustrates the use of cotton sutures in a considerable variety of ophthalmic operations. John C. Long.

Kinsey, V. E. **Spectral transmission of the eye to ultraviolet radiations.** Arch. Ophth. 39:508-513, April, 1948.

The ultraviolet absorption spectrums of various components of the albino rabbit eye have been measured. The limit of transmission for the whole eye is approximately 330 millimicrons; for the lens, 310, and for the aqueous and the vitreous and cornea, separately, approximately 280 millimicrons. In the corneal epithelium the chief absorbing element is nucleoprotein; its limit of transmission is less than 230 millimicrons. The amount of radiant energy from the sun to which the eye would have to be exposed before minimal damage occurs in the lens is calculated to be about three times the dose necessary to produce minimal damage to the cornea. So little ultraviolet radiation reaches the retina that damage would be extremely unlikely.

John C. Long.

Kugelberg, I. **On the effectiveness of tabulæ pseudoisochromaticæ B. K.** Acta ophth. 26:429-437, 1948.

This is an evaluation of pseudoisochromatic tables published in Sweden. Color plates are of little value in differentiating protanomolous and deuteranomolous vision of moderate severity, and complicated figures may cause difficulties for persons with normal color vision.

Ray K. Daily.

Macnie, J. P. **Clinical aniseikonia.** Arch. Ophth. 40:326-331, Sept., 1948.

A study was made of the 1,027 patients examined for aniseikonia at the Institute of Ophthalmology of the Presbyterian Hospital, New York, between December, 1936, and December, 1941. Aniseikonia was demonstrable in 527 and 463 received glasses. Of the latter, 365 (79 percent) were relieved of all or a part of their symptoms, and 98 (21 percent) were not benefited. In 1946, from five to ten years later, a questionnaire revealed that of 304 patients, one half were benefited. No symptoms are characteristic of aniseikonia, but symptoms associated with use of the eyes not relieved by the usual ophthalmic therapeutic measures may be due to it. The presence of aniseikonia cannot be anticipated on the basis of anisometropia or the magnitude of the refractive error. Nor is it possible to anticipate whether the correction of aniseikonia will aid the patient. Ralph W. Danielson.

Nolasco, J. B., and Rodil, D. **Responses to the Ishihara test for color perception.** Arch. Ophth. 41:20-23, Jan., 1949.

Approximately 2,000 male and female Filipino students were tested with the Ishihara color plates. The incidence of defective color vision in men was 4.3 percent; in women 0.3 or 0.2 percent, depending on which criterion was used.

Ralph W. Danielson.

Pascal, J. I. The "incident neutral" point in retinoscopy. Arch. Ophth. 39: 550-551, April, 1948.

The point where the emergent rays from the patient's eye meet is ordinarily spoken of as the neutral point. There is another neutral point which concerns the incident light and may be called the "incident neutral" point. This point is obtained when one uses a concave mirror and the incident light is made to focus in the plane of the patient's pupil. There will then be neutrality of motion irrespective of any refractive error the patient may have.   John C. Long.

Pascal, J. I. Real significance of centering a contact lens. Arch. Ophth. 39:514-516, April, 1948.

The prevailing method among physicians when centering a contact lens has been to center the cornea of the lens with the cornea of the eye. To get the best optical effect of the contact lens its cornea should be centered with the crystalline lens. Objectively this is impossible, but subjectively it can be done by observing the effect on vision of slight displacement of the position of the contact lens. Theoretical considerations of the variations in optic axis produced by contact lenses are discussed.   John C. Long.

Paton, R. T. Eye ointment dispenser. Arch. Ophth. 39:549-550, April, 1948.

A metal container is described into which the standard ointment tube is inserted. Only the tip of the sterilizable container comes in contact with the eye. (1 figure)   John C. Long.

Ríos Sasiain, Manuel. The extrafoveal sensitivity of the retina. Arch. Soc. oftal. hispano-am. 9:147-151, Feb., 1949.

Physiologic nocturnal myopia was utilized for determination of the most sensitive parafoveal area. With a black disk 9 cm. in diameter on a white background, with a controlled illumination, and regulated extrafoveal fixation it was found that the area of greatest scotopic visual acuity is 15 degrees from the fovea. (2 graphs.)   Ray K. Daily.

Rocco, Alfredo. Practical questions on color vision. Arq brasil. de oftal. 12:10-28, 1949.

A review in Portuguese of tests and theories, with bibliography.
                        W. H. Crisp.

Rubino, A., and Pereyra, L. The eye and the diencephalon. Riv. oto-neuro-oftal. 23:221-226, July-Aug., 1948.

The dark adaptation curve of congenitally amblyopic eyes were compared with similar curves of the normal eye of the same subject. The results confirm the conclusion reached by previous authors that light sensitivity undergoes no changes in amblyopic eyes. Moreover in amblyopic eyes it undergoes the same changes in "day-night rhythm" as normal eyes. These results corroborate the hypothesis that the lesion causing the amblyopia is in the intracerebral optic ways.
                        Melchiore Lombardo.

Toledo, Celso. Refractometry based on measurement of circles of diffusion. Arq. brasil. de oftal. 12:1-9, 1949.

The author describes a test based upon the apparent distance of objects of complementary colors, 5 m. or more from the patient, seen through two pinholes of complementary colors, separated from one another by a distance less than the diameter of the pupil. (7 black and white figures, references.)   W. H. Crisp.

Valente, Adolpho. Accommodation and some of its aspects in refraction. Rev. brasil oftal. 7:143-162, March, 1949.

The author's talk is clinically illustrated by three case reports, one on divergence insufficiency with a spasm of accom-

modation and convergence, one of spasm of accommodation with convergence insufficiency, and one of anisometropia with compound myopic astigmatism.

W. H. Crisp.

5

DIAGNOSIS AND THERAPY

Benton, C. D., Jr., and Heyman, A. Treatment of ocular syphilis with penicillin. Arch. Ophth. 40:302-310, Sept., 1948.

During the past three years the authors have used penicillin in the treatment of 39 patients with various manifestations of syphilis of the eye. Penicillin produced little or no immediate response in interstitial keratitis but the opacity cleared and the inflammation subsided in three to five months. Good or excellent vision resulted in 80 percent of the eyes treated in the first attack, but penicillin did not always prevent keratitis in the second eye. Penicillin treatment of six patients with acute iritis associated with secondary syphilis healed immediately and vision became normal. Papilledema associated with syphilitic meningitis responded well to penicillin therapy. In four of eight patients with primary optic atrophy the process seemed arrested 11 to 24 months after treatment. Combination with fever therapy is advised for optic atrophy. Ralph W. Danielson.

Cimbal O. The methods of penicillin therapy in eye diseases. Klin. Monatsbl. f. Augenh. 113:342-353, 1948.

The local use of penicillin in diseases of the eye is far superior to general, as only weak concentrations of penicillin reach the corneal tissue and the interior of the eye after intramuscular or intravenous injection except in pyogenous infections of the adnexa. Conjunctivitis may be treated with drops but corneal infections need repeated 15-minute applica-

tions of penicillin, 50,000 to 200,000 units per cc., by means of a cotton applicator. For penicillin therapy of the interior of the eye a cotton tampon with a few drops of 100,000 units per cc. penicillin solution is introduced into the lower conjunctival fornix. This method is preferred when pure crystalline penicillin is not available for subconjunctival injections. (References.) Max Hirschfelder.

Fedrizzi, G., and Ferri, L. Soft-ray roentgentherapy of superficial eye diseases. Boll. d'ocul. 27:697-705, Nov., 1948.

Plesioroentgenotherapy is recommended for practically any inflammatory lesion on the surface of the eye. If the equipment is not available, one may use any roentgen apparatus and apply 30 to 40 r per session until the total dose is 180 to 320 r. A short review of 31 corneal and scleral lesions shows that in some cases a satisfactory result can be obtained.

K. W. Ascher.

Fiore, Tito. Pentothal anesthesia in ocular surgery. Ann. di ottal. e clin. ocul. 74:381-395, June, 1948.

Pentothal anesthesia is preferable to inhalation anesthesia and is particularly indicated in the treatment of injuries to the globe, in acute glaucoma, in operations on the adnexa, and in enucleation and exenteration and other destructive operations. Administered by rectum it is the anesthesia of choice in operations on children.

Harry K. Messenger.

Gardilčić, A. The use of rat tail tendons as suture material in ophthalmology. Ophthalmologica 117:115-126, Feb., 1949.

As reported earlier by K. Pischel, rat tail tendons make satisfactory absorbable material for corneoscleral sutures. The author describes a convenient method of obtaining and preparing the tendon and reports experimental studies with various suture materials imbedded intracorneally

in rabbits. Rat tail tendon is better tolerated than catgut, silk or human hair.

Peter C. Kronfeld.

Gifford, H. **Motor block of extraocular muscles by deep orbital injection.** Arch. Ophth. 41:5-19, Jan., 1949.

In order to get more complete motor anesthesia and lower vitreous pressure, the author has (after considerable experimental work and cadaver dissections) devised an altered technique in retrobulbar injections which he describes in detail. Using 2 cc. of 2 or 4-percent procaine hydrochloride, with 0.4 cc. of epinephrine hydrochloride to the ounce (29 cc.), he was able to produce a better than 60-percent motor block in 74 percent of 158 cases.   Ralph W. Danielson.

Grancini, L. E. **Experimental anaphylaxis with normal placenta and with Filatow's preparation.** Rassegna ital. d'ottal. 17:357-366, Nov.-Dec., 1948.

The writer transplanted placenta under the conjunctiva 30 times in man for various intra-ocular pathological processes according to Filatow's method. Animal experiments demonstrated that the Filatow placental tissue was not anaphylactic when implanted in the peritoneal cavity or in the orbit. Fresh placental tissue, under the same conditions, produced an anaphylactic reaction. Filatow's tissue is not toxic and does not produce anaphylaxis in animals sensitized by fresh placental tissue. The conclusion is reached that the therapeutic results are no better with Filatow's material than with fresh placenta and therefore the latter is preferable.   Eugene M. Blake.

Lindsay-Rea, R. **Eyeball rotating forceps.** Brit. J. Ophth. 33:193, March, 1949.

A locking forceps, whose toothed blades terminate in sharply bent arms, which is used for rotating the eyeball is described.

Morris Kaplan.

McMackin, J. V. **Fixation light.** Arch. Ophth. 40:351-352, Sept., 1948.

In order to simplify the screen test the author has designed a light that can be displayed in the cardinal direction of gaze.

Ralph W. Danielson.

Morano, M., and Franchi, B. **Ocular therapy by low-voltage irradiation at close distances.** Boll. d'ocul. 27:625-638, Oct., 1948.

Low-voltage irradiation at close distance in corneal diseases was beneficial and the authors used the same treatment for diseases of the inner coats. They used a Goral-Siama apparatus, Chaoul type, and a 3-mm. celluloid plate to protect the surrounding ocular tissues from secondary radiation. Usually the dose was 160 to 165 r for uveal, and 190 to 195 r for deeper lesions, using 55 kV, 5 mA, focal distance 5, and the celluloid filter on alternating days for 5 or 6 applications. (3 figures.)

K. W. Ascher.

Perera, C. A. **A simple appositional suture for use in operations for cataract.** Arch. Ophth. 40:347-350, Sept., 1948.

Perera describes his method of placing appositional sutures after keratome incision.   Ralph W. Danielson.

Raiford, M. B. **Dispenser for adhesive tape.** Arch. Ophth. 39:816-817, June, 1948.

A plastic dispenser is described.

John C. Long.

Ruedemann, A. D. **Beta radiation therapy.** Arch. Ophth. 41:1-4, Jan., 1949.

The author discusses the technique of use of the beta ray application in conjunctival and corneal abnormalities and dermatologic growths of the lid. There is a twofold hazard in the use of radiation therapy: to the patient by overdosage, faulty application or severe reaction, and to the ophthalmologist. Means of avoidance are described.

Ralph W. Danielson.

Urrets Zavalía, Alberto. **The action of diamino-diphenyl-sulfone on the ocular complications of leprosy.** Arch. Soc. oftal hispano-am. 9:160-175, Feb., 1949.

This is a tabulated report of the application of this drug in 25 patients with leprosy. The drug prevents the severe uveal complications of leprosy but mild transient iritis may occur during the course of treatment. It is incapable of checking the evolution of slowly progressive ocular leprous lesions. When the anterior uvea is not involved the drug hastens the absorbtion of corneal infiltrates and brings about the disappearance of the thickened corneal nerves. It cannot arrest the progress of the lesion when the iris and ciliary body are affected.   Ray K. Daily.

6
~OCULAR MOTILITY

Berg, J. L. **Management of vertical heterophoria of paretic origin.** South. M. J. 42:220-224, March, 1949.

Bielschowsky's four types of vertical heterophoria are reviewed. The symptoms of vertical heterophoria vary from a mild drowsiness after one hour of close work to a marked blepharospasm with a chronic blepharoconjunctivitis. The amount of prism prescribed depends on the patient's occupation and upon the amount of variation in the findings between the heterophoria for near and for distance.

H. C. Weinberg.

Casari, G. F. **Clinicopathogenic importance of heterophoria.** Rassegna ital. d'ottal. 17:389-399, Nov.-Dec., 1948.

Twenty cases of heterophoria of various grades were studied and treated with vasodilators and antispasmodic drugs (nicotine amide and chloride of benzilimidazoline). The results were practically nil and not as good as those reported by Angius who administered acetyl-choline. Orthoptic exercises were more effective.   Eugene M. Blake.

Costenbader, F., Bair, D., and McPhail, A. **Vision in strabismus.** Arch. Ophth. 40: 438-453, Oct., 1948.

Conclusions are presented based on a study of 407 cases of squint. From the considerable data given, several generalizations may be made. Visual acuity can be estimated in the infant by determining the ability in foveal fixation. The greater frequency of amblyopia in patients with strabismus can be predicted from a history of "constant" or "monocular" deviation. While the average age of onset of squint may not be significant, the average duration of squint before treatment is most significant in the production of amblyopia. Amblyopia is more frequent with convergent than with divergent squint, and with mechanical convergent than with accommodative convergent squint, and is least frequent with alternating squint. The incidence of amblyopia increases directly with the degree of hypermetropia or the degree of anisometropia present. Total occlusion is the treatment of choice for amblyopia ex anopsia. Helpful suggestions for carrying out the occlusion are given.

John C. Long.

Gailey, Watson. **The crosseyed child— a social as well as a medical problem.** New Orleans M. and S. J. 101:387-389. Feb., 1949.

The psychologic problem of the child with squint is of great importance. The child withdraws from social contacts, and becomes nervous and capricious.

R. Grunfeld.

Noronha, Marianna. **Some considerations as to anomalous retinal correspondence.** Rev. brasil. oftal. 7:131-141, March, 1949.

After a general review of the subject

the author proposes there should be established in Brazil a commission, with instructions to present at the next Brazilian ophthalmological congress suggestions for uniform nomenclature of strabismus, available for scientific work and statistics. (7 figures.)   W. H. Crisp.

Swan, K. D. The blindspot syndrome. Arch. Ophth. 40:371-388, Oct., 1948.

The blindspot syndrome, of which 102 cases have been observed, consists of periodic diplopia, a concomitant esotropia of 10 to 20 degrees in which the physiologic blindspot of the deviating eye overlies the area of regard, and normal retinal correspondence. Treatment consists of correction of the refractive error, development of ample fusion by orthoptic training and slight overcorrection of the esotropia by surgical measures.   John C. Long.

7

CONJUNCTIVA, CORNEA, SCLERA

Barroquer Moner, J. I. Technic of penetrating keratoplasty. Arch. Soc. oftal hispano-am. 9:152-159, Feb., 1949.

The principal feature of Barraquer's method is the direct suture of the transplant to the cornea of the host. He uses eserine to constrict the pupil, believing that a small pupil permits of better centration of the trephine and prevents anterior synechia. (5 figures.)
                              Ray K. Daily.

Bunge, E. Keratoconjunctivitis epidemica found in lower Silesia in 1944. Klin. Monatsbl. f. Augenh. 113:369-376, 1948.

The author observed a form of keratitis superficialis punctata which probably belongs to the form of epidemic keratoconjunctivitis observed in 1938.
                              Max Hirschfelder.

Citterio, M. Two cases of metastatic furunculiform episcleritis. Boll. d'ocul. 27: 666-672, Oct., 1948.

Two mature women developed metastatic episcleritis a few weeks after infected intragluteal injections. Similar cases have been reported; their significance is the evidence of a generalized metastatic disease, possibly dangerous to the life of the patient. K. W. Ascher.

Corrado, A., and Toselli, C. Metastatic scleral abscess. Rassegna ital. d'ottal. 17: 367-378, Nov.-Dec., 1948.

All recorded instances of metastatic scleral abscess since 1881 are reviewed and abstracted. A 76-year-old man had a generalized furunculosis that had originated in the scrotum. These lesions cleared but several months later there was pain in the left eye and swelling of the lids, considerable exophthalmos, reduction of motility, chemosis with loss of corneal epithelium and a turbid aqueous. The fundus reflex was lacking. Spontaneous rupture of the abscess occurred and eventually the eye was enucleated. Six months later the other eye had an avascular keratitis punctata with absence of pupillary reaction and furuncles of the external auditory canal with staphylococcus.   Eugene M. Blake.

Ellman, P., and Weber, F. P. Sjögren's syndrome. Brit. M. J. pp. 304-305, Feb. 19, 1949.

A case of Sjögren's syndrome is presented in which the respiratory tract was involved.   Irwin E. Gaynon.

Friede, Reinhard. Medical and surgical therapy of serpigenous corneal ulcer. Acta ophth. 26:509-516, 1948.

The author applies alcoholic solutions of bacteriostatics directly to the ulcer after preliminary cocainization; the alcohol causes a flow of fluid until it is neutralized in the tissues, and the stasis about the ulcer is thus relieved. The application is made eight times daily, and

the bacteriostatic is rubbed into and under the ulcer; the necrotic tissue is wiped away. The scars following this treatment are thinner than those after caustics or cautery.

When medical treatment does not stop the progress of the ulcer, the author removes the entire area down to Descemet's membrane with a large trephine. If the floor of the trephine area is clean it may be grafted with a piece of clear cornea; if it is infected the regeneration of the parenchyma is left to itself. When the entire cornea is involved a total keratoplasty will prevent an iris prolapse, with adherent leucoma, staphyloma, and secondary glaucoma. It results in an opaque cornea, which may be dealt with subsequently by further keratoplasties.

Ray K. Daily.

Goldsmith, J. **Deep keratitis associated with atypical lichen planus.** Arch. Ophth. 40:138-146, Aug., 1948.

Deep keratitis in a soldier with atypical lichen planus associated with alopecia areata, poliosis, vitiligo and hyper-pigmentation is described. The cornea was not vascularized and the keratitis finally underwent complete regression. The patient had received 55 grams of quinacrine ("atabrine") for malaria. It is thought that quinacrine, as a sensitizing agent, and toxic products of the destructive cutaneous lesions, were probably responsible for the development of the keratitis. John C. Long.

Grom, Edward. **Limbal intrascleral cyst.** Ann. d'ocul. 182:52-56, Jan., 1949.

A six-year-old child, struck in the left eye by an arrow six years before, developed a cyst at the limbus. The eye was enucleated because of degeneration and pain. The cyst contained conjunctival epithelium and the walls were formed by sclera which had undergone hyalin degeneration. Chas. A. Bahn.

Rados, A. **Conical cornea and mongolism.** Arch. Ophth. 40:454-478, Oct., 1948.

The author has recently observed two cases of bilateral conical cornea associated with mongolism. The clinical characteristics of mongolism and the reported associated eye abnormalities are described in detail and the extensive literature on the etiology of mongolism is reviewed. The etiology of conical cornea is discussed from the standpoint of its association with vernal conjunctivitis, and with various endocrine and hereditary factors. It is possible that conical cornea may arise from endocrine abnormalities, particularly when associated with mongolism. John C. Long.

Redl, T. **Treatment of ophthalmia neonatorum at the University Eye Clinic in Vienna.** Klin. Monatsbl. f. Augenh. 113: 353-362, 1948.

The results of penicillin therapy in 37 cases are tabulated. The solutions ranged from 250 to 1,000 units per cc. and drops were used at 10-minute intervals from 3 to 12 hours. In all but five a culture was negative within four to ten hours. The author had the impression that a 1,000-unit solution is irrating and that a 500-unit solution used for 12 hours promises the best results with the least chance of recurrences. Max Hirschfelder.

Roggenkaemper. **Treatment of keratoconjunctivitis nummularis with ether.** Klin. Monatsbl. f. Augenh. 113:377-378, 1948.

The author drops 4 to 6 drops of ether on the anesthetized cornea in keratoconjunctivitis epidemica. Atropine and bandage follows this procedure. The eyes became well in six days, one third of them without any scars. Max Hirschfelder.

Rosen, E. **Interstitial keratitis and vestibuloauditory symptoms following**

vaccination. Arch. Ophth. 41:24-31, Jan., 1949.

The report by Cogan of the syndrome of nonsyphilitic interstitial keratitis and vestibuloauditory symptoms of unknown etiology has stimulated interest in this subject. Because of a suggested etiologic factor in the case reported, this paper is submitted as an introductory study of postvaccinial encephalitis. In a review of Cogan's four cases Mogan and Baumgartner's case, and the one reported present case, certain clinical features stand out rather prominently: 1. repeated negative Wassermann and allied serologic reactions in patient and parents; 2. bilateral ocular and auditory symptoms; 3. occurrence in young adults; 4. chronicity, with multiple unpredictable recurrences; 5. synchronous onset of ocular and of aural symptoms; 6. mildness of ocular symptoms; 7. aggravation of symptoms by changes in the weather; 8. striking variation in symptoms; 9. characteristic yellowish-white corneal opacities, tending toward vascularization; 10. evidence of iritis (cells in the anterior chamber and keratic precipitates); 11. leukocytosis and suggestive eosinophilia; 12. bilateral nerve deafness; and 13. constant condition of the cornea.   Ralph W. Danielson.

Silva, A. I. da. Familial dystrophy of the cornea. Rev. brasil. oftal. 7:113-129, March, 1949.

Four members of the same family were affected, two brothers and two sisters from 16 to 30 years of age. Five other children were not involved. The affection had first appeared at the ages of 7 and 5 years in the men, and in the women at 6 months. The periphery of the cornea was spared in every case. All four had extremely low vision. A small corneal biopsy in one showed epithelium in process of keratinization, irregular in thickness and generally atrophic. Bowman's

membrane was absent and replaced by amorphous hyaline structure. There had been inflammatory exacerbations. The author regards the cases as representing an atypical form of macular degeneration of the cornea. (9 figures, including 6 photomicrographs.).   W. H. Crisp.

Stansbury, F. C. Lattice type of hereditary corneal degeneration. Arch. Ophth. 40:189-217, Aug., 1948.

The lattice type of corneal dystrophy is a chronic, slowly progressive, familial disease of the cornea, inherited dominantly. It begins in the first decade of life, and usually in the first few months. It is characterized in youth by frequent recurrent erosions of the corneal epithelium, associated with severe photophobia, lacrimation and mild conjunctivitis. In adult life the recurrent attacks become less frequent and milder, but there is progressive loss of vision. The lesion is always bilateral. A detailed clinical and histologic description of the lesion is given. The etiology is unknown. The literature and classification of corneal dystrophies are reviewed. Five cases of lattice type degeneration are reported in detail. Keratoplasty was performed on one eye in each of three patients with favorable results in two. There is no assurance that the degeneration will not invade the transplanted tissue in time.
John C. Long.

Watson-Williams, E. Blue sclerotics, fragilitas osseum and deafness. Bristol Med-Chir. J. 65:82-86, Autumn, 1948.

The triad that consists of blue sclerotics, deafness and fragilitas osseum occurred in a family of four. Inheritance is dominant. The maternal grandmother was married twice. Her descendants by both husbands show the triad. (2 figures, 2 tables).   Irwin E. Gaynon.

8
UVEA, SYMPATHETIC DISEASE, AQUEOUS

Braley, A. E. The etiology and treatment of uveitis. J. Iowa St. M. Soc. 39: 57-60, Feb., 1949.

The diagnosis and treatment of uveitis are uncertain and discouraging. Observations on supposed tuberculous uveitis are contradictory. Tubercle bacilli have been found in normal retinal tissue, and the adjacent choroid and ciliary body showed extensive inflammation but no bacilli. Tissues inoculated into guinea pigs produced no reaction. In other organs tubercle bacilli are almost always associated with the lesion. Other causes are also discussed. Rather extensive experimental studies of bacterial allergy and attempts to isolate a filterable virus are being reported. In the author's laboratory intracerebral inoculations of anterior chamber fluid from about 20 eyes with uveitis were made into mice and into fluid tissue cultures but revealed no infectious agent. Ground tissue from the iris and ciliary body of five eyes enucleated because of uveitis was incubated and inoculated intracerebrally into mice, guinea pigs, and rabbits. No organism was found. Typhoid vaccine is still the treatment of choice. Antibiotics and antihistaminics have been ineffective. Bacterial allergy is probably the most important cause.

F. M. Crage.

Casanovas, Francisco. Sarcoma of the ciliary body. Arch. Soc. oftal hispano-am. 9:184-188, Feb., 1949.

The interesting features were an iridodialysis produced by the tumor, which is typical of tumors of the ciliary body and is exceptional in choroidal tumors, the formation of pseudocysts in the ciliary procesess, and inflammatory phenomena. The latter are important in differentiating tumor and tuberculoma of the ciliary body. (2 figures.) Ray K. Daily.

Marín Amat, M., and Marín Enciso, M. Leucosarcoma of the iris treated by extirpation. Arch. Soc. oftal. hispano-am. 9:180-183, Feb., 1949.

A 46-year-old woman had a small symptomless growth in the iris of the left eye for 12 years. Then hemorrhages appeared which were slight and transitory for a few months and finally filled the eyeball and obscured vision. The growth, a leucosarcoma, was extirpated. (2 figures.)

Ray K. Daily.

Rome, S., and Koff, R. Preplacement of air in cyclodialysis. Arch. Ophth. 40:134-137, Aug., 1948.

Rome and Koff have found it technically easier and safer to inject the air into the chamber through a tiny corneal incision before the cyclodialysis is done than after the operation is completed. The preplaced air cushion prevents hemorrhage instead of arresting bleeding which has already commenced. The deepened chamber facilitates the dialysis and the angle and cleft can be seen throughout the entire procedure. John C. Long.

Tower, Paul. Congenital grouped pigmentation of the retina. Arch. Ophth. 39: 536-541, April, 1948.

Two cases of congenital grouped pigmentation of the retina are presented with fundus photographs. The typical arrangement of the deposits of pigment in a triangular sector of the inferior portion of the retina suggests that this anomaly may have a cause similar to that of coloboma of the choroid. John C. Long.

9
GLAUCOMA AND OCULAR TENSION

Arruga, H. An adrenalin preparation similar to Glaukosan. Arch. Soc. oftal. hispano-am. 8:1206, Dec., 1948.

Arruga calls attention to a preparation under the name of Sol-inhal.

Ray K. Daily.

Barkan, O. **Technic of goniotomy for congenital glaucoma.** Arch. Ophth. 41:65-82, Jan., 1949.

Goniotomy is an operation for stripping or peeling embryonic tissue from the wall of the angle. If the cornea is clear, the operation is performed under direct vision with the aid of a prismatic contact glass specially devised for this purpose. If cloudiness of the cornea prevents the use of the glass, the operation is performed without it.

Goniotomy, which at the time of this writing had been performed on 76 eyes with infantile glaucoma, preserved useful vision in most cases. In 66 eyes pressure was normalized and vision maintained or restored over periods ranging from one to ten years. In 10 eyes the operation was unsuccessful. When combined with early diagnosis, it provided excellent visual results. The mode of action of goniotomy is discussed. The advantages, disadvantages, indications, contraindications and technic of goniotomy are described. The importance of early diagnosis and prompt operation is stressed.

Ralph W. Danielson.

Campos, R. **A combined antiglaucomatous operation, cyclodialysis with basal iridectomy.** Boll. d'ocul. 27:689-696, Nov., 1948.

To combat chronic simple and chronic "inflammatory" glaucoma, Campos modified Wheeler's suggestion to combine cyclodialysis and iridectomy by using a basal iridectomy instead of the complete iris excision which is too mutilating for common use. The peripheral iridectomy should be located at the site of the cyclodialysis. The latter is performed in the 12-o'clock region. A conjunctival flap is dissected to expose the upper rectus muscle and a bridle suture is introduced. Five mm. behind the limbus, a 2 to 3-mm. incision is made in the sclera, parallel to the limbus. A "first step" of cyclodialysis follows, separating the ciliary body only 3 mm. from the scleral incision without reaching the pectinate ligament. After that, another incision is made 1.5 mm. behind the limbus with a keratome, and a peripheral iridectomy is performed. The "second step" of the cyclodialysis follows. An Elschnig spatula is introduced into the anterior chamber through the first incision, and moved from the temporal edge of the coloboma to the 12-o'clock position, then from the nasal edge of the coloboma to the same meridional position. The spatula is withdrawn, re-introduced and the maneuver is repeated on the nasal side. (9 figures.) K. W. Ascher.

Crisp, W. H. **Early development of the filtration operations for glaucoma.** Ophth. ibero am. 10:211-221 (English); 222-230 (Portuguese), 1948. See Am. J. Ophth., 31:3, p. 277, 1948. W. H. Crisp.

Dellaporta, A. **Results of antiglaucomatous iridencleisis, and the value of early operation.** Acta ophth. 26:413-428, 1948.

This is a detailed analysis of the results of 224 cases operated by iridencleisis. It is just as effective as Elliott's operation without harboring the threat of late infection, and it is more effective than cyclodialysis. In noninflammatory glaucoma early operation was outstandingly more effective in preserving the visual field and reducing the tension. In late operations the number of failures was twice as large. These results are in conformity with those published by others. The earlier the operation is performed the better is the chance for normalization of tension and preservation of the visual fields. Of the 224 eyes, only 6 percent had free fistulization. The lining of the wound with protective uveal tissue accounts for the rarity of late infection after iridencleisis. (6 tables.) Ray K. Daily.

Díaz-Domínguez, D. **Glaucoma and excavation of the papilla.** Arch. Soc. oftal. hispano-am. 8:1219-1242, Dec., 1948.

This is an exhaustive review of the literature and a report of several cases of glaucoma without hypertension, in which careful investigation revealed transitory phases of hypertension. The size and depth of the excavation of the papilla have no relation to the degree of ocular hypertension. The absence of excavation in prolonged hypertension is accounted for by a diminished rigidity of the ocular walls; on the other hand, disproportional increase in the depth of the excavation is related to an increased rigidity of the ocular walls, and a vascular sclerosis in the circle of Heller. In many reported cases of glaucoma without hypertension transitory or intermittent hypertension were probably overlooked. Glaucoma is a disease of age, and the adjective "senile" may be applied to it legitimately. (5 visual fields.)   Ray K. Daily.

Esente, I. **Treatment of glaucoma with intravenously injected procaine.** Ophthalmologica 117:147-160, March, 1949.

Two to three hours after the intravenous injection of 10 to 20 cc. of a 1 to 2-percent aqueous solution of procaine the ocular tension of glaucomatous eyes drops. Acute glaucomas respond better than chronic ones. The injections must be given slowly but may be repeated two to three times daily. The possible mode of action of this medication is discussed.

Peter C. Kronfeld.

Friedenwald, J., Kronfeld, P., Dunnington, J. H., Chandler, P. A., and Vail, D. **Symposium: Primary Glaucoma.** Tr. Am. Acad. Ophth. pp. 169-237, Jan.-Feb., 1949.

Glaucoma may be primary, secondary, and congenital, and primary glaucoma may be chronic simple, acute congestive, chronic congestive, and absolute. Practically all congestive cases are of the narrow chamber angle type. Vasomotor disturbances alone are not considered causative until the chamber angle has become at least partially obstructed. Primary normal and wide chamber glaucoma is usually of the chronic noncongestive or simple type. In some cases sclerosis of the afferent arterioles of Schlemm's canal was observed. Primary wide angle glaucomas may include the low tension group. Sudden lowering of intraocular pressure apparently results in the inadequate filling of Schlemm's canal with blood. Hypotony from penetrating surgery may cause ciliary edema and change a wide into a narrow angle glaucoma.

Kronfeld, P. **Diagnosis.** Pp. 175-185.

The classification of glaucoma as to chamber angle simplifies the early diagnosis of primary types. The early diagnosis of the narrow angle groups is usually not difficult. Most congestive cases belong in this group. The biomicroscope, gonioscope and dark room test are valuable. The early stages of wide angle glaucomas are usually more difficult to recognize, and a routine procedure is outlined which will reduce diagnostic failure to a minimum. Perimetric findings and low tension glaucomas are briefly discussed.

Dunnington, J. H. **The surgical treatment of primary glaucoma.** pp. 213-224.

Surgical intervention should be promptly considered in narrow angle glaucomas, unless adequately controlled by miotics and hygienic treatment. Operations should, if possible, be performed between acute episodes. In narrow angle glaucomas scleroiridectomy is usually contraindicated after 48 hours; then iridencleisis is usually the operation of choice. The trephine and other forms of sclerectomy are more traumatizing and therefore of more limited value. Paracentesis is of no permanent value. In chronic glaucomas the age of the patient,

tension, visual acuity and fields, combined with structural ocular findings, determine the choice of iris inclusion or sclerectomy operation. In chronic narrow angle glaucomas obliteration of the angle and peripheral synechia are bad prognostic signs. Sclerectomy types of operation are usually less satisfactory than iridencleisis if extensive peripheral synechiae exist. In chronic wide angle glaucomas cyclodialysis and iridencleisis are usually preferable in less advanced cases and trephine or other forms of sclerectomy in the more advanced. Goniotomy is of greatest value in infantile glaucoma.

Chandler, P. A. **Complications of surgery.** pp. 224-231.

The causes of operative failures as well as the methods of prevention and their correction are briefly discussed. Failure in trephine operations may result from scar tissue closure in congested eyes, high tensions with subsequent lens dislocations and friable conjunctiva. Meticulous attention to details of the procedure are essential. Simple iridencleisis may not be sufficient in far advanced glaucomas, especially if the iris is atrophic.

Cyclodialysis should not be employed if the anterior chamber is very shallow, the tension high or if extensive peripheral anterior synechiae are present. Cyclodialysis should include one-third to one-fourth of the circumference.

Vail, D. **Review, summary and conclusions.** pp. 232-237.

The importance of classification of primary glaucoma by the type of angle is briefly discussed and illustrated. Repeated attacks of acute narrow angle glaucoma lay the foundation for synechiae which increase with each attack. Operations on narrow angle glaucomas tend to produce analogues of acute attacks. Trabecular pigment may be of no importance. Low tension glaucoma must be differentiated from pseudoglaucoma with cavernous atrophy. Gonioscopic examination of potential

glaucoma is advised. The early diagnosis of wide angle glaucomas may be exceedingly difficult and the five steps mentioned by Dr. Kronfeld are recommended. The importance of a synergistic combination of miotics of the different types is stressed. The authors of this symposium are in accord concerning the basic concept of the formation and drainage of the aqueous; the importance of recognizing narrow and wide angle glaucoma; the use of medical treatment especially for wide angle types only as long as it is demonstrably effective; and a careful choice of operation and thorough development of the operative techniques.

Chas. A. Bahn.

Lehrfeld, L. **Medical versus surgical treatment of glaucoma.** Arch. Ophth. 40: 332-340, Sept., 1948.

This paper is a plea for conservatism. There are innumerable cases of acute glaucoma in which operation has been performed and the tension reduced, but the visual acuity has been reduced also. The author does not have record of a single case of acute glaucoma in which a surgical procedure has not resulted in some loss of vision.

Ralph W. Danielson.

Leopold, I. H., and McDonald, P. R. **Di-isopropyl fluorophosphate (DFP) in treatment of glaucoma.** Arch. Ophth. 40: 176-188, Aug., 1948.

Di-isopropyl fluorophosphate has a prolonged miotic effect that results from an irreversible inactivation of cholinesterase. Its action is inhibited by the previous use of physostigmine or neostigmine. DFP successfully lowered ocular tension in 208 of 380 glaucomatous eyes. It was effective in concentrations ranging from 0.01 to 0.1-percent. Preparations of the drug in peanut oil were more effective than similar concentrations in liquid petrolatum. DFP lowered ocular tension successfully

in eyes with chronic glaucoma, acute glaucoma, buphthalmos, aphakic glaucoma, and glaucoma secondary to uveitis and exfoliating lens capsule, although other miotics had previously failed. The best results were seen in eyes with aphakic glaucoma. Decidedly fewer instillations of DFP were required to maintain a satisfactory ocular tension in eyes in which the tension was also controlled by other miotics. Disadvantages in its use include painful ciliary spasm, local sensitivity, and acquired resistance to its action. In six eyes a rise in tension followed its instillation. Retinal detachments have been reported to follow its use in patients with high myopia.   John C. Long.

Marín Amat, M. The true role of fistulating operations in the treatment of glaucoma. Arch. Soc. oftal. hispano-am. 8: 1249-1254, Dec., 1948.

The normal optic and metabolic functions of the eye are maintained by a neuro-vegetative intraocular center of regulation, represented by Muller's cells in the choroid, iris and ciliary body. All disturbances in the intraocular circulation, vascular or lymphatic, are compensated through this center, even if they originate extraocularly in the cortex, thalamus, medulla or hypothalamus. The primary cause of ocular hyptertension is an increase in the fluid content of the eye. Because of the compressibility of the venæ vorticosæ and Schlemm's canal, the hypertension impedes and may abolish the elimination of intraocular fluids. The interference with drainage is secondary to an overproduction of fluid. Antiglaucomatous operations should aim to decrease this fluid content of the eye by an attack on the regulating cells, situated at the root of the iris and in the ciliary body; they should in effect be arteriectomies or sympathectomies and diminish ciliary activity. Most effective are broad iridectomies and cyclodiathermies. External

operations on the sympathetic ganglia are ineffective. Fistulating operations are effective only to the extent in which they act on the primary factor of overproduction of fluid, through the concurrent iridectomy. Cyclodialysis acts by destruction of the ciliary body and not by providing drainage through the suprachoroidal space. Diathermy-coagulation of the ciliary body acts directly on the nerve cells that regulate intraocular circulation. Marín Amat is emphatic in the opinion that fistulating operations are indicated only in cases in which surgical interventions aiming at the removal of the primary cause, such as iridectomies and cyclodiathermies are inadequate.

Ray K. Daily.

Moreu, Angel. The role of the trigeminus in the regulation of ocular tension. Arch. Soc. oftal. hispano-am. 8:1193-1206, Dec., 1948.

Experimental data on dogs are presented to support the conclusion that excitation of the first branch of the trigeminal gives rise to an intraocular discharge of histamin, which through vasodilatation, increases the blood content of the uveal sponge, and raises the ocular tension. No modifications in tension were produced by the stimulation of the corneal plexus, but they appeared rapidly after irritation of the iris and ciliary body. The irritation was produced by a fine sharp needle introduced into the anterior chamber angle under gonioscopic observation, which punctured the iris or ciliary body; irritation of the iris was followed by a hyperemia of the ciliary vessels, a rise in tension, miosis, hyperemia of the iris and ciliary body demonstrable gonioscopically, and an increase of cells in the aqueous. Hyperemia of the ciliary vessels followed irritation of the cornea and conjunctiva. These experiments were repeated after modifying the neurovegetative ocular tone with mimetic and lytic

drugs. Parasympathomimetic drugs increased the effect of trigeminal stimulation and parasympatholytics were without effect. Sympathomimetics abolished the reaction of the trigeminal, and resection of the sympathetic and sympatholytic drugs exaggerated it. Acute rises in tension similar to acute glaucoma could be produced by blocking the vorticose veins concurrently with stimulation of the trigeminal. The experimental data are applied to the explanation of the pathogenesis of secondary hypertension in acute iridocyclitis. The rise in tension caused by an irritation of the trigeminus is not compensated because of the vasomotor paralysis, slowing of the circulation, and the obstruction in the venous and aqueous drainage incident to the disease. (6 graphs.)

Ray K. Daily.

Pallarés, J. Surprisingly favorable results of cyclodialysis in advanced cases of chronic glaucoma. Arch. Soc. oftal. hispano-am. 8:1244-1248, Dec., 1948.

The author's enthusiasm for cyclodialysis is based on three cases in which it was followed by a marked reduction in tension and an improvement in very narrow visual fields. (3 visual fields, 1 graph.)

Ray K. Daily.

Posner, A., and Schlossman, A. Syndrome of unilateral recurrent attacks of glaucoma with cyclitic symptoms. Arch. Ophth. 39:517-535, April, 1948.

Nine cases, forming a homogeneous group which represents a type of glaucoma intermediate between primary and secondary glaucoma, are described. The disease is unilateral. In three there was some heterochromia, and in each instance the lighter-colored eye was involved. Symptoms may be absent or there may be slight discomfort, colored halos or blurring of vision. Ocular hypertension may appear a day or so before, or simultaneously with, cells in the aqueous.

Within the next 24 hours postcorneal deposits are seen. Episodes may occur with varying frequency and without any apparent cause. It is proposed to call this condition a syndrome of glaucomatocyclitic crises. A tentative hypothesis is advanced which relates this syndrome to a disturbance of the autonomic nervous system. A classification of glaucoma associated with iridocyclitis is presented.

John C. Long.

Rubino, A. and Pereyra, L. The eye and the diencephalon. V. The "luminous sensibility" in simple chronic glaucoma. Riv. oto-neuro-oftal. 23:227-236, July-Aug., 1948.

There is a constant reduction of luminous sensibility in primary glaucoma which does not seem related to the changes of vision, visual field or tension but is attributed to a lesion of the diencephalic centers and the thalamus. (6 figures, references.) Melchiore Lombardo.

Rubino, A. and Esente, I. The eye and the diencephalon, VI. Glycemic curve and "photo-glycemic reflex" in glaucomatous patients. Riv. oto-neuro-oftal. 23:237-243, July-Aug., 1948.

Ten patients with simple chronic glaucoma showed glycemic curves that suggested changes of the diencephalic centers and also an abnormal "photo-glycemic" reflex. These observations on carbohydrate metabolism support the new concept of the relation between the diencephalon and glaucoma.

Melchiore Lombardo.

Stocker, F. W., Holt, L. B., and Clower, J. W. Clinical experiments with new ways of influencing intraocular tension. Arch. Ophth. 40:46-55, July, 1948.

The influence of the "rice diet" introduced by Kempner for the treatment of hypertensive vascular disease on the ocu-

lar tension of nonglaucomatous patients was studied. All patients showed a striking and persistent reduction of ocular tension which did not seem to be directly dependent on the reduction of the blood pressure. It is believed that a relative depletion of chlorine and sodium ions in the tissues, including those of the eye, might be the underlying factor.

Ralph W. Danielson.

Vidal, F., Brodsky, M., and Travi, O. C. **The physiopathology of simple chronic glaucoma.** Ophth. ibero-am. 10:107, 1948 (Spanish) 122, 1948 (English).

The nature and influence of three stages are discussed in detail. The exact interpretation of each developmental type permits us to avoid in future the gloomy prognosis.   W. H. Crisp.

Weekers, R., and Humblet, M. **Angioscotoma and neuroscotoma of chronic glaucoma.** Acta ophth. 26:455-467, 1948.

Every patient with early glaucoma was examined exhaustively on the perimeter and on the Bjerrum screen to demonstrate the earliest field changes in chronic glaucoma. Goldman had pointed out that increase in size of the angioscotoma is produced not by an increase in the size of the retinal vessels but by a functional inadequacy in the retinal nerve elements due to a vascular disturbance. The earliest symptom of glaucoma is a change in the physiologic angioscotoma, which goes through the three stages: increase in size, fusion, and increase in density. At the poles of the blind spot where the angioscotomas are close to one another they coalesce as they increase in size. The phenomenon is often interpreted as enlargement of the blind spot. These early changes are reversible. An increase in the density of the angioscotoma is a sign of a graver circulatory disturbance and indicates an irreversible lesion of the nerve elements. An angioscotoma with increas-

ing density soon becomes a neuroscotoma. A neuroscotoma is easy to outline, and the examination should determine its position, extent, density, margins, and progress. They are arcuate in form, and extend nasally when they reach the nasal raphe. The peripheral extension of the arcuate scotoma accounts for the peripheral constriction of the nasal field. Extension in the temporal field constricts it until only a small centrocecal island of vision is left. The early visual loss of glaucoma is demonstrable only through patient and systematic perimetric and campimetric studies, with small test objects, and variable illumination. The diagnosis of these changes is important in that they form the indications for surgical intervention at a time when it can still be effective. (8 figures.)   Ray K. Daily.

10
CRYSTALLINE LENS

Gaines, S. R. **The role of retrobulbar neuritis in the management of senile cataracts.** New Orleans M. and S. J. 101: 390-391, Feb., 1949.

Many old people have markedly reduced vision although they have no lens changes. The visual loss is due to retrobulbar neuritis on an arteriosclerotic basis. The cavernous atrophy of the nerve head in "soft glaucoma" may be caused by pressure of the sclerosed internal carotid artery on the optic nerve. One may have arteriosclerotic optic atrophy without cupping of the disc caused by total or partial obliteration of small vessels. The atrophy may be diffuse or patchy, causing generalized depression of the visual field, sector defects, or central scotoma. Patients with lens opacities not dense enough to explain the loss of vision deserve careful visual field studies and the patient should be warned that the cataract operation will restore only central vision.

R. Grunfeld.

Gjessing, Harald. **A slight improvement of the common capsule forceps.** Acta ophth. 26:445, 1948.

By filing away the next to the last tooth of the capsule forceps used for removing the anterior capsule in cases of extracapsular extraction a small hole is formed through which the lens capsule herniates as it is being grasped by the teeth. Gjessing removes a sufficiently large portion of the anterior capsule with this forceps to prevent the subsequent development of secondary cataract.

Ray K. Daily.

Huerkamp, B. **Basically different types of lens opacities within the group called "cataracta syndermatotica".** Klin. Monatsbl. f. Augenh., 113:318-328, 1948.

The cataract of neurodermatitis starts behind the anterior lens capsule, involves the anterior cortex and very slowly and progressively the posterior cortex. Cataract in sclerodermy starts in the posterior cortex and the anterior parts of the lens remain clear. Lens opacities in poikilodermy at the same time in the anterior and posterior cortex as very fine grayish points. Both eyes are involved and maturity of the cataract is reached after days or months whereas the other forms of cataract may take years to reach maturity. The article contains a chart tabulating the most important differential points. (4 figures.) Max Hirschfelder.

Jaeger, A. **Surgery of luxated lenses.** Klin. Monatsbl. f. Augenh. 113:312-314, 1948.

The author reports the result of lens extraction in 10 eyes with subluxated and totally luxated lenses. Immanent glaucoma was the indication in some. The use of a capsule forceps is recommended whenever possible. Loop extraction was necessary in nine. Two of the three eyes with subluxation had a postoperative vision near 20/100; one had an intraocular hemorrhage. Those with total luxation were much less satisfactory and must be considered poor risks.

Max Hirschfelder.

Mejer, F. **Infection of the lens after perforating injuries.** Klin. Monatsbl. f. Augenh. 113:366-369, 1948.

Thirteen cases of extraction of infected lenses after perforating injuries are described. Conservative treatment is rarely successful in spite of the newer drugs and fever shock treatment. Whenever the infection is limited to the lens and the anterior part of the globe, a satisfactory result is possible. Four of the author's cases recovered sight after extraction of the infected lens. Max Hirschfelder.

Schott, J., and Dann, S. **Werner's syndrome: a report of two cases.** New England J. Med. 240:641-644, April 21, 1949.

Two cases of Werner's syndrome are reported. It is an abiotrophic process that first becomes manifest by slow growth during adolescence and graying of the hair at the age of twenty years. Its most striking manifestation is a change in the appearance of the skin which suggests scleroderma but is the result of atrophy of the subcutaneous fat and the underlying muscle. Star-like opacities develop chiefly at the posterior pole and the periphery of the lens. F. H. Haessler.

Thomas, C. I. **Cataract extraction by the suction method.** Arch. Ophth. 39:805-815, June, 1948.

The author describes a suction apparatus modified after the instrument of Dimitry. The suction method of cataract extraction is used to its greatest advantage when 1. the lens is hypermature, 2. the capsule is tense, 3. the capsule has exfoliated, 4. the lens must be dislocated

before it is tumbled or slid out of the fossa, and 5. the capsule is friable and will not stand any tension. Pitfalls of the operation are discussed and contraindications to its use are pointed out. An analysis of 618 cases of intracapsular extraction is presented to show the comparative frequencies of rupture of the capsule.

John C. Long.

Velhagen, K., Jr. Surgery of congenital and juvenile cataract. Klin. Monatsbl. f. Augenh. 113:305-312, 1948.

Failure in the operative treatment of juvenile cataract is usually due to poor surgery. The author discusses the various complications. He emphasizes the importance of corneal incisions without bleeding. Loss of vitreous is more dangerous in children than in adults. Traction on the zonula is often followed by phthisis. The author recommends simple discission for lamellar cataract in very young children and emphasizes the necessity of doing as small an operation as sule, shrunken cataracts and tough secpossible. Cataracts with thickened capondary membranes should never be pulled out. The procedure results in phthisis bulbi. A so-called double discission is recommended, introducing two small knives from each side through small limbal incisions at the same time and cutting from the pupillary center towards the pupillary periphery. A cut with scissors may sometimes be necessary, but is more dangerous. The posterior lens capsule should not be opened as long as cortical remnants remain in front of the secondary cataract. Linear extraction in one single operation is indicated in older children and young adults only. The author prefers to operate on children with dense lens opacities at the age of 12 months. He discusses the question of early surgery in such cases. (References.)

Max Hirschfelder.

11
RETINA AND VITREOUS

Bedell, A. J. Diagnosis of retinoblastoma. Arch. Ophth. 40:311-316, Sept., 1948.

To illustrate the difficulty of diagnosis, six case reports are given, two of retinoblastoma and one each of angiomatosis retinae, leukosarcoma of the choroid, Coats's disease, and retrolental fibroplasia. Bedell advises against future pregnancy in a family in which more than one child has the disease. One case is not sufficient to condemn the family to a childless existence.   Ralph W. Danielson.

Bottasso, G. A case of retinal embolism of probable venous origin. Rassegna ital. d'ottal. 17:384-388, Nov.-Dec., 1948.

A 32-year-old man noted sudden loss of sight in the right eye 11 days after surgery for internal hemorrhoids. There was edema of the macula and in the area between it and the disc, and a sudden marked reduction in caliber at one point in an arteriole in the region. Treatment was ineffectual. It is assumed that a small embolus originated in a hemorrhoidal vein and produced a pulmonary infact from which a minute fragment found its way into one of the arteries to the eye.

Eugene M. Blake.

Carreras Matas, B. Difficulties in the diagnosis of retinal detachment. Arch. Soc. oftal. hispano-am. 8:873-878, Sept., 1948.

A woman, 40 yearrs old, had a central scotoma in the right eye, myopia, negative ophthalmoscopic findings and a recent puerpurium with a dead fetus. The diagnosis of retrobulbar neuritis was made, and treatment prescribed accordingly. Five weeks later the scotoma involved the upper nasal field, and funduscopy revealed a retinal detachment. In

the course of a perforating diathermy-coagulation a small hole was found close to the optic disc. Forty days after the operation the retina was completely re-attached, the visual field was normal, and the central scotoma corresponded to the coagulated area. The reasons for missing the diagnosis at the outset are discussed, and it is suggested that an examination of the visual field for blue, and biomicroscopy of the posterior pole of the eye might have helped to avoid the error. In retinal detachment, which disturbs the nutrition of the neuroepithelial layer, the field for blue suffers more than the red-green field. The greater magnification and intensity of illumination in biomicroscopy with a slitlamp might have revealed the retinal detachment. In general, however, this method of examination is more suitable for the study of details in a previously discovered disease than for the search for a lesion. (4 figures.)

Ray K. Daily.

De Berardinis, E., and Bonavolontà, G. **Tissue therapy in ophthalmology.** Boll. d'ocul. 27:753-772, Dec., 1948.

Among 35 patients with tapetoretinal degeneration and treated with intramuscular cod-liver oil injections 26 showed an improvement of variable degree during seven months. The authors feel that further prolonged observations will be needed. K. W. Ascher.

Di Luca, Giuseppe. **Retinal arterial occlusions.** Riv. oto-neuro-oftal. 23:106-130, March-April, 1948.

Studies of 12 patients from 16 to 76 years of age with unilateral or bilateral occlusion of the central artery of the retina or of its branches by angiospasm or endoarteritis are reported. (References and 10 figures.) Melchiore Lombardo.

Di Luca, G. **Clinical and statistical considerations of periphlebitis retinalis and recurrent vitreous hemorrhages of the juvenile eye and its connections with Buerger's disease.** Boll. d'ocul. 27:773-788, Dec., 1948.

Di Luca exhaustively studied 11 patients between 18 and 43 years of age with periphlebitis retinae or recurrent vitreous hemorrhages, and all but one showed evidence of tuberculous infection. Twenty patients with Buerger's disease were evaluated as to their ophthalmoscopic findings. Ten of the 20 showed sclerosis of the retinal arteries, 9 had engorged retinal veins, 8 peripapillary edema, 1 an inactive choroiditis, and 4 endarteritis of the retinal arteries. Summarizing his findings and those of other authors he found that among 184 patients with *periphlebitis and recurrent vitreous* hemorrhages, more than 71 per cent, had tuberculosis, and less than 1 percent showed signs of Buerger's disease. Among 138 patients with Buerger's disease only one had periphlebitis retinae and one recurrent vitreous hemorrhages. The patients with periphlebitis and recurrent hemorrhages belong to a markedly younger age group than those with Buerger's disease. There is no direct relation between th two fundus conditions and Buerger's disease. (References.)

K. W. Ascher.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.

601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month*

MISCELLANEOUS

RESEARCH PROGRAM

Papers presented at the 18th scientific meeting of the Association for Research in Ophthalmology, Inc., Philadelphia, were: "Experimental studies on sympathetic ophthalmia," Dr. Raymond C. Collins, New York; "Correlation of microscopic and slit-lamp examination of developing hereditary cataracts in mice," George K. Smelser, Ph.D., and Dr. Ludwig von Sallmann, New York; "Curare and akinesia for ocular surgery," Dr. John R. Roche, New York.

"Experiments on fatigue of accommodation with asthenopic patients. II," Dr. Conrad Berens, New York, and Saul B. Sells, Ph.D., Randolph Field, Texas; "Some effects of injection of hyaluronidase into the anterior chamber," Dr. Jay G. Linn, Jr., and Lieut. Col. Thomas L. Ozment, Pittsburgh.

"Effects of metabolic poisons and of some other agents on intercellular cohesion in corneal epithelium," Dr. Wilhelm Buschke, New York; "A study of visual mechanism as revealed by the electrical activity of optic-nerve fibers," Dr. H. K. Hartline, Baltimore; "Nutritional supply of corneal regions in experimental animals," Dr. Albert M. Potts and Dr. Lorand V. Johnson, Cleveland.

"Studies on the physiology of the eye using tracer substances: Part III. Further studies on the steady-state ratio of sodium between the plasma and aqueous humor in the guinea pig," Dr. Roy O. Scholz, Baltimore; "Studies of the eye with radioiodine autographs," Dr. Ludwig von Sallmann and Beatrice Dillon, M.A., New York; "The cyanide sensitivity and cytochrome-C content of the crystalline lens," Dr. L. O. Ely and W. A. Robbie, Ph.D., Iowa City, Iowa.

"A study of the possible conversion of dehydroascorbic acid to ascorbic acid in the aqueous humor," V. Everett Kinsey, Ph.D., Boston; "The histochemical localization of cholinesterase," George B. Koelle, Ph.D., and Dr. Jonas S. Friedenwald, Baltimore; "Polysaccharides in ocular tissue," Dr. Robert Day, Baltimore; "Problems in the histochemistry of the eye," Dr. Jonas S. Friedenwald, Baltimore.

"Beta-ray application to the eye with description of an applicator utilizing SR⁹⁰," Dr. H. L. Friedell, Dr. C. I. Thomas, and J. S. Krohmer, M.S., Cleveland; "Beta irradiation: An evaluation of a radium-D applicator for ophthalmic use," Dr.

Fred M. Wilson, Chicago; "The effect of low voltage roentgen rays on the normal and vascularized rabbit's cornea," Dr. Harold G. Scheie, Dr. Richard H. Dennis, Dr. Richard C. Ripple, and Dr. Larry L. Calkins, Philadelphia.

SECTION ON OPHTHALMOLOGY MEETING

At the meeting of the Section of Ophthalmology, American Medical Association, Atlantic City, June 8th to 10th, the following program was given:

Chairman's address by Dr. M. Hayward Post, Jr., Saint Louis, and a symposium on ocular injuries conducted by Col. William Stone, Washington; Dr. W. Morton Grant, Boston; Dr. David G. Cogan, Boston; Dr. Brittain F. Payne, New York; Dr. Don Marshall, Kalamazoo, Michigan; Dr. Alston Callahan, Birmingham; and Dr. Derrick Vail, Chicago.

"A clinical study of 200 cases of retrolental fibroplasia," Dr. Merrill J. King, Boston, with Dr. William C. Owens, Baltimore, opening the discussion; "Retrolental fibroplasia: A study of its pathology," Dr. Parker Heath, Boston, with the discussion opened by Dr. Algernon B. Reese, New York; "Prophylaxis of gonorrheal ophthalmia of the newborn," Dr. James H. Allen and Dr. Luciano Barrere, Iowa City, Iowa, with Dr. Alan C. Woods, Baltimore, opening the discussion.

"The frequency of the occurrence of cataract in atopic dermatitis," Dr. Alfred Cowan and Dr. Joseph V. Klauder, Philadelphia, with Dr. William P. Beetham, Boston, opening the discussion.

"New trends in ciliary-body surgery for the relief of glaucoma," Dr. Gambiattista Bietti, Pavia, Italy, with the discussion opened by Dr. Derrick Vail, Chicago; "Flicker fusion field: III. Findings in early glaucoma," Dr. Paul W. Miles, Saint Louis, with Dr. Lawrence T. Post, Saint Louis, opening the discussion.

"General anesthesia for cataract surgery," Dr. H. Douglas Sanders and Dr. Norman L. Cutler, Wilmington, Delaware, with Dr. John H. Tucci, Boston, opening the discussion; "The age norms of refraction and vision," Dr. Felician J. Slataper, Houston, Texas, with the discussion opened by Dr. Alfred Cowan, Philadelphia.

"The syndrome of aneurysm of the intracranial carotid: Frontal headache with oculomotor nerve paralysis," Dr. Rudolph J. Jaeger, Philadelphia, with Dr. Frank B. Walsh, Baltimore, opening the discussion; "The use of curare in intraocular surgery," Dr. Daniel B. Kirby, New York, with Dr. Frederick C. Cordes, San Francisco, opening the discussion.

SECTION EXHIBITS

Among the ophthalmic exhibits shown in the Scientific Exhibition at the A.M.A. convention were: "Hydrodynamics of the aqueous veins," Dr. K. W. Ascher, W. M. Spurgeon, and Jean Schuff, Cincinnati; "The corneal lens: Theory and application," Dr. M. W. Nugent and Dr. Kevin M. Tuohy, Los Angeles; "Pathology of the eye: New technique for preparations," Dr. Brittain F. Payne, Dr. Joseph H. Krug, and Dr. Edgar Burchell, New York; "Pathology of the eye in old age," Dr. A. L. Kornzweig, New York; "Office bacteriology of the eye," Dr. Frederick H. Theodore, New York; "Kodachrome studies of the ocular fundus," Dr. Dan M. Gordon, New York; "Cerebral angiography related to ophthalmology," Dr. Donald J. Lyle and Dr. Frank H. Mayfield, Cincinnati; "Glaucomatous excavations," Dr. Peter C. Kronfeld, Dr. Roy O. Riser, and Dr. John T. Parker, Chicago.

Dr. Georgiana D. Theobald, Oak Park, Illinois, Dr. Edwin B. Dunphy, Boston, and Dr. Phillips Thygeson, San Jose, California, comprise the exhibit committee of the Section on Ophthalmology.

SOCIETIES

READING PROGRAM

Dr. S. Gordon Castigliano, Philadelphia, spoke on "The oral cavity; the physician and the dentist," and Dr. Benjamin F. Souders, Reading, spoke on "Ocular manifestations of tropical diseases and their treatment," at the 93rd regular meeting of the Reading Eye, Ear, Nose, and Throat Society, May 18th, held jointly with the Reading Dental Society.

MILWAUKEE SOCIETY HONORS DR. HAESSLER

The May 24th meeting of the Milwaukee Oto-Ophthalmic Society was a testimonial dinner for Dr. F. Herbert Haessler in honor of his appointment as clinical professor of ophthalmology, Marquette Medical School.

Dr. Haessler, abstract editor of the JOURNAL, gave up his private practice last January in order to devote all of his time to the teaching of ophthalmology.

Among the speakers for this occasion were: Dr. Gustave Guist, professor of ophthalmology, University of Vienna, who was special guest speaker; and Dr. John Hirschboeck, dean, University of Marquette Medical School, who spoke on "Plans and objectives in ophthalmological teaching at the Marquette Medical School."

Preceding the induction of Dr. Haessler to honorary membership in the society, the annual meeting and election of officers took place.

PERSONALS

GIVES MONTGOMERY LECTURE

Dr. Daniel B. Kirby, New York, gave the Montgomery Lecture at Trinity College, Dublin, on May 12th. The subject of his address was "The preparation of the whole patient for cataract surgery." On May 23rd, Dr. Kirby presented a paper on cataract surgery before the French Ophthalmological Society in Paris.

TO LECTURE IN MEXICO

On August 15th to 27th, Dr. Brittain Ford Payne, clinical professor of ophthalmology, New York University Medical College, surgeon and director of pathology, New York Eye and Ear Infirmary, New York, will give a series of lectures and demonstrations on the "Histopathology of the eye," in Mexico City.

Among the subjects to be discussed by Dr. Payne are: "Surgical anatomy and histology of the human eyeball," "Microscopic anatomy in detail," "Normal crystalline lens," "Diseases of the cornea, sclera, and anterior segment," "Granulomas of the eye," "Glaucoma and cataract," "Traumatic lesions of the eye," and "Intraocular neoplasms."

ANNOUNCEMENT

HOME STUDY COURSES

Home Study Courses in the basic sciences related to ophthalmology and otolaryngology, offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1st and continue for a period of 10 months. Registrations must be completed before August 15th. Detailed information and application forms may be obtained from Dr. William L. Benedict, executive secretary of the Academy, 100 First Avenue Building, Rochester, Minnesota.

AMERICAN JOURNAL OF OPHTHALMOLOGY

CONTENTS

Frontispiece illustrating article by Frederick C. Cordes and Michael J. Hogan

ring hot chocolate when some of the contents splashed in his face. The left upper lid became infected. The infection subsided rapidly with Antipeol treatment. Healing was excellent and with a minimal formation of scar tissue.

DISCUSSION

One of the criticisms of the product (Antipeol) is that the ointment is too thick and difficult to remove. The greatest complaint made by the patients was that they could not get the ointment out from between the lashes without considerable rubbing. Possibly this aggravated the blepharitis which might otherwise have shown better response. If the filtrate could be incorporated in an ointment which had the consistency of the average ophthalmic ointment, this might be obviated. In addition, a softer ointment might permit better diffusion of the filtrate, with better results. At this time, a thought occurs that a filtrate of pyocyaneous germs in a suitable base might become an important adjunct in the treatment of pyocyaneous

ulcers of the cornea so common in industrial injuries.

CONCLUSION

While it is true that a great many local infections of the lids are self-limited and get well with the simple use of hot compresses, the rapid and excellent results in the 116 unselected cases reported and in a number of cases treated since are definite proof of the beneficial effects of bacterial filtrates on the ordinary pyogenic infections.

The results were more gratifying because of the complete absence of local allergic reactions. An unusual and striking phenomenon was the rapid relief from pain.

Some suggestions on the improvement of the product are offered. Wider treatment with bacterial phages and filtrates is recommended to avoid unnecessary allergic reactions and complications from the use of penicillin and sulfa drugs, which can always be used if the phages and filtrates fail.

861 Park Place (16).

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6. Grossman, H.: Eye, Ear, Nose & Throat Monthly, 24:480, 1947.
7. Combes, F. C.: New York State J. Med., 42:1143, 1942.

OPHTHALMIC MINIATURE

There is only one kind of chalazion. Its cause is the collection of a gross humor that gathers in the lid. It occurs most frequently in the outer aspect of the lid, and appears as a hard swelling, just like a hailstone.

Treatment. Dissolve gum ammoniac or galbanum in strong vinegar and rub it on the tumor; or one may apply a salve of roses mixed with wax and turpentine.

Memorandum Book of a Tenth-Century Oculist
Translated by Casey A. Wood.

REGENERATION OF THE CORNEAL STROMAL CELLS*

II. REVIEW OF LITERATURE AND HISTOLOGIC STUDY

A. EDWARD MAUMENEE, M.D., AND WALTER KORNBLUETH,† M.D.

San Francisco, California

In the course of studies on the fate of corneal grafts[1, 2] a clear understanding of the mode of regeneration of the corneal stromal cells was found to be essential in order to determine whether the cells in the donor cornea were replaced or not. A technique[3] was devised whereby the corneal cells could be destroyed with minimal inflammatory reaction and minimal disturbance of the corneal lamellae. It is the purpose of this report to describe the histologic appearance of these lesions and to establish the source of the regenerated stromal cells.

REVIEW OF THE LITERATURE

Regeneration of the corneal stromal cells has been studied extensively in the past. The types of injury used to produce destruction of these cells have been penetrating and nonpenetrating incisions into the anterior and posterior surface of the cornea and chemical burns of the cornea. Cell replacement in some cases of parenchymatous keratitis has also been studied.

It has been concluded from these observations that the stromal cells are replaced from: (1) Undamaged corneal corpuscles; (2) wandering cells from outside of the cornea; (3) a transformation of epithelial cells or endothelial cells into stromal cells; and (4) a combination of these sources.

Most workers have based their conclusions on the morphologic appearance of the cells in the regenerating area. The methods used in studying the regeneration of the stromal cells and the conclusions drawn from these studies are so similar in many instances that a detailed review of each report will not be given.

Gueterbock, Gussenbauer, Reich, Neelson and Angelucci, and others[4a-d] made incisions of various types into the corneas of frogs, rabbits, and dogs and concluded from their studies that the destroyed stromal cells were replaced from undamaged corneal corpuscles in the region of the lesions. They noted that mitotic figures appeared in the cells adjacent to the injury and that the cells became more spindle in shape before migrating into the injured area. The possibility that these newly formed cells could have originated from cells outside of the cornea was thought to have been eliminated by the scarcity of wandering cells observed in the undamaged part of the cornea.

The same conclusions were reached by Eberth,[5] Senftleben,[6] Homen,[7] and Klemensiewicz,[8] following studies on lesions produced by chemical injuries of the cornea. Elschnig[9] and Fuchs[10] studied the regeneration of stromal cells in human eyes which had been injured by inflammatory processes and had been removed for various reasons. They were not as dogmatic in their opinions as to the origin of the newly formed stromal cells but they also thought that the majority of the cells originated from undamaged corneal corpuscles. Fuchs observed the scarcity of cells containing mitotic figures and suggested that the stromal cells in some cases divided by amitosis.

Ranvier[11] offered the unique theory that wounds in the cornea were repaired by protoplasmic outgrowths from the stromal cells and not by a multiplication of these cells. Kruse,[12] who worked in Grawitz's laboratory, thought that the newly formed stromal cells arose from the "slumbering cells" of Grawitz.[13] He studied many tissues of the body and concluded that specific cells existed in the various connective tissues which could not be seen in normal tissue

with hematoxylin and eosin stain. If, however, the tissue was injured these cells became activated to repair the lesion and could be seen with routine stain. Neither of these theories has been confirmed.

Retterer[14] studied incisions in guinea pigs' corneas and concluded that the new stromal cells originated from transformed epithelial cells and a multiplication of the stromal cells by mitotic division.

Salzer[15a-e] made extensive studies on incisions performed from the external surface in the cornea of rabbits, guinea pigs, frogs, trout, chickens, pigeons, and salamanders. In a series of articles, he gradually came to the conclusion that the epithelial cells, which migrate into a wound made from the external surface of the cornea, are converted into stromal cells. As proof of this he stated that he was able to follow the transition from a typical epithelial cell to a spindle cell of the stroma.

He also thought that the nuclei of the newly formed corneal corpuscles showed a remarkable similarity to the nuclei of the epithelial cells. The protoplasma of the newly formed spindle cells (keratoblasts) stained with hematoxylin like the protoplasma of the epithelial cells.

Salzer was unable to find stromal cells in the process of multiplication and offered this as evidence against the participation of stromal cells in repair.

Wolfrum and Boehmig[16a-b] disputed the epithelial origin of stromal cells. They concluded from a series of experiments in which incisions were made into the posterior surface of the cornea that the stromal cells were replaced by mitotic and amitotic division of the corneal corpuscles and in some instances by a transformation of the endothelial cells. They thought that the leukocytes played no part in the regeneration of the stromal cells.

Hanke[17] studied perforating and nonperforating wounds in guinea pigs' corneas. He thought that the newly formed corneal corpuscles were derived from the undamaged stromal cells and, in some instances, from the endothelial cells in the deeper layers of perforating wounds. In order to determine whether or not macrophages participated in the repair of corneal stromal cells he tagged these cells by injecting trypan blue into the animals, systemically. A few cells containing this dye were found in the area of active repair. Hanke thought that these cells were not derived from outside of the cornea for he could not find cells containing the dye in the normal cornea between the lesions and limbus.

Von Wyss,[18] Bonnefont and Lacoste,[19] and Janyk,[20] on the other hand, have suggested that destroyed corneal cells are replaced by leukocytes or macrophages which wander into the cornea after injury. They thought that the stromal cells did not aid in this reparative process.

Pullinger and Mann[21] have recently studied rabbits injected with pontamine sky blue in which the corneal cells had been destroyed by applying a small droplet of liquid mustard gas to the center of the cornea. They were unable to follow the complete transition of macrophages containing this dye to stromal cells because the dye tended to disappear just at the time when the cells changed their characteristics.

However, they concluded from their experiments that most probably the principal source of newly formed corneal corpuscles was the conversion of macrophages. They pointed out that, embryologically, the corneal corpuscles were derived from wandering mesodermal cells which phagocytize vital dyes. They also stated that, in only a few instances, were corneal corpuscles observed in the process of division and therefore it was unlikely that these cells participated very actively in the process of repair.

Scelkunow[22] reported that regenerated stromal cells were derived from corneal corpuscles and leukocytes.

It may be concluded from this review of

the literature that newly formed stromal cells are derived from several sources but that there is no uniformity of opinion as to the source of these regenerated cells. The proof offered in most instances as to the origin of these cells has been based on routine histologic examinations. In only a few instances have special techniques been used to establish the source of the cells. Because of this diversity of opinion and the lack of substantial proof of any one theory it was thought that the source of the regenerating stromal cells should be investigated further.

EXPERIMENTAL STUDIES

The corneal cells in rabbits and rats were destroyed by freezing the tissue to −78°C. for 3 to 5 seconds according to the technique previously described.[3] In rabbits' corneas, 2-mm. and 6-mm. lesions produced a slight edema of the cornea which could be seen grossly 2 to 3 hours after freezing. This edema increased up to 24 hours, persisted for a few days, and gradually absorbed leaving the corneas entirely normal in appearance on gross and slitlamp examinations 5 to 7 days after freezing.

The persistence of the edema was proportional to the duration and area of freezing. Central corneal lesions on the whole caused less reaction in the conjunctiva and iris than peripheral injuries. Vascularization of the cornea was never observed in central injuries and only rarely were a few small capillaries noted to invade the cornea for a few millimeters after peripheral lesions. Secondary infection occurred in only a few instances in which over half of the corneal cells were destroyed at one time and there was persistent edema of the cornea.

Rats' corneas reacted in a similar manner but they normally contain more polymorphonuclear cells and tend to develop more inflammatory reaction. The advantage of studying rats' corneas is that the epithelium can be removed and a central 2- to 3-mm. strip consisting of the whole thickness of the stroma can be stained and examined under a microscope without sectioning. This allows a greater number of stromal cells to be observed at one time.

HISTOLOGIC STUDY

This study is based on 158 eyes removed at 5 minutes, 15 minutes, 30 minutes, 1 hour, every hour up to 4 hours, at a 3-hour interval up to 24 hours, every day up to 13 days, every other day up to 20 days, and then every 4 days up to 48 days.

Five minutes after the application of a 6-mm. solid brass applicator (cooled to −78°C.) to the cornea of a rabbit for three seconds the epithelium in the area of injury is missing. This loss of epithelium may be due to the adherence of the epithelium to the applicator.

Within 15 minutes after injury the endothelial cells in the region of freezing become flatter than normal and a few of the cells are detached from Descemet's membrane. Fibrinous exudate appears in the anterior chamber. In 30 minutes, edema can be seen in the posterior layers of the stroma. Two hours after injury a marked loss of endothelium can be observed and a few polymorphonuclear cells appear in the anterior chamber.

At this time the first changes are seen in the stromal cells. The corneal corpuscles in the area which has been frozen become thinner than normal and take a more basophilic stain. The stromal cells just adjacent to the injury become swollen. The edema which was present only in the posterior layers of the cornea can now be seen throughout the full thickness of the tissue. The corneal lamellae are separated by edema but otherwise appear normal.

At 4 hours after injury definite fragmentation of the nuclei of the endothelial cells (fig. 1) can be observed and more of these cells have become detached from the endothelium. The "stringlike" appearance of the stromal cells is more obvious. The edema
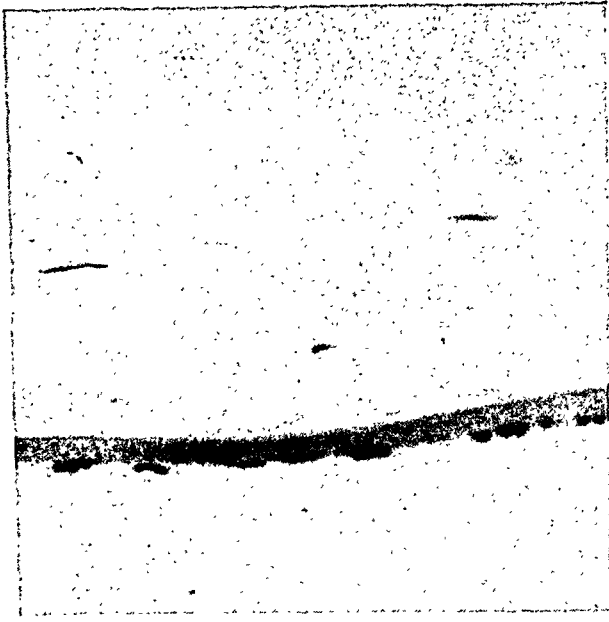
Fig. 1 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./3 sec.) four hours after injury, showing nuclear fragmentation of endothelial cells and stringlike stromal cells. (Hematoxylin-eosin stain. ×500.)
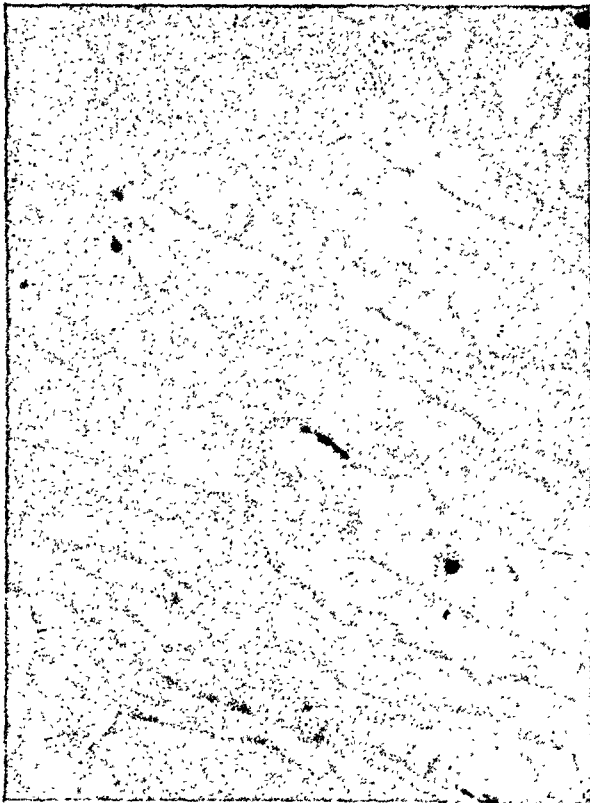
Fig. 2 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./3 sec.) 10 hours after injury, showing nuclear fragmentation of stromal cells. (Hematoxylin-eosin stain. ×500.)

of the stroma increases and a few polymorphonuclear cells can be seen outside of the vessels in the conjunctiva..

By 6 hours the endothelium is completely lost in the region of the injury. Fragmentation of the nuclei can be observed in the stromal cells and many of these cells have disappeared from the lesion.

At 10 hours most of the stromal cells have disappeared and those that remain show fragmentation of the nuclei (fig. 2). A few polymorphonuclear cells can be seen under the epithelium in the region of injury for the first time. The polymorphonuclear cells have increased in number at the limbus but the reaction is still not great. At 12 hours the cornea in the area which was frozen is practically acellular (figs. 3 and 4). The corneal edema has increased so that the thickness is now about three times greater than normal.

Very little further change is noted in the cornea until about 20 to 24 hours after freezing when definite signs of repair appear. Possible slight migration of the epithelium and endothelium occurs before this time but now regeneration of these tissues becomes definite.

The cells in the basal layers of the epithelium become flattened and at times spindle-shaped. They migrate in a single layer across the denuded cornea and the reëpithelized areas soon develop a double layer of cells. Frequent mitosis is noted in the region of repair. The endothelial cells also show evidence of repair. These cells become enlarged and spindle-shaped. They migrate individually so that at times there is a considerable space between the most advanced and next cell (fig. 5).

Mitotic figures (fig. 6) are also observed in these cells, a finding which is exceedingly rare in the normal endothelium. The stromal cells adjacent to the lesion, which up to this time have shown only an increase in basophilic staining, slight enlargement, and an increase in their protoplasmic processes, now
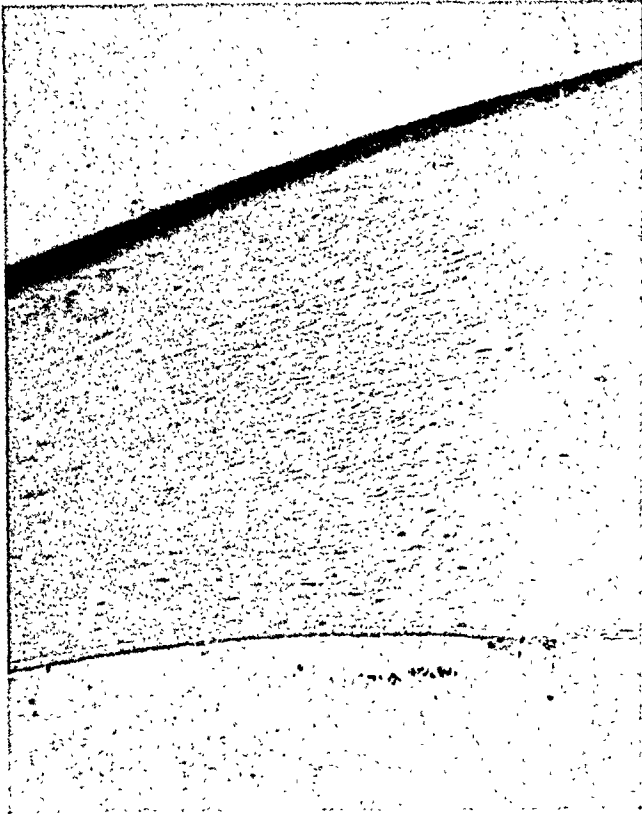
Fig. 3 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./3 sec.) 12 hours after injury, showing margin of lesion. (Hematoxylin-eosin stain. ×125.)
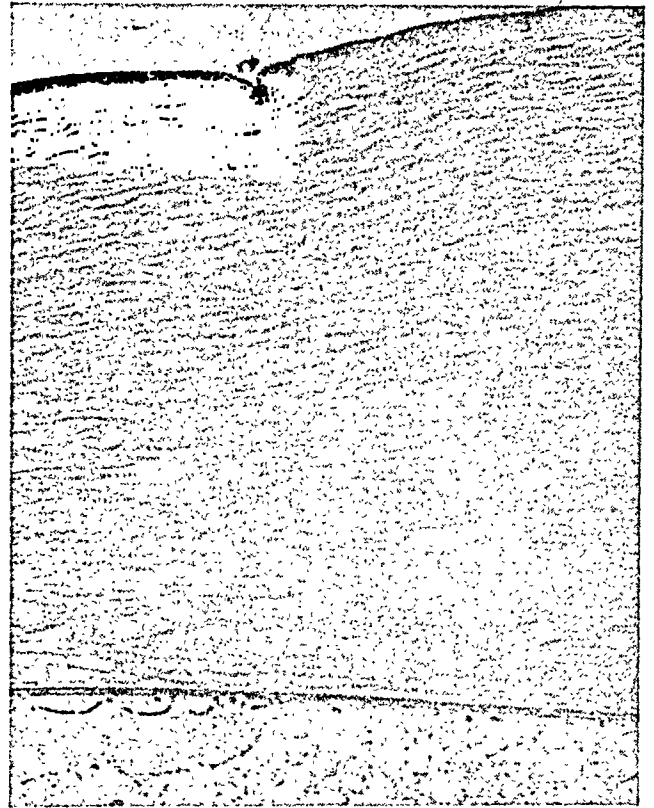
Fig. 4 (Maumenee and Kornblueth). Same cornea as in Figure 3, showing slightly more central area of the lesion. Notice complete absence of cells and edema of stroma. (Hematoxylin-eosin stain. ×125.)

show definite evidence of migration. Some of these cells become round and are difficult to differentiate from wandering macrophages with hematoxylin and eosin stain.

Other cells become more spindle in shape with long protoplasmic processes. Mitotic figures can frequently be seen in the cells adjacent to the acellular area.

Fig. 5 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./5 sec.) one day after injury, showing migration of endothelial cells. (Hematoxylin-eosin stain. ×500.)
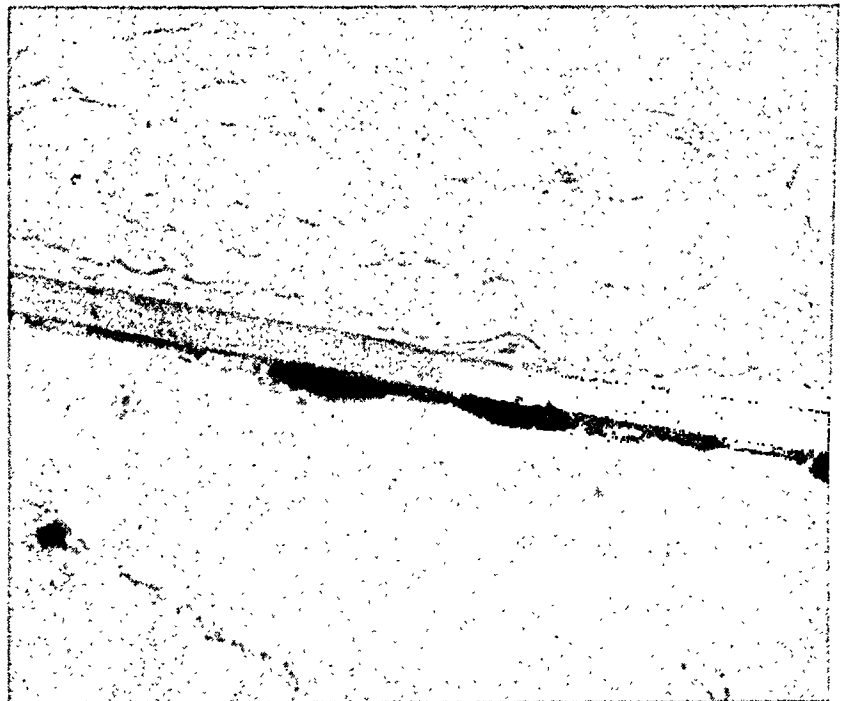
Fig. 6 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./3 sec.) 36 hours after injury, showing endothelial cell in mitosis. (Hematoxylin-eosin stain. ×500.)

Polymorphonuclear cells are conspicuously rare as they have been during the whole course of these lesions. Small monocytes however become rather prominent in the conjunctiva at the limbus and can be seen in the normal corneal stroma and near the edge of the lesion. Occasional large monocytes can also be found in the conjunctiva and normal cornea. It is difficult to differentiate these cells from the stromal cells near the edge of the injured tissue.

During the next 12 to 24 hours, the epithelium completely covers the damaged area of the cornea. The endothelial cells continue to migrate over the injured region and usually completely cover the lesion by four days. At first these cells are round or oval in shape protruding like many knots into the anterior chamber. Within a day or so, however, they resume their regular rectangular shape.

The cells in the stroma continue to invade the acellular area in a very irregular manner, some cells advancing far ahead of others. These cells vary in appearance. Some are long and spindle-shaped, with one or more nuclei; others look like small and large lymphocytes; and still others like wandering histocytes or macrophages.

Frequent mitotic figures (figs. 7 and 8) can be seen but there are not enough cells in mitosis to account for the reparative process. The occurrence of multinucleated cells would suggest that division in some instances takes place by amitosis.

By 5 to 7 days after injury, cells have invaded the full extent of the injured area. Their number and appearance however are not normal (fig. 9). The edema of the stroma rapidly subsides about this time,

Fig. 7 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./5 sec.) three days after injury, showing corneal stromal cell in mitosis (anaphase). (Hematoxylin-eosin stain. ×500.)

and by 7 to 8 days the cornea is usually normal in thickness.

The new stromal cells gradually resume their normal appearance and number and, by 10 to 12 days, the cornea appears entirely normal. At no time during this process is there any disruption or disturbance of the corneal lamellae. Vascularization of the cornea did not occur in any specimen.

The above description of destruction and repair of corneal cells was obtained from central injuries of the cornea. Lesions made in the periphery of the cornea show similar changes except for a slightly greater invasion of leukocytes and occasional invasion of the stroma for 1 to 2 mm. by small capillaries.

Fig. 9 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./5 sec.) seven days after injury, showing newly formed stromal cells. (Hematoxylin-eosin stain. ×125.)

Fig. 8 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./3 sec.) seven days after injury, showing mitosing (metaphase) and regenerating corneal stromal cells. (Hematoxylin-eosin stain. ×500.)

It is difficult to study the mode of death in the stromal cells in vertical sections of the rabbits' corneas because, frequently, the complete cell cannot be seen in a single section. Full thickness preparations of rabbits' corneas stain too deeply to allow them to be studied in toto.

Three-mm. strips of rats' corneas which had been frozen for 3 seconds and removed at various times after freezing were therefore prepared. The staining technique used was similar to that described by Buschke, Friedenwald, and Fleischmann.[23] In these preparations the full thickness of the cornea could be studied under the microscope.

It is found that, after freezing a 2-mm. area of the cornea for 3 seconds, definite fragmentation of the nuclei of the stromal cells can be seen 2 hours after injury (fig.

10). The first evidence of nuclear change is an agglutination of the chromatin into a single large clump or into many small clumps. The diffuse homogeneous staining of the nucleus becomes lighter and the clumps become more intensely basophilic. These clumps frequently migrate to the margin of the nucleus and the remainder of the nucleus becomes so pale that it can be seen only with difficulty.

Some of these cells then burst and liberate

perforating injuries. It was not possible to determine to what extent either of these two types of cells participated in the regeneration of the stromal cells nor was it possible to determine with certainty whether or not only one of these two types of cells was the sole source of the newly formed corneal corpuscles. In order to answer these latter questions further experiments were devised to study the source of the regenerated stromal cells.
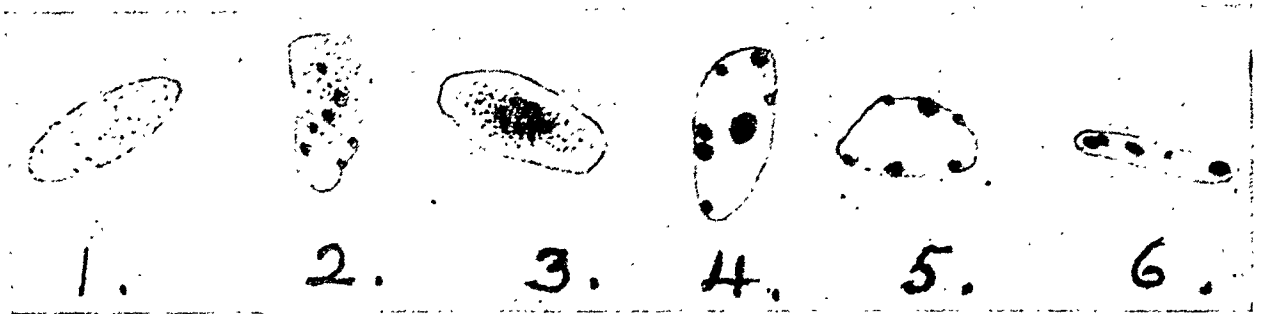
Fig. 10 (Maumence and Kornblueth). Diagram of nuclear fragmentation of corneal stromal cells of rat's cornea after freezing of cornea (2 mm./3 sec.). (1) Nucleus of normal keratocyte. (2 to 6) Various stages of nuclear fragmentation.

their granules while others shrink so the nuclei look like bits of string with 3 to 4 knots tied in it. A similar change has been observed in the stromal cells following injury by mustard and nitrogen mustard gases.[24] By 10 to 12 hours after freezing, all of the stromal cells had disappeared from the rats' corneas in the area of injury.

Several interesting conclusions were obtained from these histologic examinations.

1. The stromal cells are destroyed by nuclear fragmentation following freezing.

2. Remarkably little inflammatory reaction accompanies extensive destruction of corneal cells after this type of injury.

3. All of the cells in the full thickness of a 6-mm. area of the cornea can be destroyed and stromal cells will regenerate without leaving any residual opacity of the cornea if the lamellae are not disturbed.

4. The corneal stromal cells appear to regenerate from the undamaged stromal cells and from wandering macrophages in non-

FURTHER EXPERIMENTAL STUDIES

Participation of macrophages in regeneration of keratoblasts. A macrophage has been defined by Maximow and Bloom[25] as a cell which is capable of taking up particulate matter and storing foreign substances brought to it in colloidal solution. The simplest criteria for deciding whether a cell of the connective tissue or blood is a macrophage is the elective storing of colloidal vital dyes. The concentration of the dye must be weak for even epithelial cells will become filled with dye granules in concentrated solutions.

It is not our purpose to enter the controversial discussion of either the nature or the origin of these cells. It will suffice to mention that the macrophages participate in the phagocytosis of foreign material and repair of damaged tissues in the body. They may originate from mitotic division of preexisting fixed or wandering macrophages, by hypertrophy and development of lymphocytes

and monocytes, and by direct assumption of phagocytic activity of cells having mesenchymal potencies of development.

Tissue-culture studies of monocytes, macrophages, and fibroblasts indicate that these cells are not fundamentally different from one another but merely various stages in development of the same basic type of cell. Carrel and Ebeling[26a, b] have shown that by varying the culture media and environmental conditions tissue cultures of monocytes, macrophages, and fibroblasts may be converted from one type of cell to another.

Ebert and Florey[27] have observed the transformation of monocytes into fibroblasts in vivo by punching holes in rabbits' ears and inserting glass chambers into these areas. These chambers then became filled with blood clots. The macrophages of the blood stream were tagged by systemic injections of vital dyes (Pontamine sky blue, trypan blue, and vital new red). By the use of microphotography and microscopic examination through the glass window they were able to observe the invasion and transformation of the tagged monocytes into fibroblasts in these blood clots.

The ability of macrophages or wandering tissue histiocytes to change into fibroblasts is now generally accepted. The corneal stromal cells do not differ markedly from fibroblasts elsewhere in the body for they are derived from the same embryonic source and have the same morphologic appearance. It is, therefore, probable that damaged corneal corpuscles are replaced in some instances by macrophages originating outside of the cornea. In order to test this hypothesis the following experiments were devised.

Rabbits weighing approximately 2 kg. were injected intravenously or subcutaneously with 45 cc. per kg. of a 1-percent trypan blue solution divided into three weekly injections of 10 cc. each.

Twenty-nine corneas were injured by freezing and the eyes were removed after 3 to 30 days, fixed in Zenkers solution, imbedded in paraffin, sectioned, and stained with lithium carmin. In all eyes, trypan-blue granules were found in extravascular macrophages in the conjunctiva and iris.

The damaged corneas could be divided into two groups depending on the number of cells containing trypan blue. In corneas with dry-ice injuries at the limbus and with complete injuries, from 50 percent to 75 percent of the cells contained dye granules

Fig 11. (Maumenee and Kornblueth). Freezing (3 sec.) of whole cornea of rabbit saturated with trypan blue, 21 days after injury. Showing trypan blue granules in corneal stromal cell. (Lithium carmin stain. ×750.)

in the regenerated area. In the corneas with central lesions only a very occasional cell was found containing the dye.

In the early stages of repair, the tagged cells were round and looked like wandering macrophages. After complete recovery had occurred, the dye-containing cells in the stroma looked like otherwise normal corneal corpuscles (fig. 11). These cells were scattered evenly through the previously damaged area.

In 15 control animals saturated with trypan blue in which the corneas were not frozen, the dye was never found in the corneal stromal cells. This experiment indicated that macrophages participated in the replacement of stromal cells in peripheral and extensive injuries of the cornea but they had little to do with the repair of central lesions.

The presence of trypan-blue granules in the stromal cells cannot be considered as absolute evidence that macrophages are transformed into stromal cells; for it was possible that macrophages containing trypan blue could have entered the cornea and, at a later time, either died or expelled their granules which were then phagocytized by the stromal cells.

Stokes[28] has shown that trypan blue injected into the anterior chamber is phagocytized by the stromal cells if the posterior surface of the cornea is injured. Therefore the above experiments are suggestive but they cannot be considered as complete proof that macrophages replace injured corneal corpuscles.

In another group of rabbits in which half of the cornea was injured, it was noted that the new stromal cells appeared as rapidly from the limbal side, where there were no corneal corpuscles, as they did from the corneal side. This occurred before cells were found in the central portion of the lesion so the new keratocytes could not have originated from corneal cells. It was also noted that central 6-mm. lesions of the cornea healed only 1 to 2 days more rapidly than did 3-mm. injuries around the entire periphery of the cornea. The area of the peripheral lesions is approximately 4 times that of the central one, so if only the stromal cells participated in the repair, and the cells did not divide at a greater rate due to more extensive injury, it should have taken considerably longer for the peripheral lesion to heal.

Finally, as more extensive lesions were found to heal without residual damage to the cornea, it was thought that absolute proof of participation of cells from outside of the cornea could be obtained if all of the stromal cells were killed. To this end whole corneas were frozen by repeated applications of the metal cylinders.

Frequently these corneas became vascularized and edema persisted in the dependent portions of the cornea for 2 to 3 weeks. Some of these corneas ulcerated in the lower portions and healed with rather dense scars. However, in many of the corneas the superior portion regained its normal clarity except for a light vascularization. The failure of these corneas to heal as well as the less extensive lesion was thought to be due to the extensive destruction of the endothelium or to the destruction of some essential substance in the normal stroma.

It had been noted previously in routine histologic studies of the central lesions that the endothelium recovered more rapidly than did the stromal cells. It was, therefore, thought that if one half of the cornea was frozen, and after an interval of two days the other half and one millimeter of the originally damaged cornea was frozen, it would be possible to destroy all of the stromal cells and at the same time leave undestroyed some of the more rapidly migrating endothelial cells.

The boundary of the upper and lower half of the cornea was established by making a superficial scar in the cornea with the point of a hypodermic needle, and the two halves of the cornea were frozen as described.

Histologic examinations of corneas injured in this manner revealed that either all of the stromal cells were killed or not more than 1 or 2 percent of the cells remained in the posterior central 2 mm. of the cornea.

Regeneration of the stromal cells occurred from the periphery and was similar to the repair of other less extensive peripheral lesions of the cornea except for slightly more inflammatory reaction. Approximately two weeks after injury, the corneas fre-

quently appeared normal clinically but, on histologic examination, the stromal cells were still not normal in number, distribution, and size (fig. 12).

In most instances the corneas regained a normal histologic appearance about three weeks after operation. In a few eyes the peripheries of the corneas for about 1 or 2 mm. were invaded by blood vessels. The response of the regenerated stromal cells was normal to a second injury by freezing and these corneas supported corneal grafts as well as did normal eyes.

It may be concluded from these experiments that cells other than normal stromal cells can participate in the regeneration of keratocytes. These cells probably are the monocytes of the blood stream or the fixed macrophages of the limbal tissues which have been activated by the injury.

Participation of stromal cells in regeneration of keratoblasts. Experiments devised to prove that the stromal cells are a source of regenerating corneal corpuscles have not been as conclusive as those demonstrating the participation of the macrophages. However, some observations have been made which strongly suggest that the corneal corpuscles contribute to the replacement of the destroyed cells.

In the experiments previously mentioned, in which the animals were saturated with trypan blue, only an occasional cell containing the dye was found in the regenerated damaged area if only the center of the cornea was frozen. This is in contrast to a relatively large number of dye-containing cells found in peripheral and whole injuries of the cornea.

Secondly, in lesions in the periphery of the cornea, where half of the cornea was frozen, migration of cells and mitotic figures were found on the stromal side of the lesion before an appreciable number of wandering cells had passed through the normal cornea to reach the edge of the lesion.

Indirect evidence that the corneal corpuscles might be a source of the regenerat-

ing cells is the fact that stromal cells can be cultivated in tissue culture. These cells have the same morphologic appearance as do the cells in the intact cornea (figs. 13 and 14). While these findings are not absolutely conclusive they suggest that the stromal
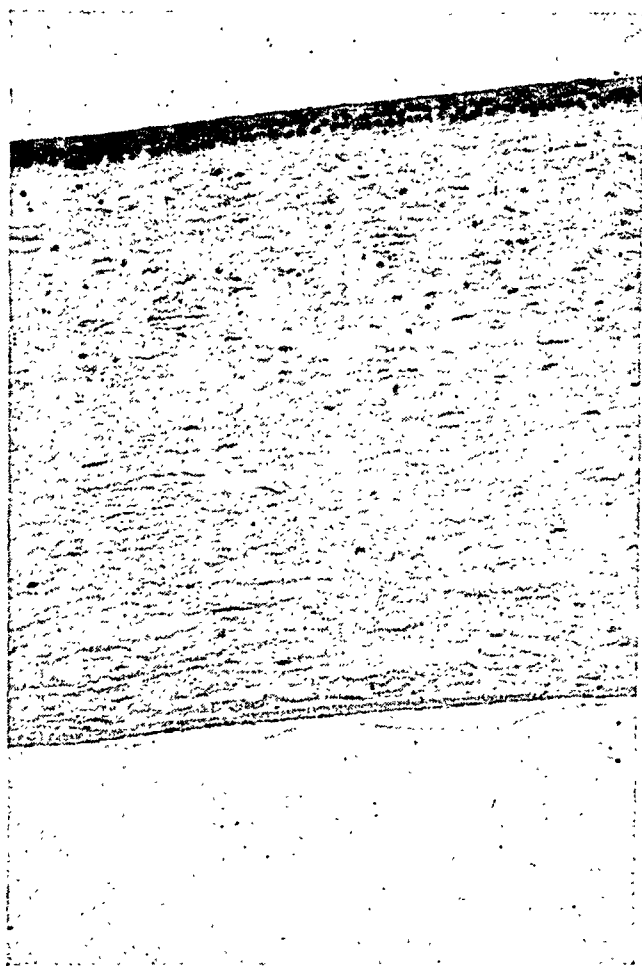
Fig. 12 (Maumenee and Kornblueth). Regeneration of corneal stromal cells nine days after freezing of whole cornea of rabbit, showing regenerated epithelium and endothelium. Slight edema of stroma, newly formed corneal stromal cells. (Hematoxylin-eosin stain. ×125.)

cells do aid in the reparative process of corneal lesions.

These experiments demonstrate that all of the cells in the full thickness of the cornea may be destroyed and, if the lamellae are not disrupted, the cornea will regain its normal clinical and histologic appearance after several weeks. The keratoblasts which replace the destroyed stromal cells originate from the remaining keratocytes and wandering macrophages from outside of the cornea.
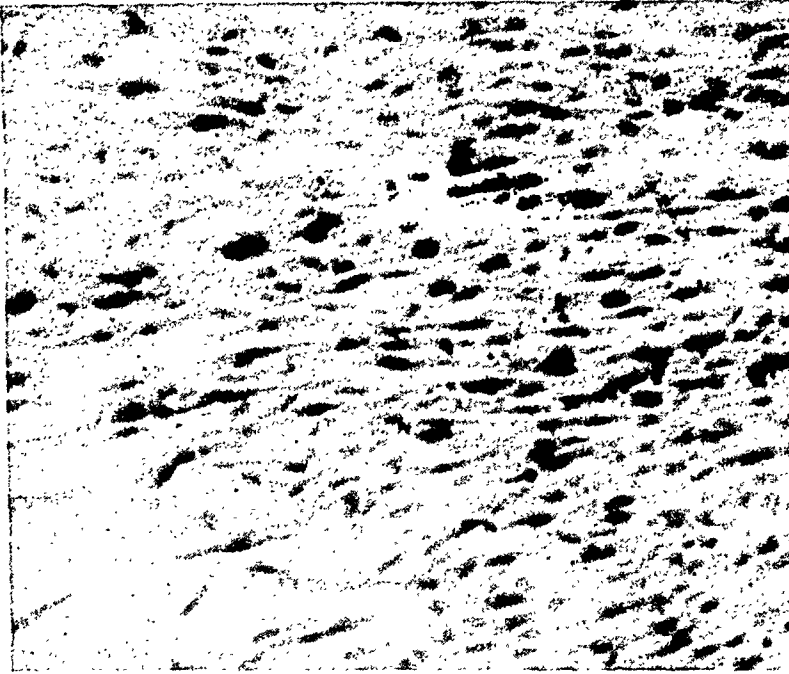
Fig. 13 (Maumenee and Kornblueth). Tissue culture of normal stromal cells of rabbit's cornea. (Giemsa stain. ×125.)

It is clear then that, if one is to establish with certainty whether or not the stromal cells in a donor corneal graft are replaced, both the keratocytes in the grafted cornea and the macrophages of the recipient animal, or the stromal cells of the donor cornea, must be tagged.

The problem of tagging these cells is not an easy one for it must be remembered that any foreign substance introduced into the donor cells may be expelled and be phagocytized by the recipient cells if the donor cells are injured or destroyed.

Fig. 14 (Maumenee and Kornblueth). Tissue culture of normal stromal cells of rabbit's cornea, showing mitosis (metaphase). (Giemsa stain. ×500.)

SUMMARY

Previous investigators have suggested that the destroyed corneal stromal cells may be replaced by migration and multiplication of undamaged corneal corpuscles and by invasion of cells from outside of the stroma. Most of the evidence set forth by these workers has been based on routine histologic studies. In this report, the mode of repair of various-sized lesions has been described in which all of the cells in the full thickness of the cornea have been destroyed by freezing. This type of lesion causes very little inflammatory reaction and, when the injury has been completely repaired, the cornea appears normal on both clinical and histologic examination.

It has been shown that keratoblasts can be derived from two sources in nonperforating lesions of the cornea: (1) The macrophages or fixed-tissue histiocytes which have been stimulated to migrate by injury to the cornea, and (2) the activated normal corneal cells. Nonirritating lesions in the center of the cornea are repaired primarily by undamaged stromal cells. Similar lesions in the periphery of the cornea are repaired by wandering macrophages and undamaged stromal cells.

These findings indicate that, if it is to be proven whether or not the stromal cells are replaced in a donor corneal graft by tagging the cells of the recipient, it will be necessary to identify both the keratocytes and macrophages. Of course, it may be possible to solve this problem by tagging only the stromal cells of the donor cornea.

CONCLUSIONS

1. Rabbits' corneas will regain their normal clinical and histologic appearance after most, if not all, of the stromal cells have been destroyed by freezing.

2. The stromal cells die by nuclear fragmentation after freezing.

3. Destroyed corneal stromal cells are replaced by migration and multiplication of undamaged corneal corpuscles and by a transformation of wandering macrophages.

Stanford University Hospital (15).

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OPHTHALMIC MINIATURE

To George Whatley

Passy, May 23, 1785

. . . By Mr. Dollond's saying, that my double spectacles can only serve particular eyes, I doubt he has not been rightly informed of their construction. I imagine it will be found pretty generally true, that the same convexity of glass, through which a man sees clearest and best at the distance proper for reading, is not the best for greater distances. I therefore had formerly two pair of spectacles, which I shifted occasionally, as in travelling I sometimes read, and often wanted to regard the prospects. Finding this change troublesome, and not always sufficiently ready, I had the glasses cut, and half of each kind associated in the same circle. . . . By this means, as I wear my spectacles constantly, I have only to move my eyes up or down, as I want to see distinctly far or near, the proper glasses being always ready. This I find more particularly convenient since my being in France, the glasses that serve me best at table to see what I eat, not being the best to see the faces of those on the other side of the table who speak to me; and when one's ears are not well accustomed to the sounds of a language, a sight of the movements in the features of him that speaks helps to explain; so that I understand French better by the help of my spectacles. . . .

B. FRANKLIN

A FURTHER, VERY DELICATE TEST FOR ASTIGMATIC AXIS, USING THE CROSS CYLINDER WITH AN ASTIGMATIC DIAL AND WITHOUT USE OF LETTER CHARTS*

WILLIAM H. CRISP, M.D.
Denver, Colorado

AND

GEORGE H. STINE, M.D.
Colorado Springs, Colorado

The purpose of the procedure as to astigmatic axis proposed in the paper presented by Crisp[1] at the meeting of the American Ophthalmological Society in 1942 was to afford a delicate control test for axis in astigmatic errors, especially of low amount, in which the test for axis with cross cylinder and test letters seemed insufficiently definite and reliable. That test utilized the wagon-wheel type of astigmatic dial, more particularly the axis chart either of Lancaster and Regan or of Verhoeff.

In the course of the preliminary clinical and photographic studies in relation to that test for axis, it became obvious that several other astigmatic dials might yield interesting results along the same lines, and brief consideration was given to the use of a rotating single cross for the purpose.

Stine proceeded to devote further attention to these possibilities, and later reported to Crisp his studies and observations. From these Stine had evolved the new test, which Crisp now proposes shall be known as the "Stine test for astigmatic axis." Both of the present writers have continued to employ this new test during the past 2 or 3 years, and have found it more definite and freer from complications than any other test known to them.

The new test is of surprising delicacy and simplicity, although like other subjective tests it demands full understanding and cooperation on the part of the patient. Like Crisp's test it is generally used as a control after preliminary testing for axis with the cross cylinder and the letter chart, and in

the light of any evidence which may be furnished by ophthalmology, skiascopy, or an astigmatic dial. In the larger astigmatic errors it may not have to be resorted to at all, although even here it may sometimes clear up doubts. In the small astigmatic errors (to which some workers pay little or no attention, but which may be quite important) it is most valuable.

The rotating cross is most conveniently and expeditiously used with a pulley mechanism for remote control from the examiner's chair near the patient, although some refractionists will rely (less conveniently) upon the services of an office helper for changing the position of the lines of the cross. Ophthalmologists who refract with a mirror and laterally inverted charts will, of course, have their charts within arm's length. The only disadvantage of the test as compared with the combined use of cross cylinder and letter charts or wagon-wheel chart is that, for absolute accuracy, the position of the rotating cross should be changed with each change of axis of the cylinder in the trial frame, although a discrepancy of a few degrees in the placing of the cross lines is usually of little practical importance.

At each step of the procedure, the lines of the rotating cross are made to straddle exactly the axis of the correcting cylinder in the trial frame. That is to say, the two lines of the dial should stand at 45 degrees to either side of the axis of the trial cylinder. The cross cylinder, usually the 0.12D. or the 0.25D., is held so that its axes correspond with the two axes of the rotating cross (that is at 45 degrees with the axis of the trial cylinder), and the cross cylinder is turned

or "flipped" in the same manner as in testing for axis with the letter chart.

The patient is asked to say with which position of the cross cylinder the two lines of the rotating dial appear more nearly matched as to blackness or sharpness, or with which position of the cross cylinder there is the lesser, amount of contrast between the two lines. The cylinder in the trial

If the choice has been made, and the position of the lens in the trial frame is changed, the position of the rotating cross must also be changed so as to straddle exactly (or at least approximately) the new position of the axis of. the trial cylinder.

The final stage of the test is reached when the patient insists that the variation of emphasis, or the reversal of sharpness or
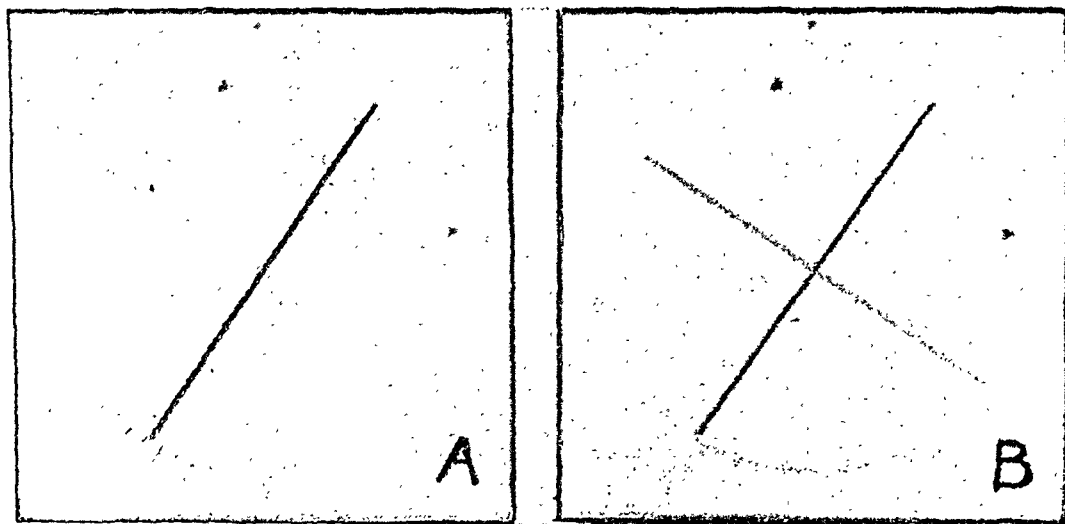
Fig. 1* (Crisp and Stine). Basic error of camera lens, rendered astigmatic, represents a final need for correction with +1.0D. cylinder axis 90°. For these two photographs the correcting +1.0D. cylinder had been placed inaccurately with its axis at 80 degrees. The two lines of the rotating cross were set respectively at 35 and 125 degrees. The cross cylinder was first placed with its plus axis at 35 degrees, and then with its plus axis at 125 degrees. The choice as to relative uniformity is obviously for the second of the two positions, indicating that the correcting plus cylinder should be turned toward 90 degrees. Astigmatic difference between the two lines in A is 0.59D., and in B, 0.09D.

frame is then moved toward the corresponding axis of the cross cylinder (plus toward plus, minus toward minus) in the position which gives greater uniformity of the lines or the lesser contrast between them.

* *Note as to illustrations.* For definiteness of illustration the basic error of the camera lens was that of mixed astigmatism, requiring a final correction with −0.25D. sph. ⊃ +1.0D. cyl. ax. 90°, and the 0.12D., cross cylinder (−0.12D. sph. ⊃ +0.25D. cyl.) was used. In actual practice it will be found that similar sharp differentiation by the patient is usually obtainable with such a weak cross cylinder and when dealing with a correcting cylinder as low as 0.25D.

The astigmatic differences between the two lines of the dial in the meridians shown in the illustrations were determined by the use of Percival's[3] equation for obliquely crossed cylinders and the law as to square of the cosine.

blackness from one line to the other, is equal in both positions of the cross cylinder; and, as under the test with cross cylinder and letters, the patient's accuracy may be cross-examined by turning the trial cylinder to each side of the selected position and repeating the test.

The patient may occasionally misunderstand the test and may answer paradoxically. Like other tests, this one is usually more reliable in the absence of active accommodation, although sometimes less accurate if the patient's vision is appreciably fogged. The use of a slightly over- or under-correcting trial cylinder affects the accuracy of the test practically not at all, although a slight overcorrection may often increase its sensitivity.

Very occasionally, determination must be made between conflicting results as to the use of this test and the use of letters with

It seems worth while to point out that, subject to spherical measurements, it is possible to accomplish all the measurements
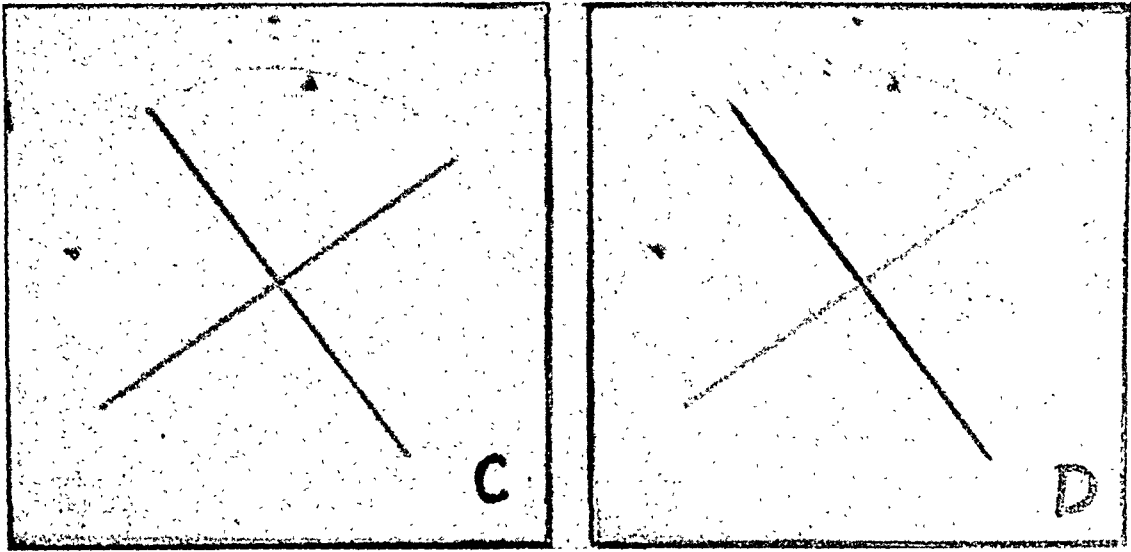
Fig. 2 (Crisp and Stine). For this pair of photographs the correcting +1.0D. cylinder had been inaccurately placed with its axis at 100 degrees. the cross was set with its lines at 55 and 145 degrees respectively, and the cross cylinder was held with its plus axis first at 55 degrees and then at 145 degrees. The choice is obviously for the former position, indicating that the axis of the correcting plus cylinder should be turned toward 90 degrees. Astigmatic difference between the two lines is 0.09D. in C, and 0.59D., in D.
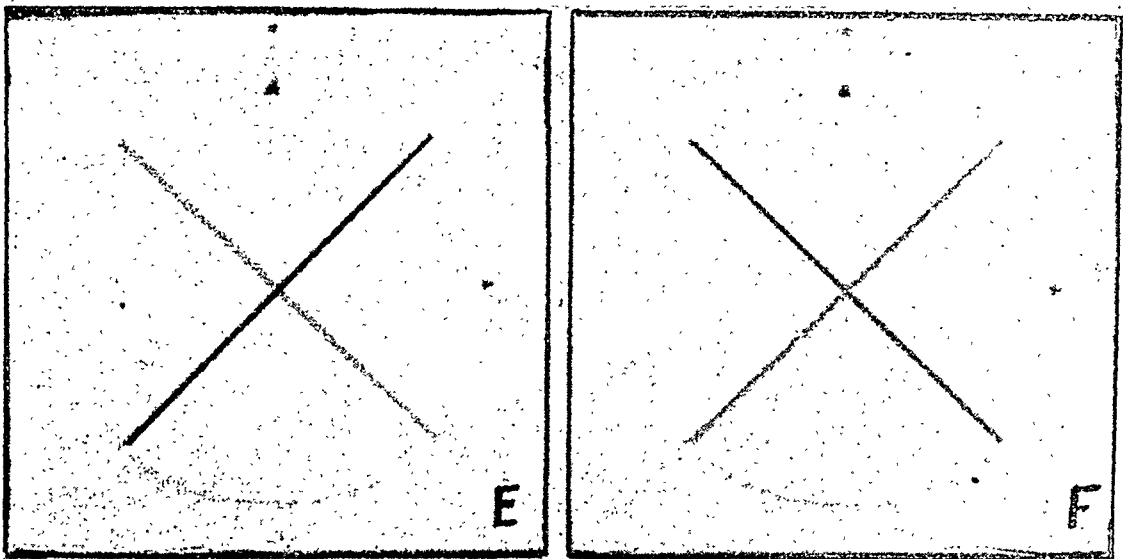
Fig. 3 (Crisp and Stine). For these two photographs the correcting plus cylinder was placed with its axis in the proper position, namely at 90 degrees. The rotating cross was placed with its lines respectively at 45 and 135 degrees, and the cross cylinder was held with its plus axis first at 45 and then at 135 degrees. There is obviously no choice as to the "equal inequality" of sharpness of the two lines on the rotating cross, indicating that the correcting cylinder is now at the proper axis. Astigmatic difference between the two lines is 0.25D. in both E and F.

the cross cylinder. But, generally speaking, the test with cross cylinder and rotating cross is as delicate and reliable as any procedure in refractive work, or more so.

(axis and strength) for astigmatism by means of the rotating cross, without resort to the letter chart. As demonstrated by Crisp in 1917,[2] the rotating cross may be

conveniently used in combination with a low cross cylinder for extreme refinement as to the exact fraction of astigmatism.

For this purpose, the axis having been determined, and the cross having been rotated so that one of its lines coincides with the axis of the trial cylinder, the cross cylinder (usually the 0.12D.) is held with the plus or minus axis alternately parallel with the axis of the trial cylinder. If both lines of the cross are actually equal, each position of the cross cylinder will slightly sharpen one of the lines of the cross and will slightly blur the other.

Thus, the patient's selection may be made to discriminate as to the error being slightly above or slightly below an exact eighth of a diopter of astigmatic difference. If the patient's response is paradoxical, all that is necessary is to inquire which position makes the two cross lines more equal in sharpness. The definiteness of this test may, of course, be vitiated by the presence of irregular astigmatism.

As to the axis test which is the main topic of this paper, a further application of the same principle may be made during determination of the axis by cylinder skiascopy. In this application, a cross cylinder of proper strength (as demonstrated by experience in the individual case) is held with its axes at 45 degrees with the axis of the cylinder before the patient's eye, and the examiner decides which way there is less suggestion of uncorrected astigmatism. But, as stated in regard to use of the test at the trial case (subjective test), in most patients, except those with larger errors or amblyopic eyes, such doubts may be settled more expeditiously and more conclusively along subjective lines.

1276 Emerson Street (3).
23 East Pikes Peak Avenue.

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OPHTHALMIC MINIATURE

To evert the upper lid grasp the eyelashes between the thumb and index finger of the left hand and draw the lid down towards you, pressing the center of it back with the handle of your sound before the eye is opened and the lid released. It will then be everted so that its inner surface is fully exposed for accurate, deliberate and complete treatment.

The everted lid should be gradually returned to its proper place; do not allow it to snap back suddenly—a bad practice

Memorandum Book of a Tenth-Century Oculist
Translated by Casey A. Wood.

FIXATION DISPARITY AND THE FUSIONAL PROCESSES IN BINOCULAR SINGLE VISION*

KENNETH N. OGLE,† PH.D., FRANCES MUSSEY, M.A., AND
AVERY DEH. PRANGEN,‡ M.D.
Rochester, Minnesota

INTRODUCTION

We have two eyes, therefore two retinal images, but we experience ordinarily a single perception of space. The normal physiologic and psychologic means through which this phenomenon takes place are called the fusional processes.

If, while one is looking at a distant object, a prism, base-out (for example), of not too high power is suddenly interposed before one eye, momentarily two objects are seen. These two, however, immediately move rapidly toward each other, the speed seeming to increase as the separation becomes less, as though each were attracted to the other by a magneticlike force. Then they suddenly coalesce, the final single impression giving no hint of its dual character. This phenomenon is said to illustrate the compulsion for fusion, a reflex to prevent diplopia. Under this compulsion eye movements occur such that the eye behind the prism turns to fixate the image of the object now seen through the prism. The movements of the eyes necessary for the reunification of the images are known as fusional movements. As usually stated, once the attention is directed to a given object the reflex to fusion so directs the pointing of the eyes that the images on the two retinas will fall on corresponding retinal elements or as near as possible to those elements. When this has taken place, one assumes that the neural excitations that arise from the two eyes are transmitted as "cortical" images to identical centers or regions of the visual cortex where unification takes place, the unification occurring prior to the conscious awareness of the perception.

The ophthalmologist needs a measure of the strength of the compulsion to fusion as an indication of the efficiency of the binocular visual mechanism and its ability to cope with muscle imbalances. The only measures available are the so-called prism vergences or fusional amplitudes. In the test for these, the eyes of the patient are directed to a target and then forced to converge (or diverge) by means of prisms placed before the eyes, base-out (or base-in). The prism power in each case is gradually increased until the patient reports a doubling of the target. At this report the prism power is noted. The findings so obtained for the convergence and the divergence are used as a measure of the fusional ability of the patient. Sometimes the prism strengths at which "blur" occurs and at which fusion is regained are also considered. Attempts are made to relate these data to the degree of lateral heterophoria present and finally to the ocular comfort of the patient.

That prism vergences are, at least in part, measures of the fusion ability is clear, since the fusion reflex cannot be separated from the convergence mechanisms and since it must demand particular muscular synergies of the oculorotary muscles of the eyes. However, it is questionable whether fusion power alone is being measured.

In prism vergence tests, probably three variables are involved: (1) The degree of the forced convergence (or divergence), (2) the strength of the fusion compulsion reflex, and (3) the degree to which the otherwise normal accommodative-convergence reflex is altered or embarrassed. The stimulus to accommodation (the target distance) is constant throughout the test.

The introduction of prism power before the eyes ordinarily sets up a stress in the normal accommodative-convergence reflex relationship, as long as the images remain fused. An accommodative change demanded by the changed convergence does not occur because of the compulsion to maintain clear vision, and it has been shown that over fairly wide limits the accommodative change in these tests is small, except as the prism strength approaches the diplopia point.[1]

In the prism vergence test it is the increasing stress in the convergence-accommodation reflex together with that of the musculo-mechanical processes which is pitted against the compulsion for fusion as prism power is increased. Diplopia occurs either when that stress is so great as to overcome the reflex innervation to maintain single binocular vision or when the mechanical limits of the oculorotary muscles are reached. Certainly, there is an expenditure of energy involved, and also a fatiguing of the muscles in the process. Both the magnitude of this stress and the strength of the fusion compulsion will undoubtedly vary from individual to individual.

Experimental evidence indicates that in spite of the compulsion to register the dioptric images of the two eyes as near as possible on corresponding retinal points, there occur an actual small deviation of the eyes and a corresponding slipping of the cortical images, although fusion is still maintained.

Identical target patterns observed on the two sides of the stereoscope will appear under normal conditions single, and then the images of these patterns are said to be "fused." Dissimilar (and unfusable) details *centered* on each of the same two patterns will under certain conditions appear decentered, that is, will appear displaced relative to each other, in spite of the fusion of the images of the identical patterns. This displacement occurs especially when the observer is heterophoric, or when the convergence and its normal corresponding stimulus for accommodation are altered. This phenomenon has been designated a *fixation disparity* (formerly, a "retinal slip") because the evidence indicates that the retinal images of the point of fixation may be actually disparate.

While this phenomenon may be a common observation among those who use the stereoscope or haploscope, it was Lau[2] who first described and correctly interpreted it while performing experiments on a different problem. He did not recognize any relationship between it and phoria.

He used targets, as illustrated in Figure 1A, in a haploscope, before the left and right eyes. Each target consisted of a long central line and a pair of shorter parallel lines that extended only to the center of each target. On one, the two short lines could be adjusted laterally by means of a screw, and the displacement could be measured by a scale and vernier. While the observer fixated the central line, and its images were fused, Lau adjusted the one pair of lines until the two opposing ones appeared in alignment. In every case, he found that both lines had to be displaced a small distance in the *same* direction. The magnitude of the displacement increased somewhat if the convergence of the arms of the haploscope was increased.

The interpretation given was that the true chief rays for the corresponding elements at the foveas of the two eyes were actually diverging slightly behind the position of the fused central line, the line of fixation.

Hofmann[3] reported the lag in the pointing of the eyes with rapid movements of the arms of the haploscope. Also, in commenting on Lau's work he expressed the belief that the phenomenon was associated with the interference in the normal accommodation-convergence reflex.

Lewin and Sakuma[4] set a playing card on each side of the haploscope; a four of diamonds before one eye and a five of diamonds before the other as illustrated in figure 1D. On looking into the haploscope the observer easily fused the images of the

four outer diamonds. The central diamond seen by only one eye, however, appeared decentered with respect to the outer four, especially as the convergence of the arms of the haploscope was changed.

In 1928, under the designation of "retinal slip," Ames and Gliddon[5] reported experiments with the haploscope in which targets (fig. 1B or fig. 1C) were used. They were able to show that the direction of the dis-

arrows seen by the left and right eyes on each side of the binocularly observed center appear displaced in the same direction. In fact, this displacement appeared to be a contributing factor to the lowered precision of measurements in the horizontal meridian, compared to those in the vertical, especially at the reading distance. The apparent magnitude of the displacement cannot be predicted, however, by the degree of the phoria.
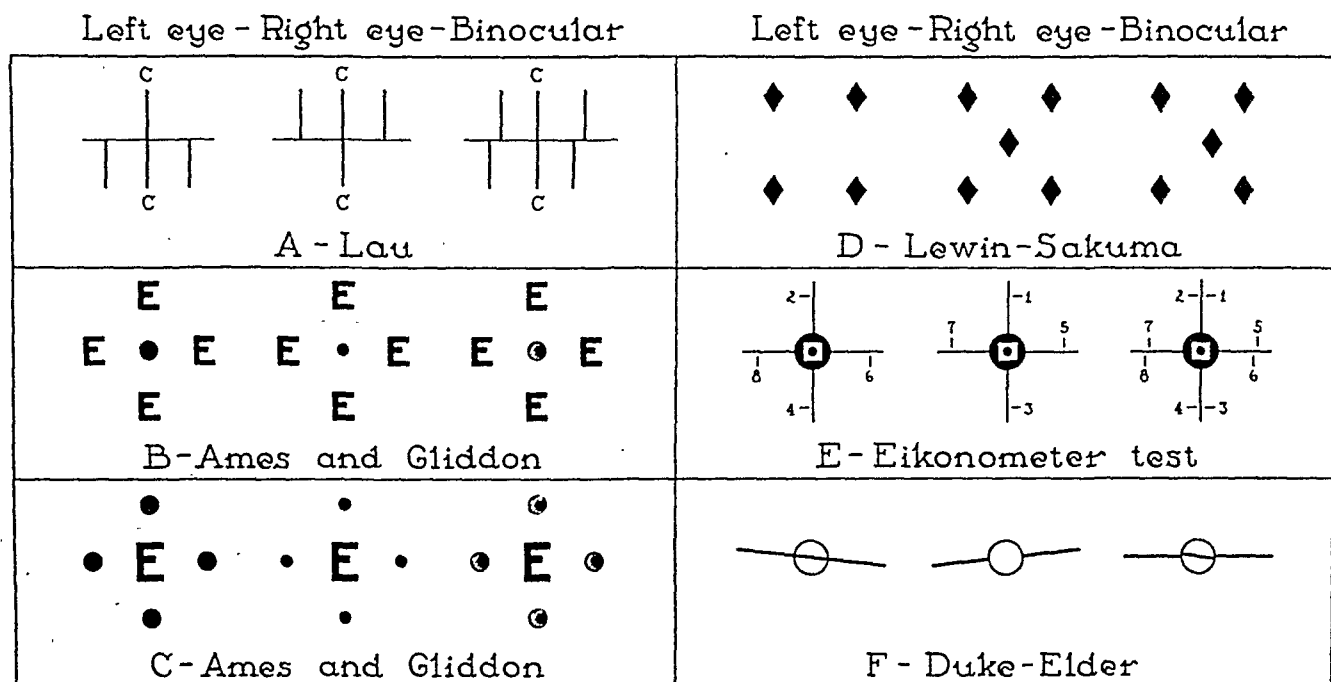
Fig. 1 (Ogle, Mussey, and Prangen). Types of targets used by different authors for haploscopic observation with which fixation disparity was evident.

placement of the small discs within the larger ones was generally the same as the direction of the phoria of the observer. Also, they found a fair correlation between that convergence of the haploscope arms necessary to eliminate the displacement of the discs, and the magnitude of the phoria measured under the same conditions. The close similarity of the results from the two types of targets suggests that the phenomenon occurs irrespective of whether the fusion is in the central or in the more peripheral parts of the binocular visual field.

In the use of the eikonometer with the direct comparison targets (fig. 1E),[6, 7] it is a common observation that for the average patient who has heterophoria the opposing

Duke-Elder[8] illustrates a pair of targets (fig. 1F) which show that this same phenomenon can also occur as a cyclotorsional displacement of the monocular images compared to the binocularly fused portions of the targets.

This phenomenon rests on the well-known fact that disparate images in the two eyes can be fused, if that disparity is not too great, that is, if they fall within the so-called Panum fusional areas.[9] These areas increase with peripheral angle; they are 6 to 10 minutes of arc near the macula. Disparate images are those which do not fall on corresponding retinal elements of the two eyes. Images which fall on corresponding points of the two eyes give rise to the ex-

perience of the same *primary* subjective sense of direction, as though each eye were used alone.

Were it not for the existence of the fusional areas, physiologic diplopia (or, better, double images) could be demonstrated for all images of objects in space which did not fall exactly on corresponding retinal points. Thus, in the fusion of disparate images, where a single sense of direction is experienced, that subjective direction must be a compromise between the primary directions associated with the two noncorresponding retinal elements on which the two disparate images are falling.

Objects in the binocular visual field which are so arranged (for example, by haploscopic, Polaroid, or red-green glass methods) that they can be seen only by one eye are experienced in a subjective direction corresponding to the primary uniocular organization of the retinal elements on which the images fall, unless those images are near other images of binocularly seen contours the images of which are fused.[5]

Therefore, if the eyes tend to overconverge or overdiverge, owing to innervations or mechanical stresses ordinarily manifested as a phoria when the eyes are disassociated, they could actually deviate from exact fixation, so that the images of the point of fixation would be disparate to an extent limited by the size of Panum's fusional areas. The subjective direction of the fused images of the point of fixation would be a compromise between the two foveal elements in the two eyes on which the images fell as in normal stereoscopic vision. Objects in the field of view seen monocularly would be seen in the subjective direction according to the primary characteristic of the retinal elements on which the images fell.

That this is actually the case is illustrated by data that have been obtained for the longitudinal horopter[10] as determined by the nonius method. In Figure 2,* the eyes fixate

a point on an object at F. On either side a number of narrow vertical rods are so mounted that they can be moved nearer or farther along fixed tracks. Before the eyes is placed a special illuminated screen with apertures cut out in such a way that, except for the fixation object F, the upper halves of the rods are seen by one eye, and the lower halves are seen by the other eye. All the rods are properly shielded from the surroundings and are observed against a uniformly illuminated background. As any rod is moved along its track the two halves of the rod appear displaced laterally relative to each other, the apparent displacement changing with the position of the rod. The observer adjusts the position of each rod until the two halves appear collinear, that is, in the same subjective direction. The rod at this position, then, by definition, has images in the two eyes that stimulate corresponding retinal meridians. Experiment shows that generally the esophoric subject tends to set all the rods in a curve that lies entirely in front of the point of fixation (fig. 2a), while the exophoric subject tends to set all entirely behind the point of fixation (fig. 2b). Thus the images of the point of fixation are actually disparate, uncrossed in the first instance and crossed in the second.

The phenomenon of fixation disparity, which is found in a majority of subjects, implies that the cortical images arising from the two eyes are actually slipped or displaced a small amount with respect to each other. The angle of fixation disparity is a measure of the degree to which the images have slipped, in the same sense that Panum's area, although measured as a retinal dimension, pertains to a cortical area within which disparate images are fused. The processes involved in the compulsion for fusion normally strive to keep the images from the two eyes as nearly as possible on corresponding points. The phenomenon of fixation disparity shows, however, that the fusion is not exact when a tendency for a disassociation exists (a heterophoria), although the unification of the images is preserved.

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* In these figures, for simplification in representation, the angle of fixation disparity is shown as though originating in only one eye.

Fixation disparity as a measure of the displacement of the cortical images will depend on the strength of the innervations and stresses of heterophoria, the strength of the fusion processes themselves, and the amount and complexity of the detail in the binocular field of view.

The purpose of this paper is to report a series of systematic measurements of the fixation disparity as influenced by a number of factors. The experiments were prompted

pair of Polaroid plates (5-cm. square) before the two eyes with the planes of polarization at right angles to each other. This Polaroid attachment could be turned down out of a field of view, and the two plates could be interchanged before the eyes if desired. The target for fusion stimuli consisted of Snellen letters projected by a lantern, the total field subtending an angular size of about 20 degrees. A small central area of a given size could be blanked out at
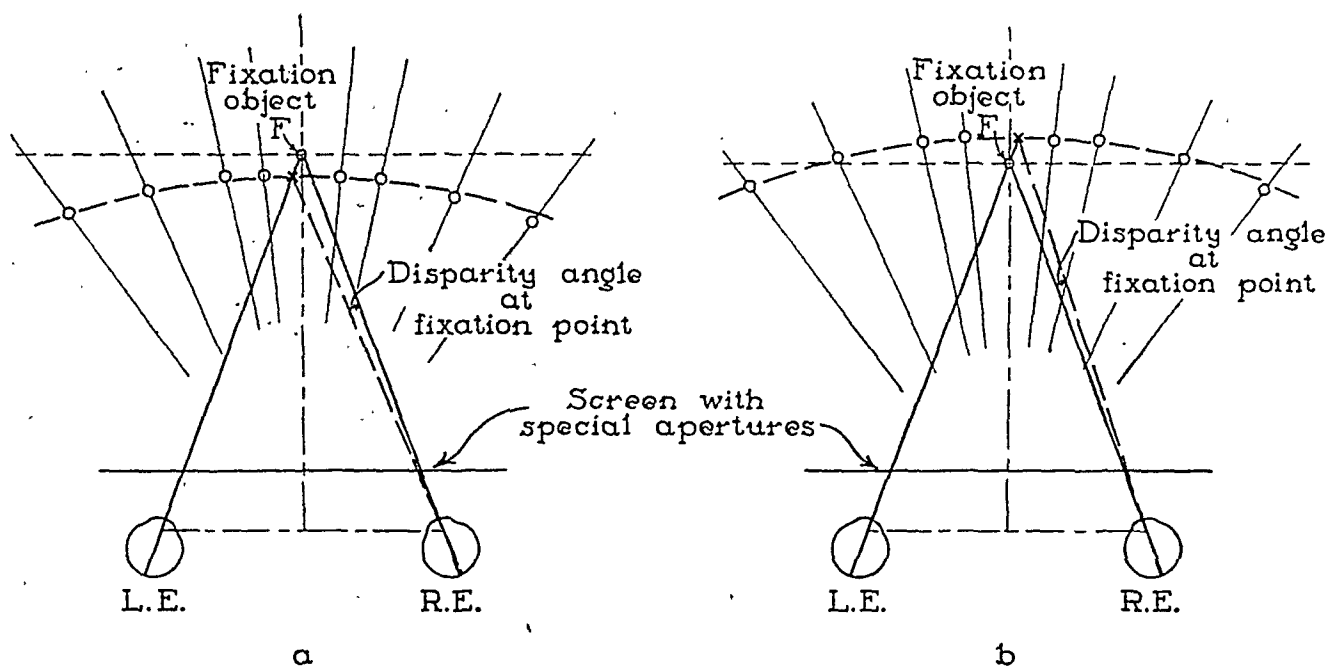
Fig. 2 (Ogle, Mussey, and Prangen). Schematic representation of horopter experiments which show that the point of fixation may not have images that fall on corresponding points.

by the thought that the fixation disparity might be an estimate, if not an actual measure, either of the strength of the fusional reflex or conversely of the strength of those forces—innervational, anatomic, and so forth—which tend toward an incorrect pointing of the eyes, while the images of the two eyes are actually fused.

PRESENT EXPERIMENTS

DISTANT-VISION TEST

Instrumentation. On an aluminum-coated screen, set up 2.5 meters from a subject's eyes, patterns and special test configurations were projected by suitable lanterns (fig. 3). The subject observed the screen through a phorometer, to which had been attached a

the center of the target and thus appear black to the subject. The size found convenient is a square that subtends a visual angle of about 1.5 degrees to the subject. With this center no stimuli for fusion are present within the foveal regions of the two eyes, but details for fusion exist everywhere outside this area.

The test configuration was projected on the blank square at the center of the screen by a second lantern into which a special slide arrangement had been built. The test details (see insert in fig. 3) consisted of a horizontal bright line, 28-cm. long and 5-mm. wide, and a pair of opposing (vernierlike) short vertical bright lines (arrows), 2.3-cm. high and 2-mm. wide (2.5 minutes of arc).

The arrows were polarized by Polaroid

film in the slide, so that one arrow would be seen by one eye and the other by the second eye, when viewed by the subject through the Polaroid plates. The upper arrow was fixed (stationary) but the lower could be displaced horizontally by means of a special mechanical arrangement in the lantern, which was operated by a screw and knob on the outside.

The displacement of the two arrows was

The general illumination of the room was kept subdued, and the luminosity of the screen and fusion detail were the same throughout the experiments. The binocular visual field was restricted wholly to the details on the screen.

Procedure. The phorometer is adjusted to the subject's head so that the eyes are centered. With the Polaroid plates before the eyes, the visual acuity of each eye is checked
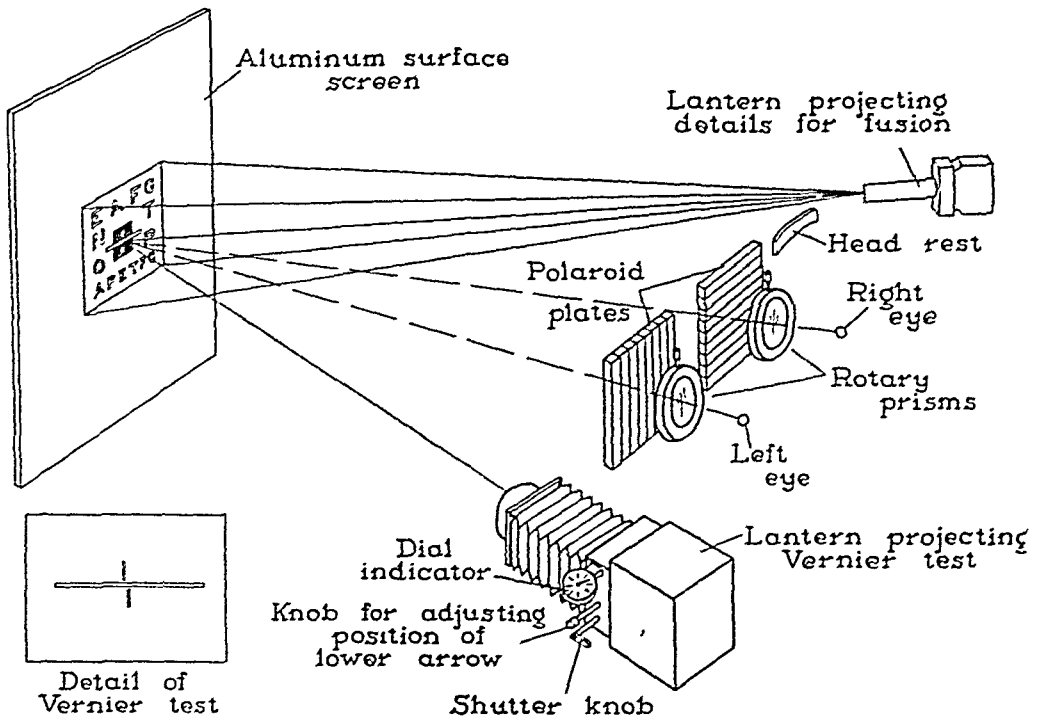
Fig. 3 (Ogle, Mussey, and Prangen). Perspective drawing of the instrumentation used to measure fixation disparity.

read by the experimenter from an accurate *dial indicator on the lantern, to an estimated 0.2 minute of arc (angle subtended to the subject), which is well within the maximal sensitivity found. By means of a shutter arrangement, the lower arrow could be occluded or flashed onto the screen at the will of the operator.*

A light-green filter could also be placed over the upper arrow, if needed for making the identification of the arrows easier for the subject. The long horizontal line prevented fusion of the arrows and possibly reduced any tendency for a vertical deviation.

by means of the Project-O-Chart, the test target being projected on a screen. After this the phoria is estimated by the Maddox rod and also by the double prism test, a spot of light being projected on the screen in a room totally dark.

The target (with the 1.5-degree square) and the test arrows are then projected on the screen. With the Polaroid plates removed (both eyes observing the target), a determination of the dial reading is made for which the arrows appear in alignment, as well as of the least perceptible displacement (*a measure of the precision*) that can be detected. The operator instructs the subject

to look at the upper arrow, and then he flashes the lower arrow for a fraction of a second, after which he asks the subject whether that arrow was to the right of, to the left of, or was centered with the upper arrow. Between flashes the lower arrow is displaced to a new position. By the method of limits the average midpoint and precision are determined. The zero of the dial indicator is then adjusted to that reading for

position and the limits can be found within which he reports that the two arrows appear aligned. The actual displacement of the arrows is expressed by the angle, in minutes of arc, subtended at the eyes of the subject.

The experiment then proceeds by the determination of the fixation disparity for different values of prism power introduced by Risley rotary prisms* before the patient's eyes. For most subjects the prism power

TABLE 1

TYPICAL DATA OBTAINED ON THREE SUBJECTS SHOWING THE MAGNITUDE OF FIXATION
DISPARITY, σ, (MINUTES OF ARC) AND THE PRECISION OF THE MEASUREMENT
FOR VARIOUS DEGREES OF FORCED CONVERGENCE AND
DIVERGENCE; CENTRAL SQUARE 1.5 DEGREES

Prism power	Subject F. M. 1.5Δ exophoria		Subject W. A. P. 6Δ–8Δ esophoria		Subject K. N. O. 2Δ–3Δ esophoria	
	σ	Limits	σ	Limits	σ	Limits
Zero	0	±0.7	6.6	±1.7	2.7	±1.3
4Δ B.O.*	−0.8	±0.7	3.3	±1.7	2.0	±1.0
2Δ B.I.	2.3	±0.7	8.3	±1.7	6.0	±1.3
8Δ B.O.	−2.0	±1.0	2.3	±2.7	1.7	±1.3
4Δ B.I.	1.7	±1.0	23.3	±2.3	15.0	±1.7
12Δ B.O.	−2.7	±1.0	−0.7	±1.0	2.3	±1.3
6Δ B.I.	5.0	±1.0	30.0	±3.0	21.7	±5.0
16Δ B.O.	−4.0	±1.3	−1.7	±1.7	1.3	±0.7
8Δ B.I.	6.3	±1.7	Diplopia		Diplopia	
20Δ B.O.	−5.7	±1.3	−4.0	±3.3	1.3	±1.0
10Δ B.I.	13.3	±2.3	Diplopia		Diplopia	
24Δ B.O.	−6.0	±1.7	−11.7	±3.3	1.3	±1.3
12Δ B.I.	Diplopia		Diplopia		Diplopia	
28Δ B.O.	−7.3	±2.0	Diplopia		1.0	±1.7
32Δ B.O.	−9.6	±3.3			0.7	±1.0
36Δ B.O.					0.0	±2.7
40Δ B.O.					−1.7	±1.0

* B.O. = base-out; B.I. = base-in

which the subject reports that the arrows are in alignment. This procedure eliminates the constant personal and instrumental errors. Only small variations between subjects are found.

The Polaroid plates are raised and the operator checks that the right eye sees only the upper arrow and the left sees only the lower arrow, and that ghost images are absent. By means of the shutter the lower line is then exposed for short intervals of about 0.25 second, and the subject is asked to judge whether this arrow was right or left of the upper arrow, or even with it. By adjusting the amount of displacement, and obtaining the patient's response, the average

was placed alternately base-out and base-in; the base-out in 4Δ steps and the base-in in 2Δ steps. The alternation of base-out and base-in procedure was found necessary to avoid cumulative effects.

Thus, while following to some degree the procedure in the test for fusional amplitudes, here one measures any deviation of the eyes

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* It is unfortunate that rotary prisms introduce optical distortion. However, the advantages of the continuously adjustable prism power over the fixed steps of loose prisms, the axes of which are also difficult to adjust accurately, outweigh the possible disturbing effects of the distortion. Cursory experiments showed that this distortion had no significant effect on the measurements, in spite of the fact that theoretical arguments might anticipate such effects.

from their positions for exact fusion that may occur during the procedure. The change in the actual deviation during the test provides new data for studying the fusional processes as the eyes are subjected to changes in convergence by prisms and changes in the stimulus to accommodation by lenses.

parity and the limits within which the arrows appeared aligned are given. The direction (sign) of the deviation is taken as positive if it indicates an overconvergence of the eyes and as negative if the deviation
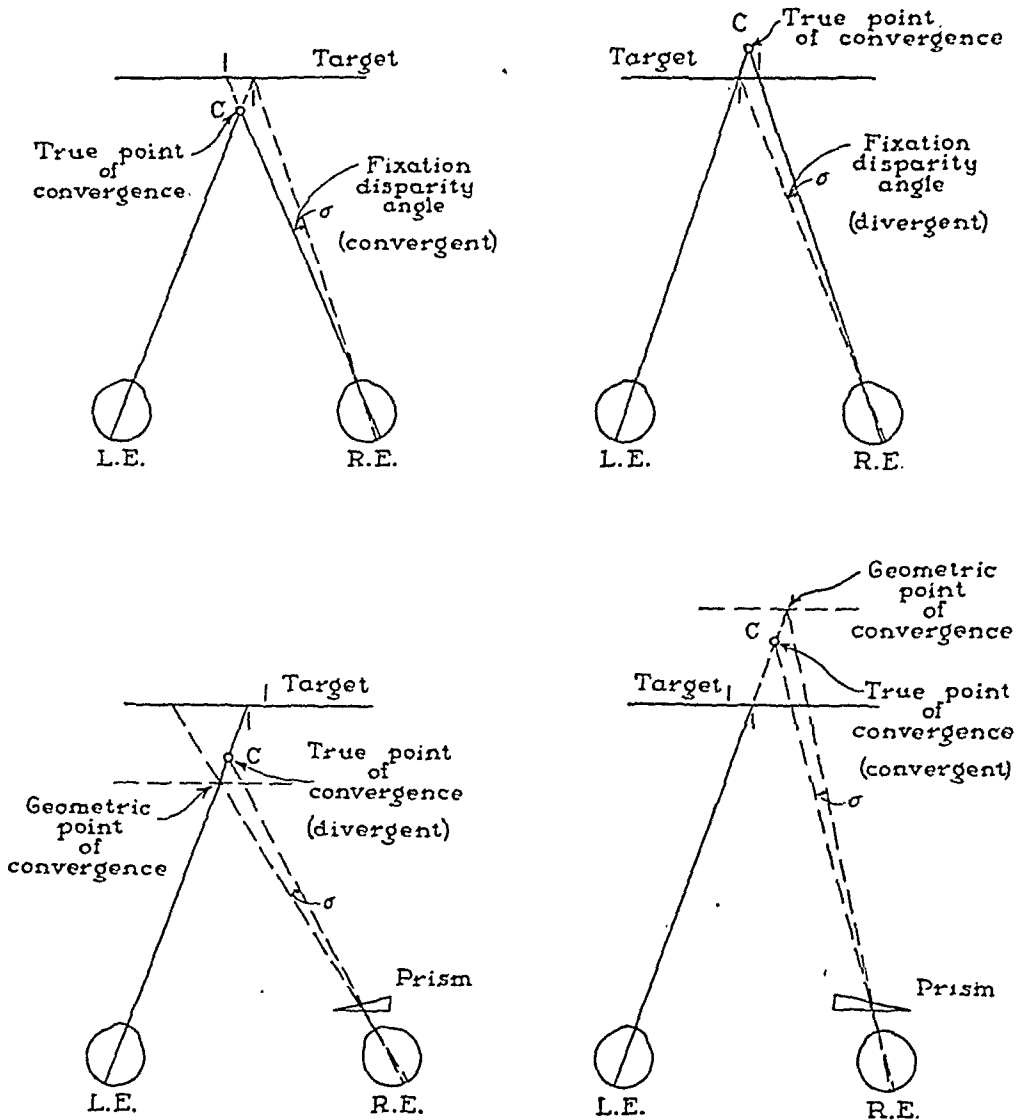
Fig. 4 (Ogle, Mussey, and Prangen). Relationship between the displacement of the polarized arrows, when they appear aligned, and the existence of an overconvergence or underconvergence of the eyes (fixation disparity).

Results. Typical data obtained are given in Table 1, and with others are illustrated in figures which follow. In the first column of the table, the prism power used is listed in the order in which the data were taken. In the two columns for each subject, the corresponding measure of the fixation dis-

indicates an underconvergence (overdivergence), that is, positive if the eyes are actually converged in front of the target or the geometric position of that target when prisms were used and negative if actually converged behind the target. Figure 4 illustrates schematically the positions of the arrows when they appear aligned, and the patient overconverges or underconverges relative to the target fixated. When prisms are used

before the eyes, of course, the images of the targets are so displaced that the eyes must converge or diverge if fusion is to be maintained.

The results of eight subjects are shown in Figures 5 and 6. In these graphs, the positive for convergence and negative for divergence. The measured fixation disparity in minutes of arc is plotted on the ordinate, being taken as positive if the deviation of the eyes is convergent and negative if divergent. It is evident that a large proportion
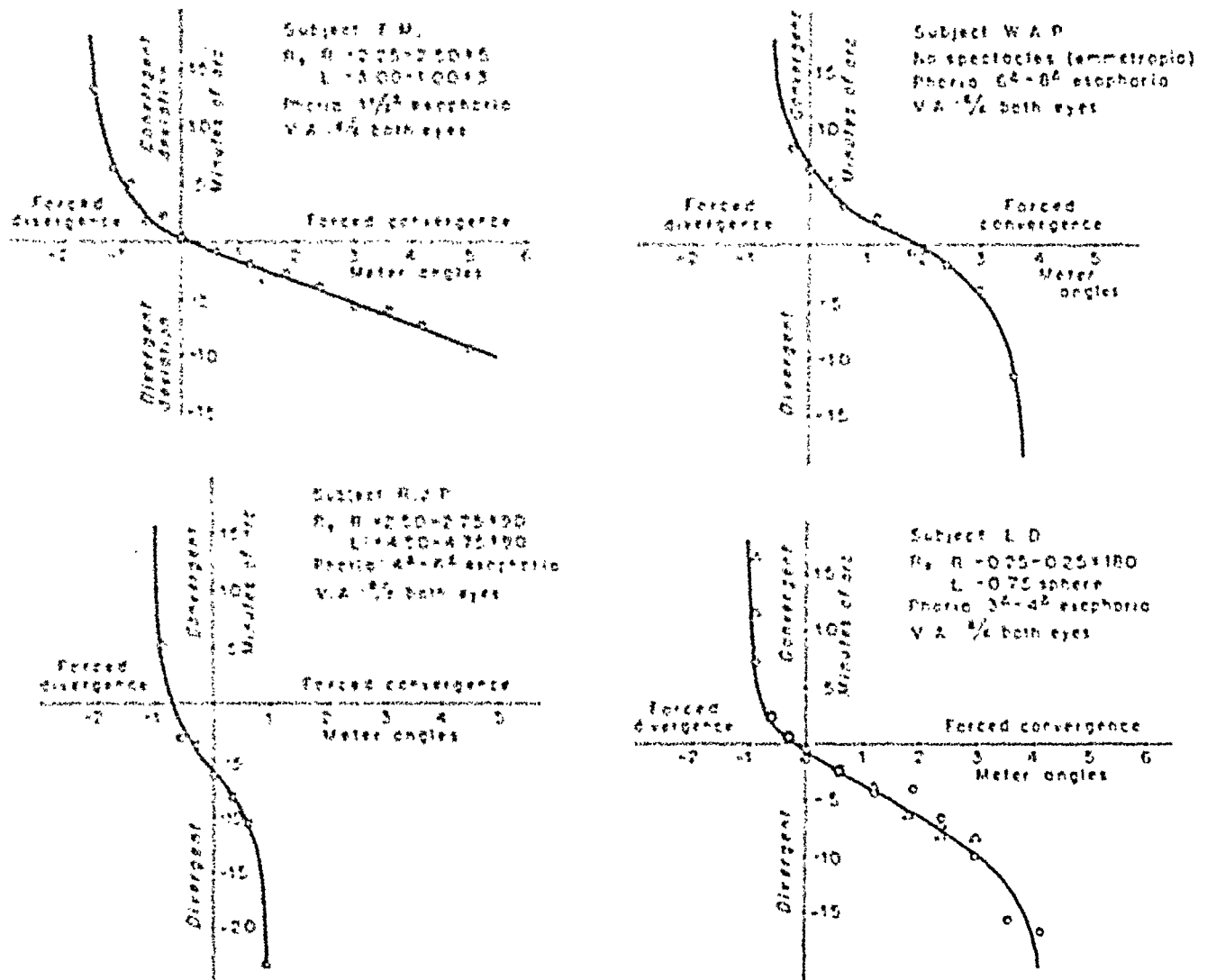
Fig. 5 (Ogle, Mussey, and Prangen). Typical data of subjects for whom the fixation disparity changes with forced convergence and divergence caused by the prisms before the eyes.

difference in the angle of convergence caused by the prisms compared to that for the 2.5-meter observation distance, measured in meter angles,* is plotted on the abscissa.

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* The meter angles are readily obtained by dividing the total number of prism diopters by the interpupillary distance (in cm.), or roughly by 6. Meter angles are to be preferred over prism diopters or centrads, for they indicate more clearly the degree of convergence, and the corresponding demand on the accommodative mechanisms of the two eyes.

of all subjects exhibit a fixation disparity of different amounts, even when no prisms are used.

Inspection of Table 1 and Figures 5 and 6 shows that points representing the data for each subject describe a sigmoidlike curve, the shape of which is different for different subjects. However, two fairly definite types of curves are distinguishable. Typical graphs illustrating these two groups are shown in Figure 5 and in Figure 6.

Consider for discussion the data for W. A. P. in Figure 5. This subject is nearly emmetropic, with a visual acuity of 6/6 in both eyes, but shows an esophoria of 6 to 8 prism diopters for the 2.5-meter visual distance. With no prisms before the eyes (or the rotary prisms set for zero power), the two arrows had to be displaced 6.6 minutes

forced convergence would be manifested as an exophoria or a decreased esophoria if the fusion were not present, or as a change in the fixation disparity in the direction of a divergence. Such a reaction is demonstrated in this subject.

When prisms are placed base-in before the eyes a divergence of the eyes is forced, and
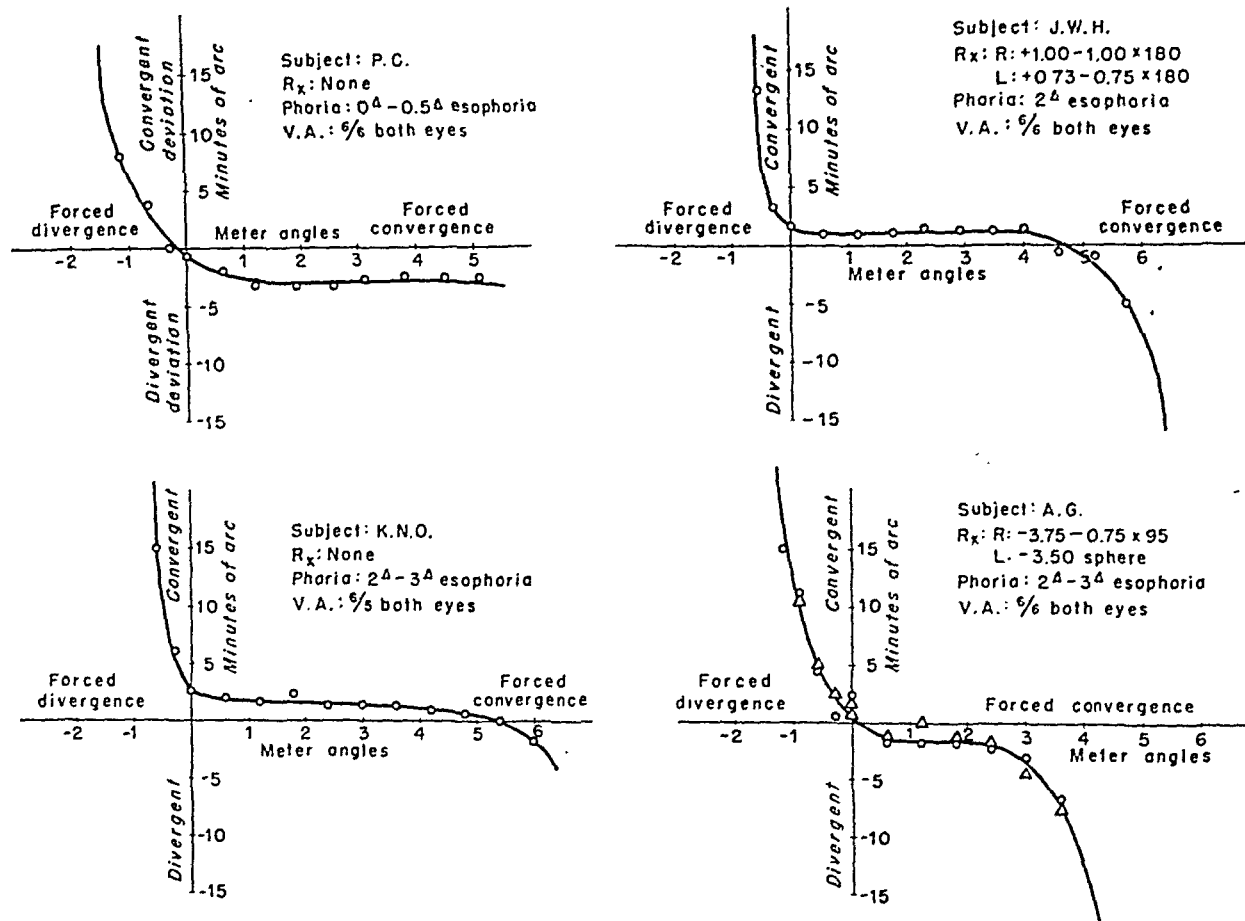
Fig. 6 (Ogle, Mussey, and Prangen). Typical data of subjects for whom the fixation disparity changes only slightly with forced convergence except at the limits of the fusional amplitudes.

of arc for them to appear aligned. This finding shows that the eyes were actually over-converged by 6.6 minutes of arc, which is in the same direction as the phoria.

When prisms are placed base-out before the two eyes, a convergence is necessary if fusion is to be maintained. This convergence of the eyes is made, but if the convergence-accommodation reflex is active, this convergence will be resisted because the accommodation cannot change appreciably without blurring the vision. This resistance to the

the reverse behavior in the fixation disparity is to be expected. Since the limits of prism vergences base-in at this fixation distance* are not large, the fixation disparity increases rapidly because the point of diplopia is quickly reached.

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* For the fixation distance b, the distance from the target to the true fixation point Δb is given sufficiently accurately by $\Delta b = b^2/2a \tan \delta$, where δ is the fixation disparity and $2a$ is the interpupillary distance. For a visual distance b = 2.5 meters, this distance is roughly 3 cm. for a fixation disparity of 1 minute of arc.

Considerable difference between subjects is found in the limiting prism power for forced convergence caused by prisms base-out. On approaching that point, fusion may become too unsteady for reliable measurements and diplopia may occur intermittently. In several subjects (fig. 5), the data could not be obtained to the point of diplopia because of blurring, micropsia, and the ocular discomfort associated with the sustained convergence.

Precision of the data. One of the striking aspects of these data is the smallness of the quantities being measured and the precision within which they are obtainable. As is the case in many other psychophysical measurements, the observer feels that his judgments are very uncertain, but the actual objective accuracy proves surprisingly great.

If the visual acuity is high and the muscle balance is fairly normal, it is usual to find the limits within which the two arrows appear in alignment of the order of 1 minute of arc, and often less. The precision decreases with lowered visual acuity, and decreases considerably as the degree of the forced convergence or divergence becomes large, because the relative positions of images seem more unstable and liable to change (see table 1).

Several subjects, however, showed poor precision for the entire curve, in spite of good visual acuity and low phoria. It should be clear that the limits as determined here are larger than the mean error or the standard deviation would be in other types of experimental technique.

Repeatability. Data of the nature of those described in these experiments cannot fail to vary somewhat from day to day, depending on rather intangible factors associated with the individual. For some subjects the precision of measurements seemed to vary from one day to the next for no obvious reason, although fatigue, previous excessive use of the eyes, and even disinterest may have been specific factors. However, in spite of this variation, the general curve obtained

for a given subject after the lapse of several days agreed remarkably well with that previously obtained.

Figures 5 (L. D.) and 6 (A. G.) show two sets of such data identifiable by the circles and triangles. A small training effect is to be expected, but this seems to manifest itself in an increased precision and an increased amplitude of base-out prism vergence, rather than a change in the curve that represents the data. This must not be taken to imply that no changes are found, for frequently the second curve may be displaced from that taken first by a small degree, in the same sense that the phoria will change from day to day.

The particular technique used in exposing the arrow also generally had no significant effect on the curve obtained. In one technique the lower arrow was not flashed at all, the subject merely reported when he saw it to the right and when to the left of the upper arrow, as it was slowly displaced one way and then the other by the operator. The flashing technique was preferred, for it tended to reduce any alignment of the two arrows due to "desire for symmetry" and any influence of after-images, although these factors actually appeared to have only a minor effect, if any.

The small normal involuntary eye movements that are always present and which appear to increase with the stress accounted for occasional spurious responses. As the prism vergence approached the point of diplopia, fusion of the images became more uncertain, and here greater discrepancies in the repeated data were found. However, the values for the fixation disparity were already comparatively large in these regions, so that the curves themselves were only slightly modified by the variations in data. Reversing the Polaroid plates before the eyes, so that the arrows would be seen by opposite eyes, had no influence on the data.

For some subjects a second set of data obtained immediately after the first resulted in a slightly different curve. An accumulative

effect of the sustained use of prisms base-out toward the end of the test appeared to leave a residual esophoric stress evident by the vertical displacement of the curve and sometimes also by an increase in the slope (rate of change of the deviation with convergence) especially in the center of the curve. The effect may persist for several hours after the original experiment.

Care was taken not to obtain data for a curve immediately after prism vergence tests or unusual use of the eyes. In order to avoid cumulative effects during the experiment, the prisms, base-out and base-in, were alternated and frequent short rest periods were allowed. This influence of sustained base-out prisms on fixation disparity is interesting, for in obtaining prism vergence limits it is believed that the use of prisms base-out has less effect on data subsequently obtained than has the use of prisms base-in.[11]

Subject groups. An inspection of the curves selected shows rather strikingly the manner in which the subjects tend to fall into two groups according to the characteristics of the curves found. Subjects with curves intermediate between these two will probably be found, however. In the first group (fig. 5) the fixation disparity increases with the forced convergence (or divergence) of the eyes, and in the middle range the increase is almost directly proportional to the prism power. For these subjects, as the prism power is increased, the cortical images from the two eyes increasingly "slip" and the fusion of these images becomes increasingly less exact, until finally a confusion and then a diplopia occurs. Although the rate of change in the deviation with prism power suggests itself as a measure of the strength of the fusion reflex (the higher, the poorer the fusion), this is not borne out.

In the second group (fig. 6) the eyes maintain more or less the same degree of fusion, over wide ranges of forced convergence, as evidenced by the fact that the fixation disparity changes little between the limits near which sudden increases are found. The fusion of the two images for these subjects appears to be tightly held in spite of the increased prism power. Even for high degrees of forced convergence certain of the subjects showed only a small increase in the disparity (data K. N. O. and J. W. H.), until the point was reached where abrupt changes might be expected.

This second type of curve is not unexpected, for it might be anticipated that the fusional processes would hold the images tightly together during the entire prism vergence test, until a sudden giving way would occur at the limits with resultant diplopia. However, one would expect the fixation disparity to be zero between these limits. The anomalous factor shown in these data is that more or less constant actual fixation disparity is maintained between those limits. The precaution taken at the beginning of the measurements to determine the "zero" for each observer precludes the possibility that this displacement is a constant personal or instrumental error. The direction of this disparity in the level portion of the curve appears generally to be in the direction of the phoria.

Blurring the retinal images. There would be reason for expecting that the fusion in the face of opposing stresses would be more difficult when the retinal images are blurred, because all contours on which fusion will depend would be less distinct. However, it is well known that in prism convergence tests on the major amblyoscope or synoptophore the fusion of the images seems to hold well even after the images are so blurred as to be almost unrecognizable. The fixation disparity curve as obtained here also does not change appreciably when the images of both eyes are blurred by plus ophthalmic spherical lenses at distant vision or with occluder (special etchedlike) glasses.*

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* These glasses were supplied by Dr. E. D. Tillyer of the Scientific Department of the American Optical Company. They consist of a series of glasses manufactured by a special process for reducing visual acuity in fixed steps.

However, if the image of only one eye is blurred, the fixation disparity does change with prism vergence, which indicates a less exact fusion. In these experiments the images were blurred by a +1.0D. sph. and the special occluder glass, both of which reduced the acuity of the eye to about 20/70. The effect of the blurring of the image of one eye on fixation disparity was somewhat different according to the two groups of subjects described previously. Figures 7 and 8 show the results obtained. In Figure 7, the curve changes markedly when the image is blurred, both for forced convergence and for forced divergence. In Figure 8, the change appears as a vertical displacement of the curve and occurs more significantly for divergence than for convergence.

Peripheral fusion. If the details for fusion are limited more and more to the peripheral

Fig. 7 (Ogle, Mussey, and Prangen). Influence of blurring the image of one eye on the fusion.

visual field, the fixation disparity curves change markedly, although again this is different in the two groups of subjects. By increasing the size of the blanked-out square in the projected fusion pattern on the

screen, in the center of which the vernier arrows are seen, the images which can be fused are restricted more to the periphery of the retinas.

Voluntary eye movements do not occur,

Fig. 8 (Ogle, Mussey, and Prangen). Influence of blurring the image of one eye on the fusion.

for the eyes are fixated at the center if they are to see any displacement of the arrows. Squares used to test this effect were of angular sizes of 0.75, 1.5, 3, and 6 degrees of arc subtended at the subject. The results obtained on two subjects, as examples of the two groups, are illustrated graphically.

In the first case (fig. 9) for a given convergence the fixation disparity increases rapidly as the size of the blanked-out area increases. Since Panum's areas in the periphery are many times larger than those in central vision, such increased disparity is possible while still maintaining fusion. The precision of the data decreased also. The response of this subject is entirely consistent with the previous data (compare Figure 5 for F. M.).

Figure 10 shows how peripheral fusion influences the fixation disparity in the second type of subject (compare Figure 6 for K. N. O.).

The data were obtained for the series of target sizes at each prism setting, in the same order as shown in Table 1; hence the

Fig. 9 (Ogle, Mussey, and Prangen). Influence of peripheral fusion on fixation disparity.

results found were not cumulative effects of the forced vergences. Again the data are consistent. The fixation disparity increases as the fusion is pushed into the periphery, but here this is evident by a vertical displacement of the curve in the convergent direc-

Fig. 10 (Ogle, Mussey, and Prangen). Influence of peripheral fusion on fixation disparity.

tion. As the forced convergence increases, the deviation then changes rather slowly toward the divergent direction.

For the subject whose data are illustrated in Figure 9, the curves for different-sized, central targets deviate even more if a red glass is used before one eye and a green glass before the other (fig. 11). This suggests that a red-green visual rivalry (such rivalry was experienced during the test) acts as a further hindrance to exact fusion.
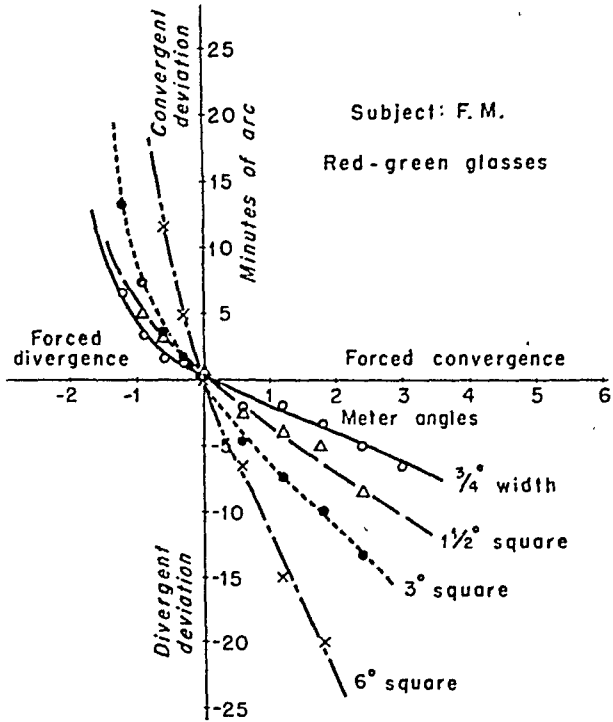
Fig. 11 (Ogle, Mussey, and Prangen). Influence of red-green glasses for different degrees of peripheral fusion on fixation disparity.

However, the red-green glasses on the second subject had only a small effect on the results obtained, and almost no rivalry was experienced.

Effect of lenses. Because the change in fixation disparity with forced convergence or divergence is probably associated with the convergence-accommodation reflex, similar changes might be expected when the stimulus to accommodation was also changed, as, for example, when spherical ophthalmic lenses are placed before the eyes. Such a
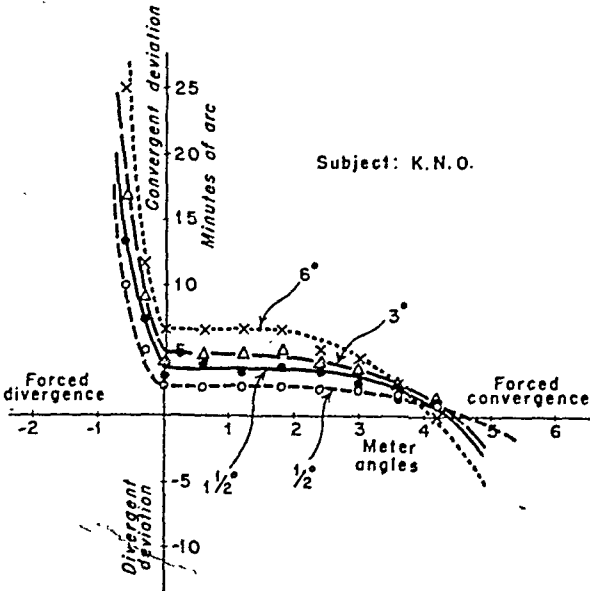
change has been reported in the displacement of the longitudinal horopter as determined by the nonius method, when plus lenses were worn by the esophoric observer. Certainly the problem being studied would not be complete without such a consideration.

The procedure was to obtain data for the curves for the fixation disparity with forced changes in the convergence while spherical lenses are placed before the two eyes, for both distant and near vision.

NEAR-VISION TEST

Instrumentation. For the near-vision tests new instrumentation was necessary. A light box with a transparency plate in front was used instead of the projector lanterns and screen. Figure 12 illustrates the apparatus schematically. The features are essentially the same as those for the distant-vision apparatus, and no further description is necessary.

The fixation distance was 29 cm. (3.4
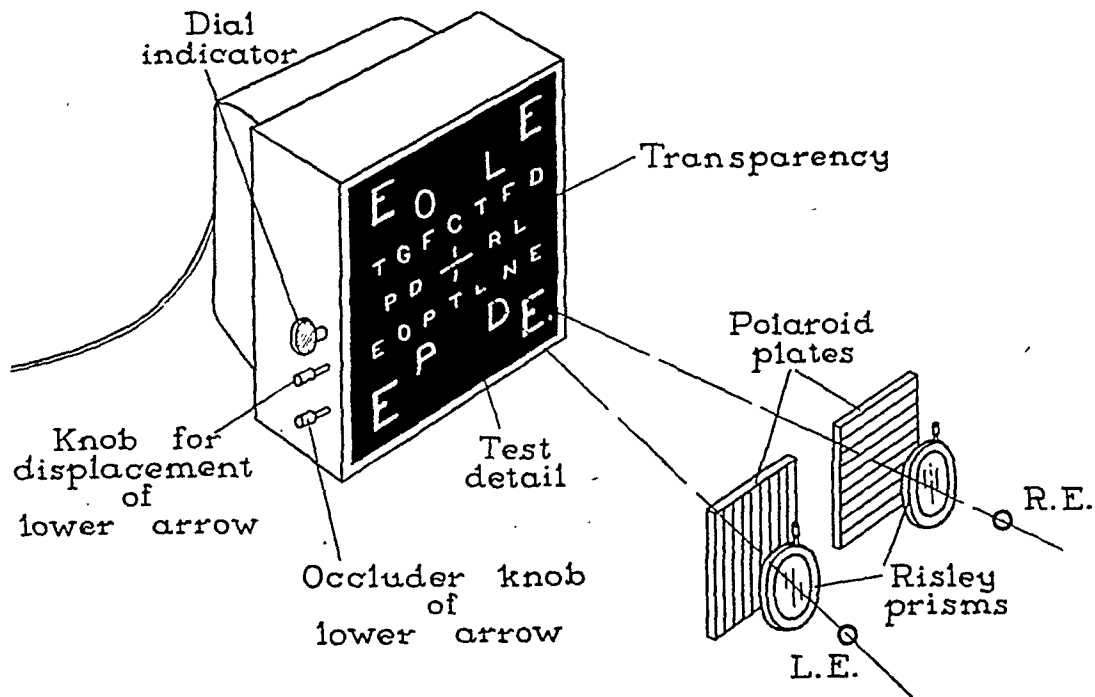
Fig. 12 (Ogle, Mussey, and Prangen). Perspective drawing of apparatus for measuring fixation disparity at near visual distances.

For distant vision, three sets of data were obtained: with the usual or with no refractive correction, and with supplemental lenses of +1.0D. sph. and —1.0D. sph. before both eyes. In each case the added sphere caused a displacement of the curves. As would be expected, the fixation disparity changes in the divergent direction with plus spheres, and in the convergent direction with minus spheres, which is in the direction that the phoria would also tend to change. The addition of the plus spheres in both cases blurred the vision somewhat, but not sufficiently to prevent data being taken, although the sensitivity was reduced.

diopters). If the subject had adequate accommodation, supplemental lenses of +2.0D. sph. and —2.0D. sph. were used, while if not, as in beginning presbyopia, supplemental lenses of +2.0D. sph. and +4.0D. sph. were used.

Characteristic curves were obtained, showing the marked influence of the stimulus to accommodation, and of the probable accommodation which took place, on the fixation disparity. Figures 13 and 14 show results of two subjects, characteristic of the two types.

It is of special interest to derive from these curves the various combinations of spheres
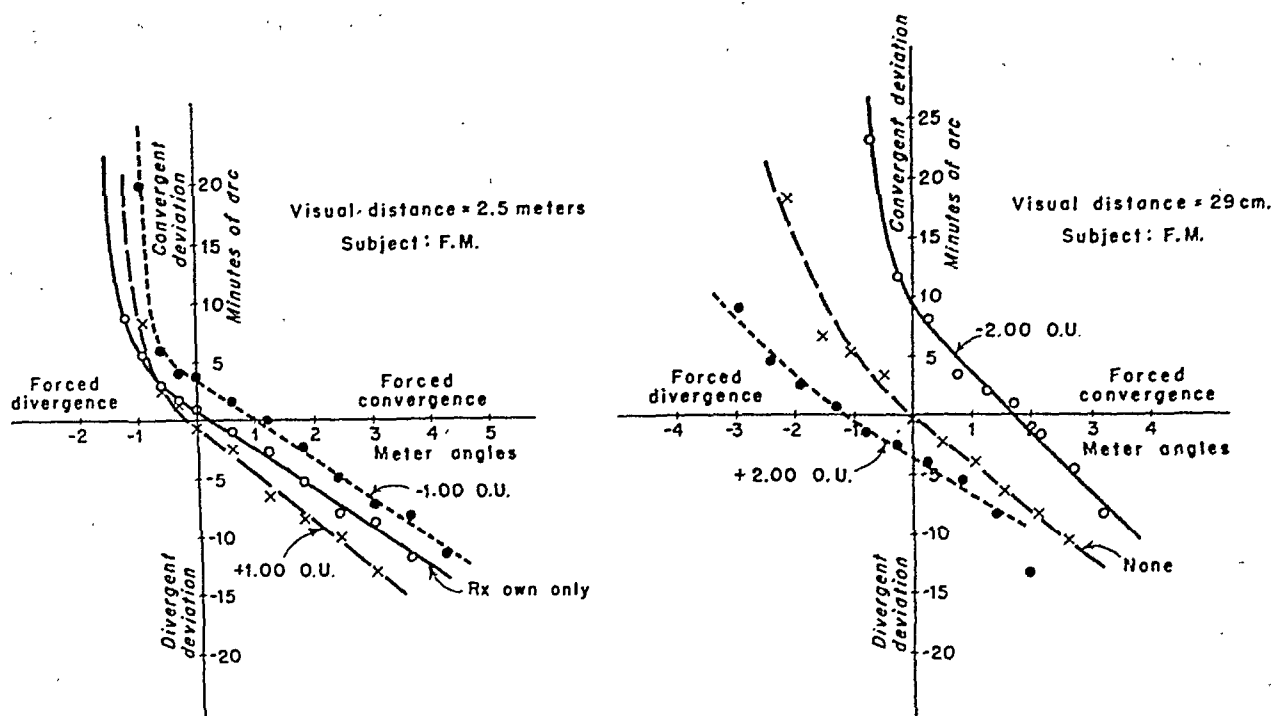
Fig. 13 (Ogle, Mussey, and Prangen). Effect of spherical lenses on the fixation disparity-convergence curve for visual distances of 2.5 meters and 29 cm.

and meter angles of convergence (prism power) each of which results in a given fixation disparity, especially a zero disparity, for then the cortical images would be exactly superimposed. Examples of such derived data are illustrated in Figure 15, for the two subjects for both distant and near vision.

In these graphs the abscissa represents the lens power and the ordinate the forced vergence—convergence positive and divergence negative. The values for forced vergence are measured from the meter angles of convergence corresponding to the distance of the target. Some inaccuracy cannot be avoided in selecting the place where a given
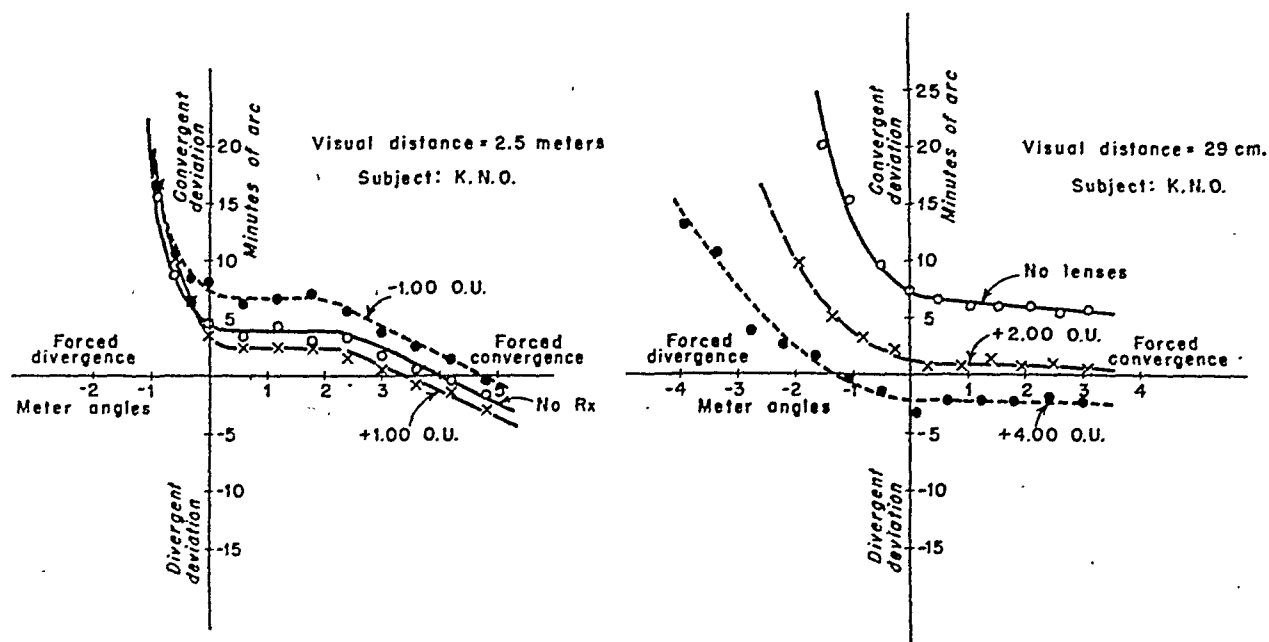
Fig. 14 (Ogle, Mussey, and Prangen). Effect of spherical lenses on the fixation disparity-convergence curve for visual distances of 2.5 meters and 29 cm.

curve in the original graph intersects the ordinate of a given fixation disparity. However, the results are not much in error.

The average slope of these lines is a measure of the comparative influence of prisms and lenses on fixation disparity and the convergence-accommodative relationship. For the two subjects illustrated here about 0.6 to 0.8 meter angle of convergence (3 to

tainly this could be taken as the condition of no muscular imbalance and perfect fusion, and as such it would be desirable. As far as the spherical lenses are concerned, it appears that when the subject wears the proper refractive correction the fixation disparity is small, if not actually zero.

The deficiency in the experimentation reported here lies in the fact that the actual
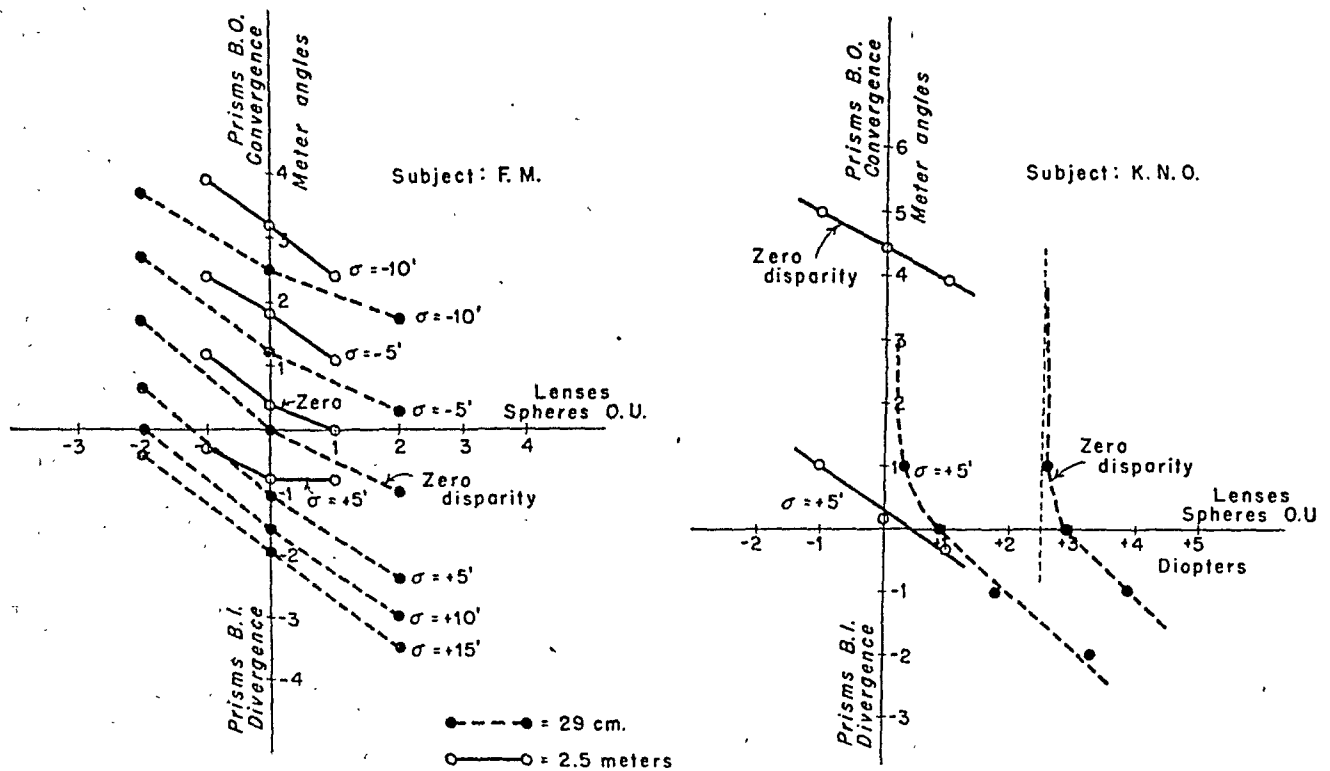
Fig. 15 (Ogle, Mussey, and Prangen). Derived data from Figures 13 and 14 showing comparative influence of prisms, forced vergence, and spherical ophthalmic lenses.

4 prism diopters) has the equivalent effect on fixation disparity of 1 diopter of lens power before the two eyes.

The approximate parallelism of the lines in these derived graphs certainly can be taken as evidence that the fixation disparity is a specific measure of the stress of muscle imbalance during fusion. The approximate parallelism of the lines indicates also that the addition of the spherical lenses has caused in the main a displacement of the curves, that is, has added a constant factor.

At this time it is not possible to attach special significance or functional importance to the "zero" disparity line, although certainly

state of accommodation in any given combination of lenses or prisms can only be presumed from the presence or absence of blur (loss of visual acuity). Reliance was placed on previous experimentation by one of us, which showed that the maximal change in accommodation with prism vergence was of the order of ±0.25 diopter, and on the literature, for the statement that the accommodation changes only very slightly for forced convergence or divergence except near the limits.

COMMENT

A fixation disparity can be measured in most subjects who show a heterophoria, re-

gardless of the type of fusion detail used in the target. This means, in general, that the retinal images of the point of fixation do not fall exactly on corresponding points.

Although ideally the fusion compulsion reflex strives to direct the pointing of the eyes so that the images fall as nearly as possible on corresponding retinal elements, it may only be able to keep the images within Panum's areas of fusion because of innervations or mechanical stresses which make up muscle imbalances. Thus the two cortical images arising from the two eyes will be slightly displaced or slipped with respect to each other.

By and large the direction of the fixation disparity is the same as that of the hetero-phoria, although apparently not correlated quantitatively with it, probably because the phoria is a phenomenon of the disassociated eyes. Fixation disparity *a priori* need not always be associated with a phoria. The stresses of dynamic muscular balance active during actual fusion may be the result not only of mechanical and tonic neuromuscular effects but also of functional innervations, all of which would not necessarily be present when the eyes are disassociated.

Occasionally, the initial fixation disparity is found in the direction opposite to the phoria, and generally this occurs in the case of a small esophoria which nevertheless exhibits a divergent deviation. The possible influence of "instrumental convergence" must not be excluded in the phoria measurement.

The subjects seem to fall into two more or less distinct groups according to the way in which the fixation disparity (cortical image slip) changes with forced convergence and divergence of the eyes. In the first group, the deviation increases with the degree of forced convergence, while in the second, the fixation disparity remains nearly constant with the degree of forced convergence or divergence, except near the limits of the fusional amplitudes. From one point of view these data indicate that in the

first type, fusion is more loosely held and the cortical images are more liable to slipping than in the second type, in which the fusion is more tightly held until the limits of fusional amplitudes are reached.

The existence of a more or less constant fixation disparity in the second type is difficult to account for. In a tightly held fusion, the second type of curve would be expected, but with the greater part of the curve coinciding with the abscissal axis, that is, with the fixation disparity zero. Only near the limits of the fusional amplitudes would there be a sudden change in the curve. The measurements of the fixation disparity as the fusion details are confined more and more peripherally constitute a crucial experiment. Otherwise, it might be argued that the constant deviation in the second group might be the result of an adapted change in the sensory subjective direction, in the same sense of an anomalous correspondence, developed by a constant fixation disparity under the influence of a neuromuscular tension.

The better explanation for these results is that the stress set up in the accommodative-convergence relationship produced by the prisms differs greatly with different individuals. Here two groups could be differentiated. In the first, a real stress is caused by the prisms, in an effort to resist the forced convergence. In addition to these stresses, there must be those manifested by the phoria. In the second group, the disproportion between the accommodation and the convergence due to the prisms introduces little or no additional stress at all; there is practically *no resistance to the prisms*, as though the accommodation and convergence relationship was exceedingly elastic, until the degree of convergence or divergence becomes great. Thus, in spite of the forced convergence caused by the prisms, only those stresses manifested by the phoria remain as the sole source for the ocular deviation. Hence, the fixation disparity would tend to remain constant. It would tend to be constant for a given pattern of fusion detail and only

secondarily to be influenced by a change in phoria with convergence.

Since the accommodative-convergence relationship is affected by lenses, which change the stimulus to accommodation, as well as by prisms, the fixation disparity is changed by lenses. In general it appears that the fixation disparity-prism vergence curves are displaced laterally, as though the lenses merely added a constant equivalent prism vergence change. The magnitude of this equivalence is about 0.6 meter angle (3.5 to 4 prism diopters) to 1 diopter lens power, although in one case of probable convergence insufficiency this was only 0.2-meter angle (1.5 prism diopters) to 1 diopter lens power.

These results show that fixation disparity is an indication, if not an actual measure, of the muscular imbalance when the images in the two eyes are fused. The magnitude of the fixation disparity, however, will depend not only on the stress of that muscular imbalance but also on the strength of the fusional reflex processes.

These results also suggest that the therapeutic results from the prescription of prisms would be different for the two groups of subjects as well as in specific cases. In the first they might prove helpful, in the second not at all. One could argue, however, that a much tighter fusion exists in the second group than in the first.

The interpretation of the prism vergence or fusional amplitude tests should be different for these two types of subjects.

Mayo Clinic.

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ANTISTINE: A STUDY OF ITS TOXICITY ON TOPICAL APPLICATION TO THE EYE*

T. F. SCHLAEGEL, JR., M.D.

Indianapolis, Indiana

Antistine hydrochloride is a relatively new antihistaminic available for topical application to the eye. The oral use of such drugs as Benadryl and Pyribenzamine for the ocular symptoms of allergy has been disappointing.[1] The probable explanation is that insufficient drug reaches the site of the allergy.[2] Antistine, developed in an attempt to overcome this disadvantage, gives promise of symptomatic relief.[1] Since Antistine was the only antihistaminic commercially available for topical application to the eye at the time of these experiments, this study was limited to Antistine.

Clinical trial has not demonstrated any unusual reactions. Occasionally conjunctival congestion occurs and rarely an allergic reaction may be seen.[2a, 2b]

Recently Grant and Loeb reported on the toxicity of several different antihistaminics on the rabbit eye.[3] They studied the approximate maximum concentration at which no alteration in the rabbit cornea occurs, as shown by examination with the slitlamp, after a single drop of solution. For Antistine hydrochloride this concentration was 1.5 percent. At slightly higher concentrations, a temporary keratitis epithelialis develops. At still higher concentrations, corneal edema and loss of epithelium occurs. They found from the subjective standpoint that 0.75 percent Antistine produced the same discomfort as 0.5-percent tetracaine (Pontocaine) hydrochloride in human eyes. By altering the pH of the solutions, it was found that the discomfort was not attributable to excess acidity or alkalinity. None of the drugs produced anesthesia on the application of a single drop.

Recently Hurwitz gave the most comprehensive report of the clinical use of 0.5-percent Antistine. He found that 42 of 50 patients with various external ocular allergies obtained significant symptomatic relief.[1]

CHEMISTRY

Antistine hydrochloride[†] is a synthetic preparation bearing the chemical name of 2-phenyl-benzylaminoethyl-imidazoline hydrochloride. The structural formula is as follows:
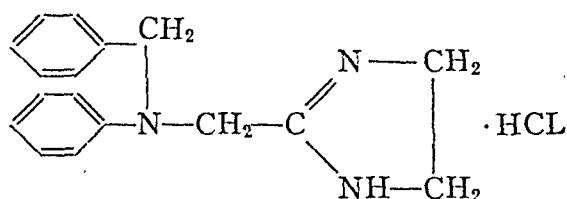
The crystals are white, odorless, and have a bitter taste. Solutions for ocular application originally contained the sulfate salt and it is this product upon which Hurwitz reported.[1] It is now made as the hydrochloride in 0.5-percent concentration with a pH of 6.94 which is close to the pH of tears (7 to 7.5).[4] It is made as an isotonic buffered solution of the following formula:

Antistine hydrochloride	0.50
Boric acid powder U.S.P.	1.20
Sodium carbonate anhydrous	0.05
Potassium chloride C.P. anhydrous	0.15
Distilled water q.s.	100.00

According to Bourquin, Antistine may be combined with other substances such as penicillin, zinc, argyrol, mydriatics, and miotics.[5]

PHARMACOLOGY

A common feature of antihistaminics is an antagonism of all of the major effects of

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† Manufactured by Ciba Pharmaceutical Products, Inc.

histamine except its gastric secretory activity.[6a, 6b] They differ greatly in other respects. Some show an atropinelike action, while others exert a spasmogenic effect in moderate or higher doses. Certain ones augment the pressor effect of epinephrine, while others block or even reverse it. Landau and Gay in Dale tests (inhibition of guinea pig gut contractions) found that within one minute Histadyl, Bromothen, Chlorothen, Pyribenzamine, and Neoantergan completely counteracted five times as much histamine. Within one minute, Benadyl completely antagonized an equal amount of histamine, but Antistine was fully effective against only one half the amount of histamine.[7]

In experiments to counteract the effect of histamine intoxication and anaphylactic shock on guinea pigs, Antistine was again found to be the weakest of the antihistaminics tested.[8] However, no parallel existed between effectiveness against histamine in guinea pigs and their effect against human allergy.[9] Antistine is used systemically in doses larger than that of other compounds (100 mg. tablets). It was found by Gay and others to be the most effective antihistaminic against urticaria and angioneurotic edema and against dermatitis and pruritic conditions of various etiology, and it produced the smallest number of side effects (18 percent).[9]

Despite conflicting reports the consensus is that antihistaminics influence allergic symptoms by a specific antagonism of the pharmacologic effect of histamine.[6a, 10] Although there is no proof of the mechanism of action, the current belief is that they compete with histamine for the same receptor cell, displacing histamine from its point of action.[6a]

EXPERIMENT 1

Effect of Antistine on normal cornea. Since clinical trial has demonstrated an apparent lack of damage to the cornea, it was thought that a preliminary test on a small series of rabbits would be adequate before a more

careful determination of its effect on the normal human cornea. It was found that staining with fluorescein was no more common in eyes treated repeatedly with 0.5-percent Antistine than in normal untreated rabbit eyes.

Effect on human cornea. Ten medical-student volunteers were selected. Both eyes of each were flushed with fluorescein and examined with the slitlamp prior to the experiment. The effect of 0.5-percent Antistine hydrochloride was compared with that of a buffered isotonic control. At intervals of one-half hour for 12 times two drops were instilled above the limbus of each eye. Antistine was used in the right eye and the control solution in the left eyes. The formula for this buffered isotonic control was:

Sodium carbonate anhydrous	0.016
Potassium chloride	0.028
Boric acid crystals	2.500
Distilled water q.s.	100.000

The pH of this solution was 5.80 and was raised to 6.94 by the addition of a few drops of concentrated sodium hydroxide. The experiments of Friedenwald and Buschke have shown that wound healing in the corneal epithelium occurs at a pH from 4.5 to 9.5.[11]

Subjective comments. Burning for a minute or two occurred after application of drops of both Antistine and the control solution but was slightly more pronounced with Antistine.

Gross objective findings. The characteristic reaction to the frequent instillation of drops was a mild to moderate congestion, mainly bulbar in distribution. It was slightly greater in the right eyes receiving Antistine.

Biomicroscopy. At the end of the day, both eyes were again flushed with fluorescein and examined with the slitlamp. In only 1 of the 10 volunteers (number 6) was any change noticed. This volunteer was an agitated "expectant" father. In the right eye treated with Antistine there were small punctate points joined to produce horizontal linear streaks below and nasal to the pupil. In the left eye treated with the control solution a

superficial punctate area, about 3 mm. in diameter, was found near the limbus at the 8-o'clock position. Since the staining was bilateral and more severe in the control eye, it was felt that some intercurrent factors were involved.

Summary. A 0.5-percent solution of Antistine hydrochloride instilled at half-hour intervals for 12 times in 10 human eyes produced no discernible corneal damage attributable to the drug. Bulbar congestion occurred in both eyes, but was slightly greater in those treated with Antistine; the subjective sensation of stinging was slightly greater in the Antistine-treated eyes.

EXPERIMENT 2

The effect of Antistine upon reëpithelization of the denuded rabbit cornea. It is generally known that agents that are noninjurious to the cornea and conjunctiva of the

the fingers. The epithelium was then completely removed by abrasion with sterile gauze. The completeness of denudation was checked by instillation of 2-percent sodium fluorescein followed by a gentle flushing from an eye dropper with a solution of penicillin-G potassium, 2,500 units to the ml., which does not delay healing.[13] Two drops were instilled above the limbus of each cornea five times a day.

In Group I the right eyes received 0.25-percent Antistine, and the left eyes, the control solution.

The right eyes of Group II received regular 0.5-percent Antistine, and the left eyes, the control solution.

The right eyes of Group III were given 1-percent and the left eyes 2-percent Antistine.*

TABLE 1

THE DAY OF THE EXPERIMENT ON WHICH DENUDED RABBIT CORNEAS HEALED WHILE UNDER TREATMENT WITH BUFFERED ISOTONIC CONTROL OR WITH VARIOUS STRENGTHS OF ANTISTINE SOLUTION

Drug		Day of Experiment													Average
		4	5	6	7	8	9	10	11	12	13	14	15	etc.	
Group I	Control		2	3	3	1									6.3
	Antistine (0.25%)	1	3	1	4										6.3
Group II	Control			2	4	3	1								7.3
	Antistine (0.5%)		1	1	4	2		1			1				7.9
Group III	Antistine (1%)					3	2	1	1			2			10.3
	Antistine (2%)						3			1		5			12.5

rabbit are equally or even less irritating to that of the human eye and that the cornea is an excellent medium to ascertain information relative to the local tissue effect of drugs.[14]

To test the possible toxic effects of Antistine upon the rabbit cornea more carefully, 30 young adult pigmented rabbits with normal eyes were selected and divided into 3 groups of 10 rabbits each. Four-percent cocaine was used for anesthesia and to loosen the epithelium. To expose and fix the eyes, they were proptosed and held between

Complete denudation has been used frequently.[13-15] Other methods such as disc denudation outlined with a cork borer,[15] strip denudation outlined with double-bladed corneal knife,[16] and needle prick have been employed.[11] De Roetth objected to complete denudation because he felt that it was diffi-

* Supplied through the courtesy of Dr. F. L. Mohr and Ciba Pharmaceutical Products, Inc., Summit, New Jersey. All of the Antistine solutions were formulated to be isotonic and buffered with a constant pH of 6.94 so the only variable was the drug used. The 0.25-, 0.5-, and 1-percent strengths were made as the hydrochloride but the 2-percent strength had to be made up as the sulfate since the hydrochloride is not sufficiently soluble.

cult to be certain that one is producing constant damage.[17]

This objection has validity and is the reason for our separating Group I from Groups II and III in Table 1. The reason for this was that the day following the denudation it was obvious that the first 10 rabbits (Group I) had not been denuded as completely as the last 20, for in the first 10 the epithelium had already begun regeneration but had not in the last 20 rabbits. That this difference was not due to the drugs employed was indicated by the fact that the left eyes of Group I and the left eyes of Group II both received the same control solution. That the completeness of denudation was reliably equal within the groups was indicated by observation and by standardization upon previous rabbits and by frequent repetition of the same maneuver.

Results. The regeneration in uncomplicated cases is easily followed since the crescent of reëpithelized cornea at the limbus stands out brilliantly clear and normal against the greenish stained haze of the denuded area. The eyes were examined daily by staining with fluorescein and flushing gently with a solution of penicillin. Obvious secondary infection was rare. Only one rabbit in Group I was discarded because of delay in healing from secondary infection, while one rabbit in Group III died of intercurrent disease.

Group I. Except for the one discarded rabbit the corneas reëpithelized from the 4th to the 8th day with an average healing time of 6.3 days with both the 0.25-percent Antistine and the isotonic buffered control.

Group II. There was no significant difference in the healing time of the right eyes treated with regular clinical 0.5-percent Antistine hydrochloride (average 7.9 days) and the left eyes treated with the control (average 7.3 days).

Group III. Healing in Groups I and II was complicated only by a faint diffuse haze which was considered the result of super-

ficial stromal damage at the time of denudation. The use of stronger strengths of Antistine caused greater conjunctival congestion, a definite delay in healing, and other evidence of corneal damage. This delay with 1-percent Antistine hydrochloride was moderate (10.3 days) and the corneal damage

Fig. 1 (Schlaegel). Grossly relucent and vascularized rabbit cornea that had been treated with 2-percent Antistine. This cornea had apparently healed as indicated by lack of gross staining with fluorescein.

was moderate with superficial vascularization.

The healing time with 2-percent Antistine sulfate was pronouncedly increased (12.5 days) and the corneal damage was severe. In five of the rabbits, most of the cornea not protected by the nictitating membrane was rendered grossly relucent, densely vascularized, and very slow to heal (fig. 1).

Although clinically healed on the 15th day, microscopic sections revealed that the stroma was covered not by epithelium but by a hyaline membrane 1 to 2 times as thick as Descemet's membrane (fig. 2). Van Gieson stain indicated that the hyaline membrane was modified superficial stroma.

Summary. The use of Antistine five times a day on completely denuded rabbit corneas demonstrated that the 0.25- and 0.5-percent solutions do not delay healing over that of the control solution, but that the 1-percent and especially the 2-percent strengths are definitely toxic, resulting in delayed healing and vascularized scars.
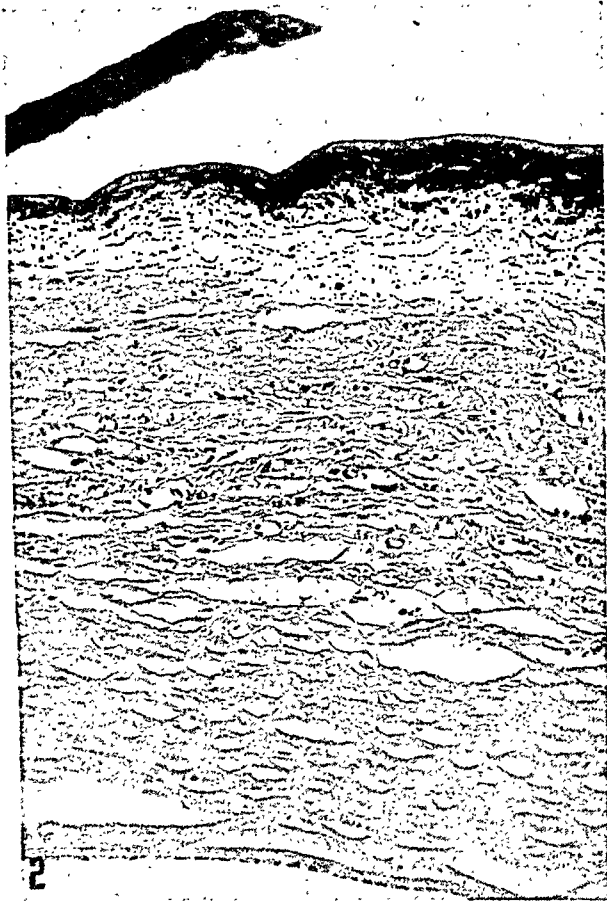
Fig. 2 (Schlaegel). Microscopic sections revealed that the cornea had not become reëpithelized, but that the superficial stroma had developed a hyaline membrane. Degeneration, vascularization, and cellular infiltration of anterior two thirds of stroma.

EXPERIMENT 3

Effect of Antistine on the size of pupil and upon accommodation. Since some of the antihistaminics demonstrate an atropinelike, spasmogenic, or adrenergic response, it was felt necessary to check the pupil and ciliary body for signs of effect. Harris, McGavack, and Elias found that Benadryl applied topically to the bulbar conjunctiva in 0.5-percent aqueous solution produced a moderate mydriasis of readily measurable proportions which appeared within 15 minutes and became maximum within one hour.[18] The capacity for accommodation was simultaneously decreased. Benadryl enhanced the mydriasis of homatropine and lessened the miosis of eserine. However, no effect on the pupil was noted from the oral use of 400

mg. of Benadryl daily. In their studies of Antistine hydrochloride, Benadryl hydrochloride, Decapryn, Histadyl, Neoantergan, Pyribenzamine, Thenylene, and Thephorin, Grant and Loeb noted that only Benadryl hydrochloride had a noticeable mydriatic or cycloplegic effect.[3] Using Benadryl, Antistine, and Pyribenzamine, von Sallmann found that only Antistine did not weaken the miotic action of di-isopropyl fluorophosphate.[19]

Methods. Under constant conditions of illumination, the apparent size of the pupils of the 10 human volunteers previously mentioned was measured before and after the day of drop instillations. Reading was permitted during the experiment. Using a Prince rule with Duane line for test object the nearpoint of accommodation of each eye was checked 10 times both before and after the experiment by bringing the test object toward the subject to the point of blur. Since only the relation between "before" and "after" was desired the total cycloplogic error was not determined and glasses were worn only if desired.

Results (Pupil). Table 2 clearly demonstrates an absence of effect on the pupil. *(Accommodation).* Table 3 gives the results of the average value of the 10 measure-

TABLE 2

THE APPARENT PUPILLARY DIAMETER IN MM. OF THE EYES OF 10 HUMAN VOLUNTEERS "BEFORE" AND "AFTER" 12 INSTILLATIONS OF ANTISTINE (0.5 PERCENT) TO THE RIGHT EYES AND CONTROL SOLUTION TO THE LEFT EYES

Volunteer	Right Eyes (Antistine)		Left Eyes (Control)	
	Before	After	Before	After
1	4.50	4.50	4.00	4.00
2	4.50	5.00	4.50	5.00
3	3.50	3.50	3.75	3.50
4	3.50	3.50	3.50	4.00
5	4.50	4.50	5.00	5.00
6	4.50	4.50	4.50	4.50
7	4.00	4.75	4.50	5.00
8	4.00	4.00	4.00	4.50
9	5.00	5.00	6.00	5.00
10	5.00	4.50	5.00	4.50
Average	4.30	4.38	4.48	4.50

ments of accommodation of each eye both before and after the experiment. The average for the 10 subjects indicates an increase in accommodative power of the right eyes (Antistine) of 2.3 cm. and an increase in the left eyes (control solution) of 1.2 cm.,

TABLE 3

THE AVERAGE OF 10 DETERMINATIONS OF THE NEAR POINT OF ACCOMMODATION MEASURED IN CM. FOR EACH EYE OF 10 VOLUNTEERS BOTH "BEFORE" AND "AFTER" 12 INSTILLATIONS OF ANTISTINE (0.5 PERCENT) TO THE RIGHT EYES AND CONTROL SOLUTION TO THE LEFT EYES

Volunteer	Right Eyes (Antistine)		Left Eyes (Control)	
	Before	After	Before	After
1	22.7	16.4	17.9	14.3
2	16.1	16.1	15.3	16.1
3	17.0	11.5	15.2	12.6
4	9.4	8.5	9.2	9.7
5	13.0	12.9	12.8	13.9
6	13.0	12.9	13.8	12.9
7	18.7	13.7	18.1	15.7
8	13.5	14.4	12.7	10.8
9	14.7	15.6	15.9	15.7
10	17.8	10.4	14.2	11.4
Average P.P.	15.5	13.2	14.5	13.3
Standard Deviation	3.5	2.4	2.5	2.1

but statistical analysis indicates that none of these differences is significant.

Summary. Antistine hydrochlroide (0.5-percent) applied as drops 12 times in one day to the eyes of 10 human volunteers failed to affect the size of the pupil or the accommodation.

COMMENT

Experimental studies of the toxicity of antibiotics on the cornea indicate that many of them, especially in the powder or ointment form, produce some damage.[12, 14-16,20] It has also been shown that anesthetics and antiseptics commonly employed in ophthalmology are even more toxic to the cornea.[13, 21, 22] Since Antistine hydrochloride solution in 0.25- and 0.5-percent strengths did not produce corneal damage in these experiments, Antistine as commercially supplied (0.5-percent solution) should be a safe drug to add to our armamentarium.

GENERAL SUMMARY

1. Antistine hydrochloride (0.5-percent) instilled repeatedly in 10 human eyes produced no discernible corneal damage. Bulbar congestion and subjective stinging were slightly greater with Antistine than with the control solution.

2. The use of Antistine on completely denuded rabbit corneas demonstrated that 0.25- and 0.5-percent solutions do not delay healing longer than does a control solution, but that the 1-percent and especially the 2-percent strengths are definitely toxic.

3. Antistine hydrochloride (0.5-percent) applied as drops 12 times in one day to the eyes of 10 human volunteers failed to affect the size of the pupil or the accommodation.

CONCLUSIONS

These experiments indicate that 0.5-percent Antistine hydrochloride is not toxic to the cornea and does not affect the pupil or accommodation.

1040 West Michigan Street (7).

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THE EFFECT OF DICUMAROL ON THE VISUAL FIELDS IN GLAUCOMA*

A PRELIMINARY REPORT

WILLIAM P. McGUIRE, M.D.
Winchester, Virginia

The problem of progressive loss of visual field following a successful filtration operation in glaucoma is one that has plagued ophthalmologists for years. The general consensus seems to be that these changes are due to an irreversible vascular process which is set up while the tension is above normal limits and has progressed sufficiently so that when the tension is reduced, either by surgical or medical means, there is no regression, but apparently a continued progression of the vascular process.

As far as can be determined, no completely satisfactory pathologic observations have been made on the ocular vascular system in early cases of chronic simple glaucoma. Duke-Elder[1] states that there is a vascular stasis and quotes three individual case reports by Levinsohn, 1908, Ronne, 1913, and Hanssen, 1918, in which all showed evidence of circulatory stasis and vascular lesions, either of periphlebitis or endophlebitis of the episcleral or vortex veins, with areas of leukocytic infiltration.

Knapp,[2] in reporting on cases of atrophy of the optic nerve with cupping and low tension, states that "atheromatous carotid arteries cannot alone cause this descending atrophy, but the condition must be caused by simultaneous circulatory disturbances in the optic nerve from arteriosclerotic vascular changes."

Best[3] called attention to the fact that arteriosclerotic changes in the small nutrient vessels may damage the optic nerve, while Siegert[4] and von Stief[5] believed that the cause of optic atrophy in cases of "pseudoglaucoma" are the result of arteriosclerotic changes in the vessels supplying the optic paths.

Gradle,[6] in discussing glaucomatous cupping and atrophy of the optic nerve in cases where the tension was never found to be elevated, held that the condition begins as a low-grade neuritis limited to the anterior third of the optic nerve, the vessel-bearing portion, and leading to an absorption of the nerve fibers, producing the cavernous changes in the nerve described by Schnabel.[7] Lagrange and Beauvieux[8] found sclerosis and obliteration of the small nutritive vessels of the nerve in several cases of primary glaucoma.

Loewenstein[9] demonstrated changes in the walls and thromboses in the small vessels of the optic nerve, producing cavernous degeneration and sclerotic plaques. He concluded that the degenerative changes found in the nerve in glaucoma are the result of vascular damage with impairment of nutrition rather than the effect of increased intraocular pressure.

It is interesting to note that the recent studies of Putnam[10] and his co-workers on the etiology of disseminated sclerosis present some evidence that vascular thrombosis has a definite bearing on the formation of the plaques found in nerve tissue in this disease. This group has recently treated a series of cases of acute disseminated sclerosis with dicoumarin and report encouraging results in those cases which are characterized by remissions and exacerbations.

Rintelen[11] has described the histologic findings in cases of arteriosclerotic atrophy of the optic nerve. He believes that sclerosis of the central retinal artery has little or no effect on the nerve and that the damage in these cases is due to sclerosis of the small nutrient vessels. Vail[12] states, "It is entirely probable that vascular disease of the nerve may account for the progress of cupping,

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atrophy, and field changes that frequently occur after the ocular hypertension has been quite controlled in true glaucoma, especially in the aged."

In view of these facts and hypotheses it would seem that the most reasonable explanation for the progressive field changes in chronic-simple glaucoma is arteriosclerotic changes in the nutrient vessels of the optic nerve. These changes may involve slowing of the blood stream, narrowing of the lumen of the vessels, formation of atheromatous plaques in the endothelium, and formation of mural thrombi.

In searching for some method to treat these patients, many of whom seem to be in desperate straits, it was believed that a vasodilator might be of benefit if the vasodilatation could be prolonged. Further, it seemed that a drug with anticoagulant properties which would inhibit the formation of thrombi might possibly be of value in the treatment of these cases. The only drug which met both of these requirements was dicumarol.

Schofield,[13] in 1924, and Roderick,[14] in 1929, reported on hemorrhage disease in cattle following ingestion of spoiled sweet-clover hay. In 1939, Link[15] and his associates isolated and crystallized the active principle in spoiled sweet-clover hay that was responsible for this disease of cattle. Since that time a great number of experimental and clinical investigations have been made on 3,3'-methylenebis (4-hydroxycoumarin), better known as dicoumarin or dicumarol.

Meyer, Bingham, and Axelrod[16] reported that the administration of the chemical, either orally or intravenously, is succeeded by a protracted prolongation of the prothrombin time and coagulation time. This effect follows an initial latent period of 24 hours following administration of the drug. In therapeutic amounts no untoward symptoms were produced but excessive quantities produced spontaneous hemorrhages and fatalities in dogs.

Bingham, Meyer, and Pohle[17] first noted

that the most constant pathologic change produced by the substance is a widespread dilatation of capillaries, arterioles and venules, and this finding has been confirmed by Wright and Prandoni,[18] Bollman and Preston[19] and Townsent and Mills.[20] It is of interest to note that this vasodilatation occurred in animals whether they died from overdose of the drug or were destroyed for study following therapeutic dosages.

In treating patients suffering from arteriosclerosis obliterans or thromboangiitis obliterans with dicumarol, Wright and Prandoni[18] noted an increased tendency to bleed at the site of ulceration and attributed it to the dilatation of minute vessels. Allen, Barker, and Waugh[21] believe that something in the body is necessary for the action of dicoumarin because if the drug is added to drawn blood, the prothrombin time is not affected. The bleeding time is not affected by the clinical use of the drug but the sedimentation rate is routinely increased.

The method used in administration of the drug in the cases to be reported consisted in hospitalizing the patients and, on the first day of hospitalization, the administration of 300 mg. of dicumarol by mouth.

Routine determination of the prothrombin time, according to the method of Quick[22] was started on the second day in the hospital and carried out daily thereafter. According to this method the normal prothrombin time runs around 11 to 13 seconds. By the administration of dicumarol the prothrombin time was elevated to between 35 to 45 seconds and maintained at that level during the period of hospitalization. The amount of dicumarol to be given each day is determined by the reported prothrombin time of that day. On the average it was found that after the initial dosage of the drug a daily dosage of 100 mg. was sufficient to maintain the desired level in the blood, although on occasion the dose had to be decreased or increased for a day or so.

It is of interest to note in this connection that, if there appears to be some danger of

hemorrhage, the prothrombin time can be reduced dramatically by the intramuscular injection of 50,000 units of penicillin. This will reduce the prothrombin time but will not prevent it being raised again to the desired level by the administration of dicumarol, while the intravenous use of vitamin K will not only reduce the prothrombin time but keep it at low levels for several days in spite of the continued use of the anticoagulant.

Of the nine cases to be reported in this paper, dicumarol was initially administered for a period of two weeks only. However, several patients have had a second course of the drug because, while some improvement was noted after the first course, it was felt that further improvement was desirable and consequently further treatment was advised.

The first case reported was perhaps the most dramatic of all. After the first course of dicumarol, from which there was a most striking, and to me unbelievable, response, the fields held well for a period of 10 months. At this time it was noted that there was again a marked lower nasal field cut to within 10 degrees of fixation. The patient was given a second course of the drug and one month after this the field had again become almost normal while a month later it was within normal limits and has remained so until the present, 8 months after the last course of dicumarol.

This quite naturally brings up the question as to whether it is necessary to give repeated courses of the drug and at what intervals these should be given, or whether, as in the case of some patients who have suffered thrombosis of the coronary artery, a maintenance dose of the drug should be given for some months or years. I am not prepared to answer this question definitely at the present time, although I do have three elderly patients with advanced field changes on a maintenance dose at this time. These patients all had increased intraocular pressure which was reduced by operation, but I believe that the field changes in them were more characteristic of an arteriosclerosis of

the vessels supplying the optic pathways than of those which we ordinarily associate with glaucoma. It is too early to speculate what the outcome will be in these elderly patients for if, after further study, this therapy proves to be of value in treating the visual changes in long-standing glaucoma it is my belief that the older patient with advanced field changes, due in all probability to arteriosclerosis, will prove to be the most intractable type of case for such treatment.

Again, although I have not yet carried out such a procedure, I have the feeling that, if dicumarol proves to be of value in these cases, probably the most advantageous use of the drug would be its long-continued administration over a period of years with weekly checks on the prothrombin time after the blood level is finally stablized.

CASE REPORTS

Case 1. W. G., aged 44 years. This Negro was first seen on December 12, 1944, complaining of early presbyopic symptoms. He stated that the vision in the right eye had been failing for some years but he thought the left eye was all right and that all he needed was some reading glasses. There was no history of pain or congestion in the eyes at any time. Vision was: O.D., hand movements at one foot; O.S., 20/30.

External examination was negative with the exception of the pupils which were semidilated and reacted poorly. The media were clear while the fundi showed a minimal arteriolar sclerosis and a deep cupping of each disc of the glaucomatous type, the pallor of the nervehead being more marked in the right eye.

The vision in the right eye could not be improved while in the left it was improved to 20/20 by +0.5D. sph. Intraocular pressure was O.D., 29 mm. Hg; O.S., 42 mm. Hg (Schiøtz). No visual field was obtainable in the right eye while that in the left eye revealed a marked defect in both the upper and lower nasal quadrants. Pilocarpine (2 percent) was ordered to be instilled four times daily and the patient asked to report in two weeks. At this time the tension was O.D., 25 mm. Hg; O.S. 35 mm. Hg; and operative intervention was advised for the left eye.

On January 7, 1945, a modified Lagrange operation was performed on the left eye. The postoperative course was uneventful, and one month after the surgical procedure tension was O.D., 25 mm. Hg; O.S., 17 mm. Hg. From that time until the present the tension in the left eye has never been above 17 mm. Hg nor below 13 mm. Hg on repeated examinations.

However, on March 31, 1945, almost three months after operation, the field in the left eye showed a good deal more contraction, and three months later the contraction was even more marked. Following this there was a more gradual contraction of the field until December, 1946. At this time the best corrected vision in the left eye was 20/30, but it should be emphasized that at no time during the observation of this patient had the blindspot showed any variation from normal.

weeks later, on November 15th, the field had again returned to normal limits and the corrected vision was 20/20. He was last seen in February, 1948, and the field was holding well.

Case 2. M. W. P., a white man, aged 60 years, was first seen in October, 1936, when he stated that he had lost the sight in the right eye four years previously. He had not consulted a physician and came in merely to see about getting some reading glasses.

Fig. 1 (McGuire). Case 1.

Fig. 2 (McGuire). Case 1.

Dicumarol therapy was ordered on December 12, 1946, and the patient was kept on the medication for 10 days. He was seen again on January 11, 1947, and the field was found to be much improved. Two months later, on March 15th, three months after the dicumarol therapy, he was again checked and the field found to be full in all meridians.

In June of 1947 the field remained normal and he was asked to report again in three months. On September 27, 1947, the field had begun to show a temporal contraction and a marked lower nasal quadrant cut to within 10 degrees of fixation. The blindspot remained unaffected and the best corrected vision was 20/25. At this time he was put on dicumarol for two weeks and on October 18, 1947, the field had shown marked improvement while four

There was no history of pain or inflammation in either eye. There was no light perception in the right eye while the vision in the left was 20/20.

The external examination was negative with the exception of the right pupil which did not react to light and was partially dilated. The media were clear. The fundi showed marked glaucomatous atrophy of the right nervehead and some shallow cupping of the left disc. There was a slight upper nasal contraction of the left field.

Intraocular pressure was: O.D., 48 mm. Hg; O.S., 35 mm. Hg. Pilocarpine was ordered for each eye and under this regimen the tension was reduced to: O.D., 30 mm. Hg, and O.S., 17 mm. Hg. No essential change was noted in the eyes until the middle of 1940, four years after the patient was

first seen, when, in spite of the continued use of miotics the tension began to rise slightly in the left eye. Between May and December, 1940, the tension varied between 17 mm. Hg and 35 mm. Hg in the left eye with a base curve which was showing a slow but constant increase. On December 31, 1940,
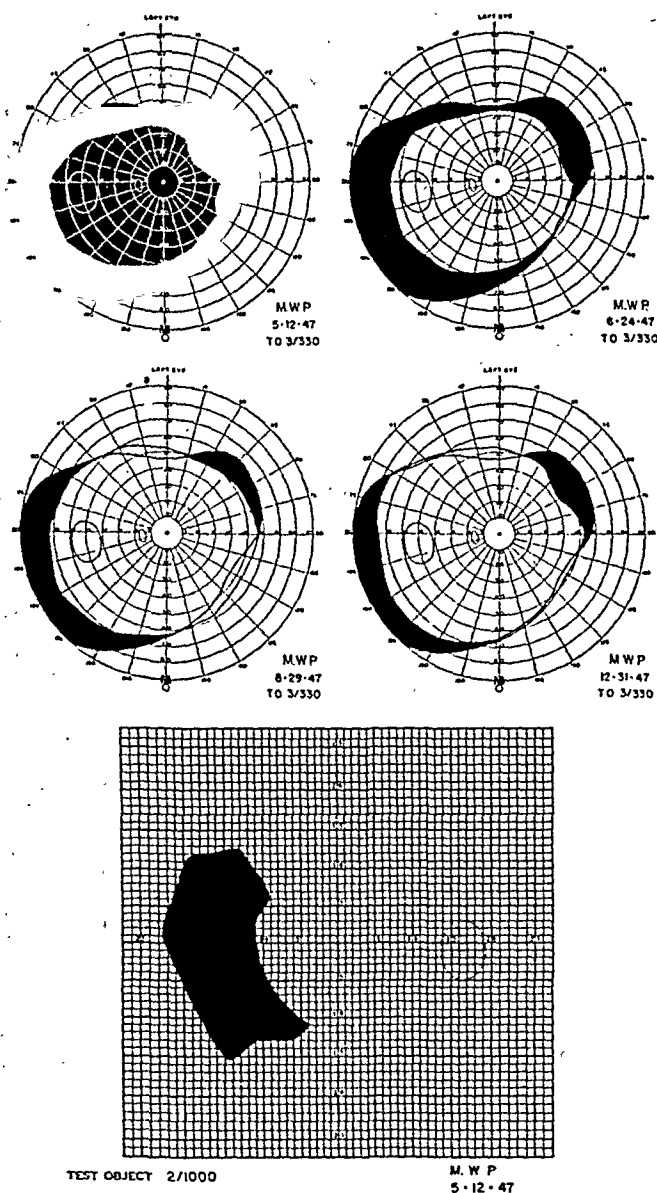
Fig. 3 (McGuire). Case 2.

a trephination was done on the left eye, following which the tension was reduced from 40 mm. Hg to 15 mm. Hg, in which neighborhood it remained for several years.

During late 1943, the patient developed an acute exacerbation of the glaucoma in the blind right eye and a complete iridectomy was performed by Dr. Louis S. Greene in January, 1944. This served to reduce the tension for only a few months and then the patient began to develop spontaneous hemorrhages from the iris in the right eye and the globe was enucleated in May, 1945. In the meantime the tension and the field in the left eye had been holding well. In August, 1946, it was noted that the field in the left eye had begun to show a little more

contraction and a 48-hour tension curve was done with the highest tension recorded at 22 mm. Hg (Schiøtz).

In May, 1947, the field was found to be more contracted and the blindspot definitely enlarged. Dicumarol therapy was advised and the patient entered the hospital for this therapy on May 15, 1947. He had two weeks on the drug and, on June 24th, it was noted that the nervehead was of better color and the field was improved. On August 29th the field showed continued improvement and the
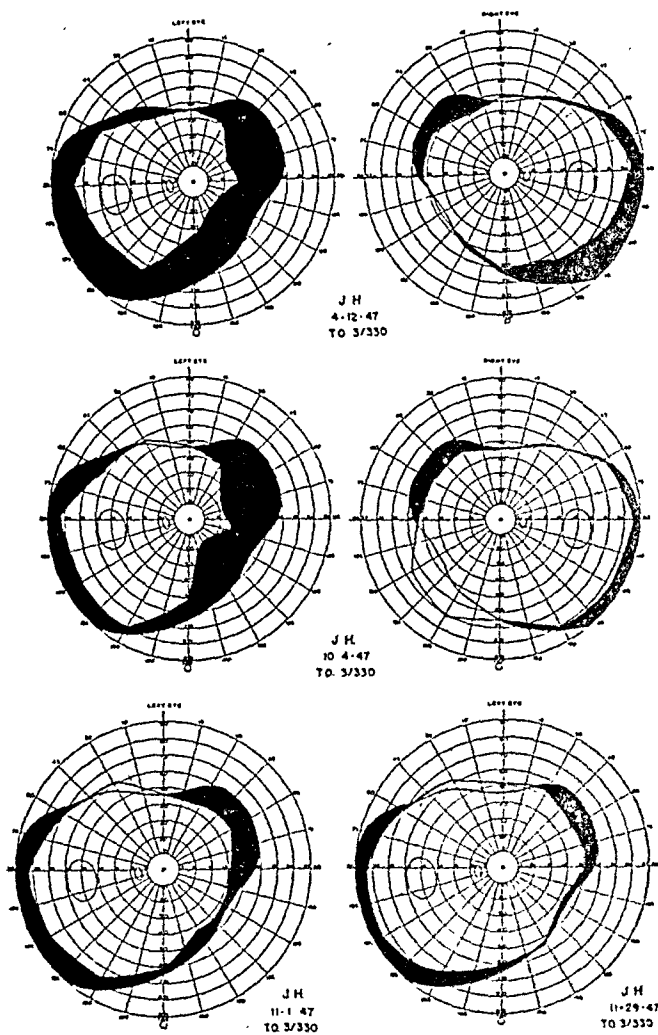
Fig. 4 (McGuire). Case 3.

blindspot was about normal in size, while the fields were maintained at the same level on December 31, 1947.

In this case the central vision in the left eye has never been worse than 20/30, corrected, and, when the patient was last seen, it was corrected to 20/20.

Case 3. J. L. H., a white man, aged 45 years, was first seen in August, 1944, when he came to the office for a change of glasses. There was no history of ocular trouble other than the usual presbyopic symptoms. The vision was 20/20 in each eye, corrected to 20/15 in the right eye and 20/15 in the left. The external examination was negative and the media were clear. The fundi were normal with
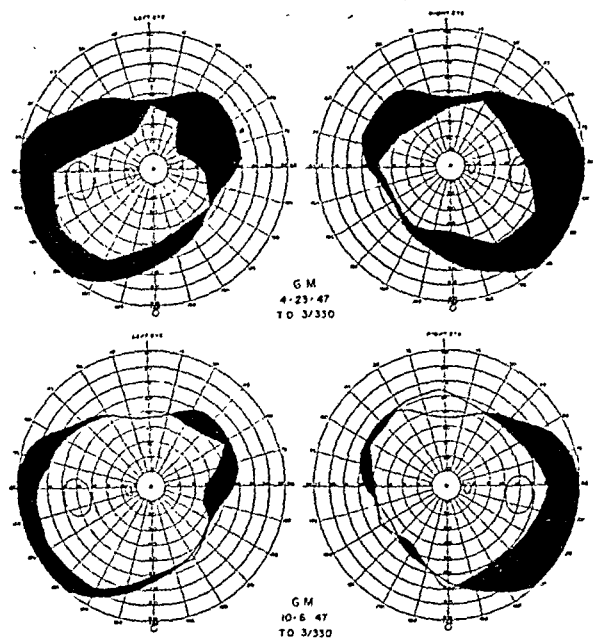
Fig. 5 (McGuire). Case 4.
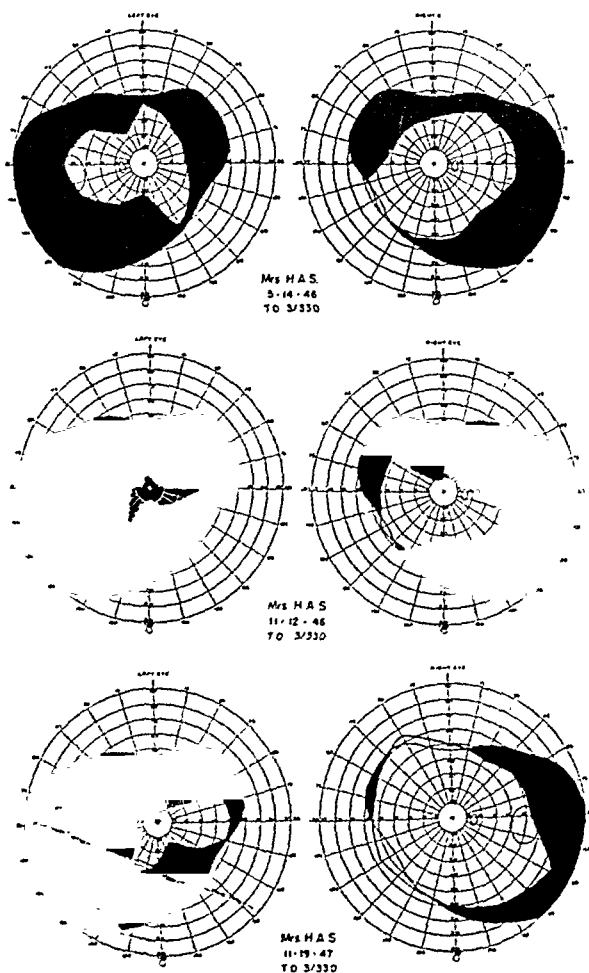
Fig. 6 (McGuire). Case 5.

the exception of the left nervehead which showed a moderate pallor and a shallow cupping.

Intraocular pressure was: O.D., 17 mm. Hg; O.S., 29 mm. Hg. The right field was full while the left showed some upper nasal contraction, although this was not marked. The patient was placed on pilocarpine but the tension remained unchanged.

TEST OBJECT 2/1000   Mrs C B
                                  6-25-47
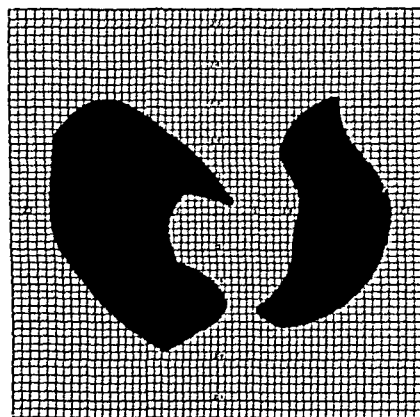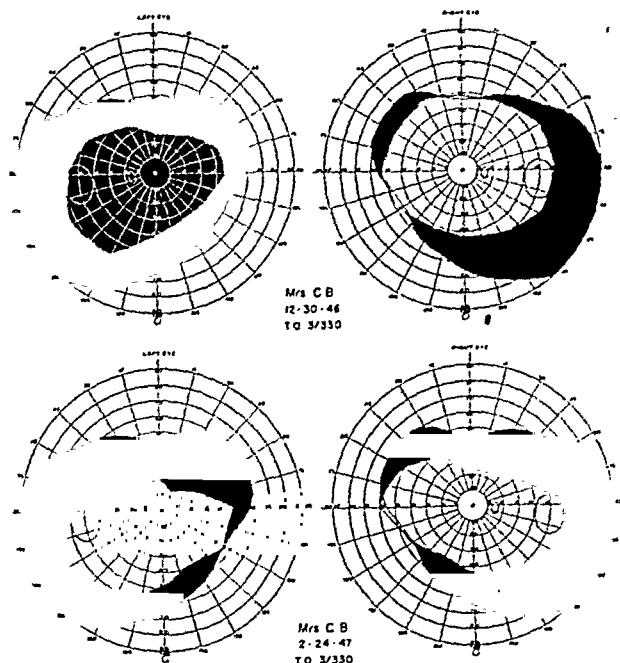
Fig. 7 (McGuire). Case 6.

On December 2, 1944, a trephination was done on the left eye. Following this procedure the tension dropped to 6 mm. Hg but, within a month, had risen to 35 mm. Hg. Miotics were again ordered and the tension was slowly reduced to normal limits.

From June, 1945, until April, 1947, the patient did not report for a checkup and, when he finally was seen on April 12, 1947, he reported that his eyes had been comfortable but that he thought he needed more help in reading. At this time the corrected vision was 20/15 in the right eye and 20/25

in the left. The fundi showed no appreciable change. Tension was: O.D., 17 mm. Hg; O.S., 22 mm. Hg.

The left field showed more contraction. On October 4, 1947, the field showed even more contraction and the blindspot a marked enlargement. Dicumarol therapy was advised. The patient entered the hospital on October 8th and received dicumarol for two weeks. On November 1st, the field showed marked improvement and, on November 29th, slightly more improvement was apparent while the

blindspot had been materially reduced in size. At this time the corrected vision remained at 20/25 and the tension at 22 mm. Hg in the left eye. When last seen in April, 1948, the field and blindspot showed no appreciable change over a period of almost five months.
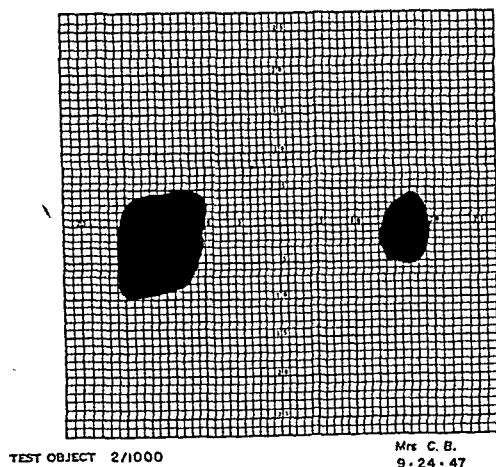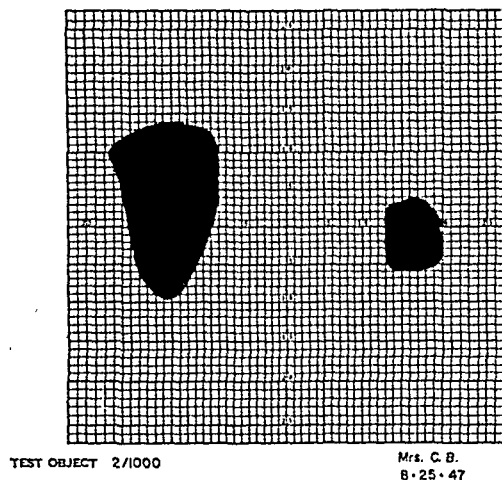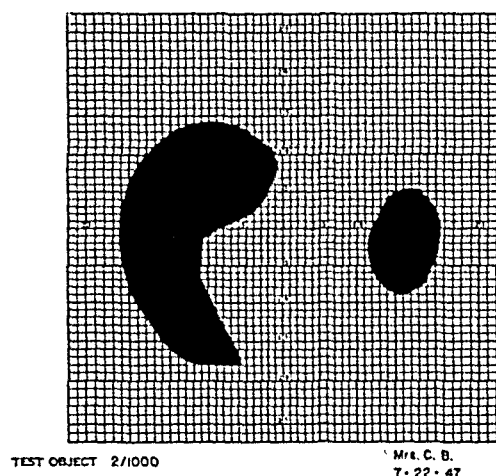
Fig. 9 (McGuire). Case 6.

Fig. 8 (McGuire). Case 6.

Case 4. G. W. M., a white man, aged 74 years, was first seen in April, 1944, with a vision of 20/200 in each eye, corrected to: O.D., 20/70; O.S., 20/20—. There was a nuclear sclerosis in each lens and a shallow cupping of each disc.

Intraocular pressure was: O.D., 29 mm. Hg; O.S., 40 mm. Hg, and there was a slight concentric contraction of the visual field in each eye. The patient was ordered to use miotics and was followed in the office at intervals. By April, 1947, the tension had risen to 40 mm. Hg in each eye and the fields showed more cut in each eye.

In May, 1947, a flap sclerotomy was done bilaterally and dicumarol was administered for two weeks. Following operation the tension has re-

mained within normal limits and in October, 1947, the field showed marked improvement. At the last visit, October, 1947, the nuclear sclerosis had increased markedly and the best corrected vision was 20/100 in each eye.

In spite of being advised to return for periodic checkups, this patient, who lives at a considerable distance, has not returned and I have, unfortunately, lost contact with him.

There was no appreciable change in conditions until March, 1940, when the patient was hospitalized for a 24-hour tension curve. During this period and, in spite of the continuance of pilocarpine as before, the tension was found to be elevated in the early

Fig. 10 (McGuire). Case 7.

TEST OBJECT 2/1000   Mrs M. F.
                                          3-14-47
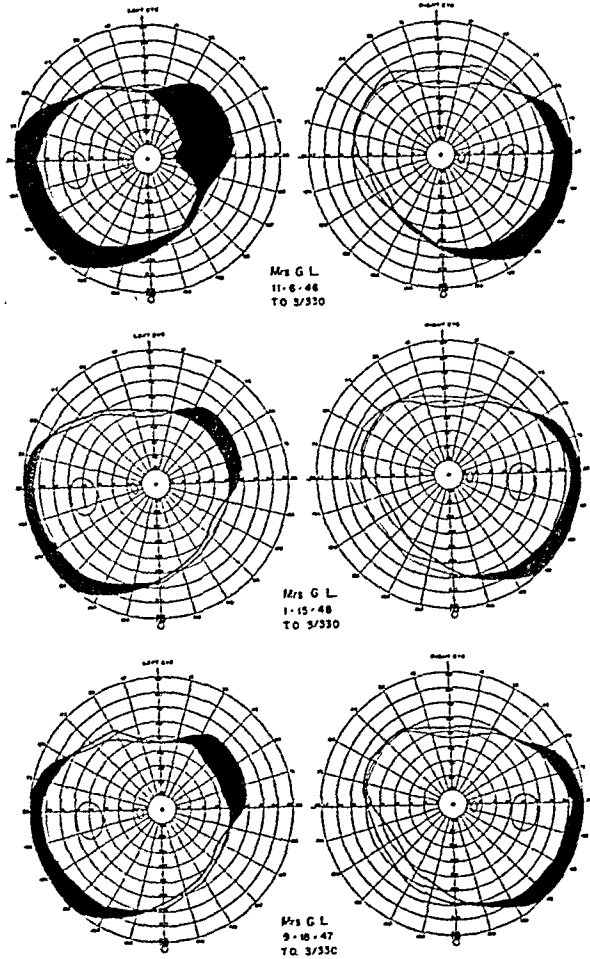
Fig. 11 (McGuire). Case 8.

Case 5. Mrs. H. A. S., aged 67 years, white, was first seen in June, 1945, when she stated that she thought she needed a change of glasses. Upon questioning she stated that for several years she had noticed that she could not see objects to the side of her direct line of vision but that she had paid no attention to this phenomenon.

Vision in the right eye was 20/50—, corrected to 20/20; in the left, 20/70—, corrected to 20/40—. The media were clear and the fundi revealed a Grade-2 retinal arteriolar sclerosis and a marked cupping of the glaucomatous type in each nerve, associated with an extreme pallor. Both visual fields showed a great deal of constriction, the left being more marked than the right. Tension was: O.D., 25 mm. Hg; O.S., 35 mm. Hg. Pilocarpine (2 percent) was prescribed four times daily.
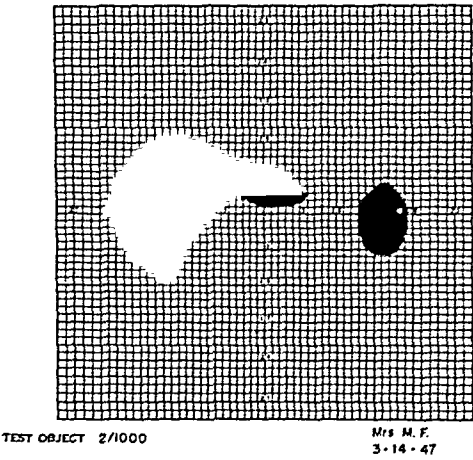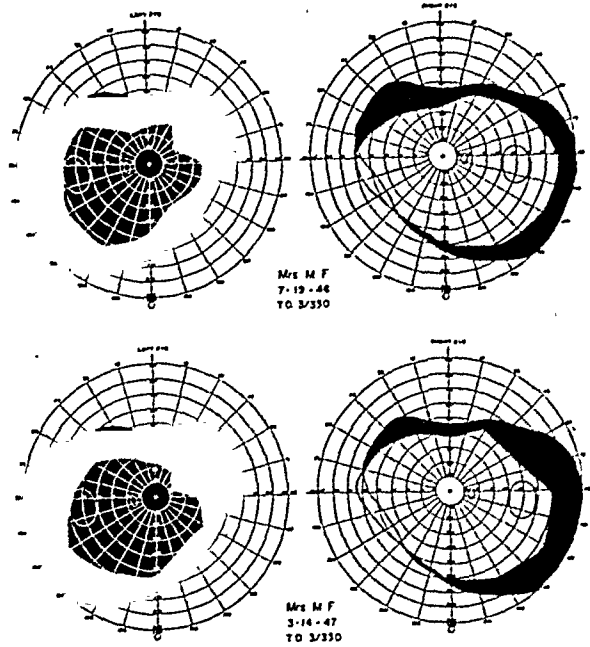
morning hours to: O.D., 35 mm. Hg; O.S., 48 mm. Hg. Iridencleisis was performed on each eye with an interval of one week between operations. Immediately after operation the tension was reduced to O.D., 19 mm. Hg; O.S., 11 mm. Hg and, since operation, has never been found above 22 mm. Hg in either eye.

While the patient was still convalescent it was noted that the vascularity in each nervehead was improving, so much so in the left eye that the vessels on the left disc looked like a Medusa head of capillaries, and the color of the discs in general was much improved. When the fields were checked in May, 1946, two months after operation, they were found to be much improved, but by November 12th

of the same year they had again begun to contract. They remained in about the same stage until August, 1947, when the patient entered the hospital for dicumarol therapy which she had for two weeks.

On November 19, 1947, the right field had improved very strikingly while the left showed marked contraction with a central defect. At this time the corrected vision in the right eye was 20/20—, and in the left, 20/60 eccentric.

June, 1946, a bilateral iridencleisis was done. Since operation, the tension has remained within normal limits but, by February, 1947, the fields showed more contraction, particularly in the upper portion, while by June 25th of that year, the blindspots had markedly increased in size.

The patient was placed on dicumarol for two weeks and one month later the central fields had improved to some extent. On August 25, September
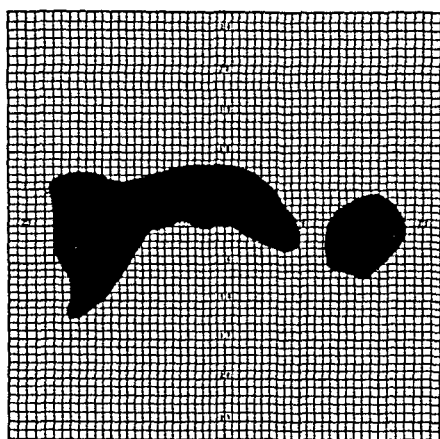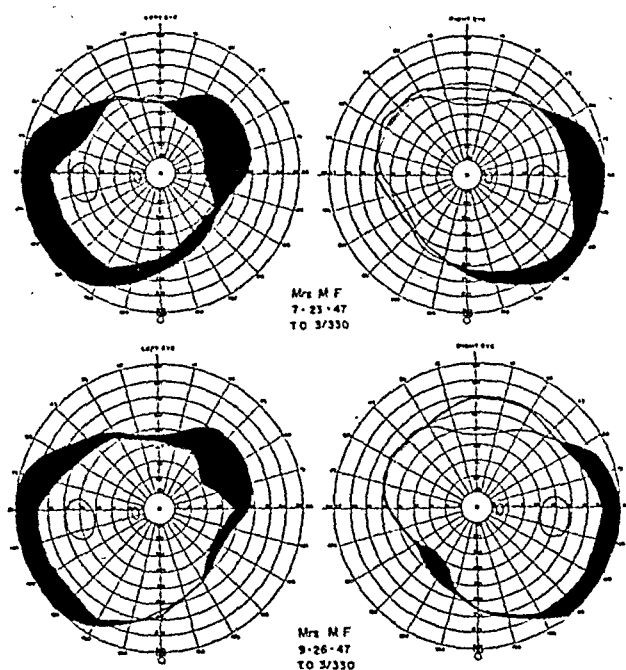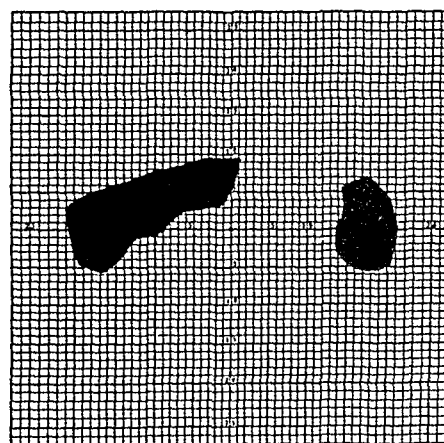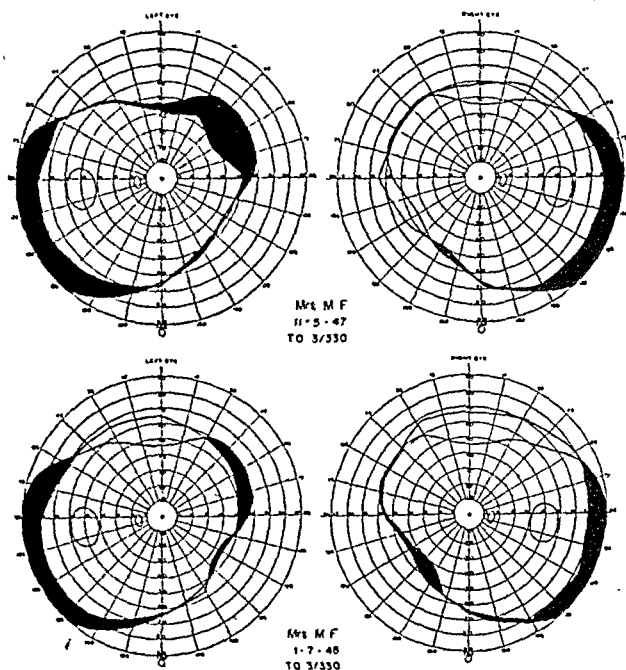
Fig. 12 (McGuire). Case 8.

Fig. 13 (McGuire). Case 8.

Case 6. Mrs. C. B., aged 73 years, white, was first seen in January, 1946, with a corrected vision of 20/20 in each eye. Tension was: O.D., 26 mm. Hg; O.S., 22 mm. Hg. There was a faint nuclear sclerosis in each lens and a shallow cupping with some pallor of each disc. The fields showed some slight bitemporal contraction and there was some enlargement of the blindspots. Roentgen examination of the skull was negative with the exception of calcified posterior clinoid ligaments.

In spite of the use of miotics the tension varied between 22 and 30 mm. Hg in each eye and in

24, November 5, 1947, and January 9, 1948, a progressive improvement was noted in both the peripheral and central fields. The corrected central vision in each eye has steadily become worse due to the development of lenticular opacities. This patient was last seen in April, 1948, when it was found that the fields and blindspots were virtually unchanged in the 3-month period.

Case 7. Mrs. G. L., aged 47 years, a white housewife, first presented herself on September 4, 1947, stating that she did not think she saw well enough

with the glasses that she was wearing. She had had them for several years. Her husband was a photographer and she had made a practice of helping with work in the developing room. She had noticed that recently, after working in the darkroom for several hourse, she would have a headache and pain in the eyes.

Vision in the right eye was 20/30—, and in the left, 20/40—, each correctible to 20/15—. The media

Fig. 14 (McGuire). Case 9.

were clear. The fundi were normal with the exception of the left disc which showed a very shallow cupping with a questionable pallor. Intraocular pressure was: O.D., 22 mm. Hg; and O.S., 26 mm. Hg.

Visual fields showed an upper nasal cut in the left eye and a slight concentric contraction temporally in both eyes with a beginning enlargement of the blindspot in the left eye. Two-percent pilocarpine was prescribed for each eye four times daily and, when the patient was next seen in early November, the tension was O.D., 19 mm. Hg; O.S., 22 mm. Hg. There was no change in the fields and the patient still complained of the same symptoms following work in the darkroom.

An iridencleisis was performed on the left eye on November 19, 1946, and on the right eye the following week. The postoperative course was uneventful and, upon repeated checks since operation, the tension in either eye has not varied from a low of 15 to a high of 19 mm. Hg. There was no
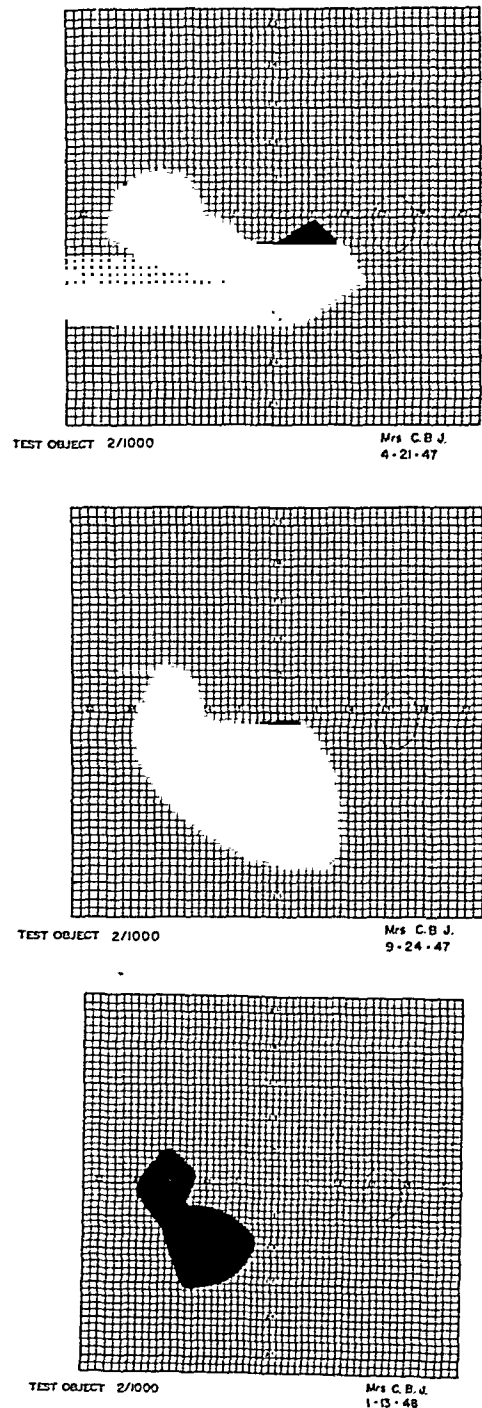
Fig. 15 (McGuire). Case 9.

material change in the fields through June, 1947, but at this time the best corrected vision had decreased to: O.D., 20/20; O.S., 20/25—.

Two months later, on August 23, 1947, the fields were unchanged from the preoperative appearance

but the left blindspot had enlarged slightly while the right was a little larger than normal.

Dicumarol therapy was advised and during the first two weeks in September the patient was in the hospital for a course of the drug. On September 18, 1947, the field and blindspots showed some improvement, while on January 15, 1948, the blindspots were normal in size and the only remaining peripheral field defect was a slight concentric contraction in the upper nasal quadrant of the left eye. At this time the corrected vision in each eye was 20/15—.

Case 8. Mrs. M. F., aged 52 years, white, was first seen in the office in June, 1945, at which time she complained of gradual loss of vision in the left eye. Vision in the right eye was 20/100 corrected to 20/15, while that in the left eye was 20/70—, unimproved. Tension was 19 mm. Hg in the right eye and 35 mm. Hg in the left eye. Nothing remarkable was noted in the examination other than a rather marked cupping and pallor of the left disc with some loss of field and a large Bjerrum scotoma above in the left eye. The patient was placed on miotics and the tension was found to be: O.D., 19 mm. Hg; O.S., 22 mm. Hg, when she was next seen several weeks later.

One year later, in spite of maintaining normal tension at every office visit the field showed more cut, while in March, 1947, there was an even greater defect in the field. At this time a flap sclerotomy was performed on the left eye and the patient was given dicumarol for two weeks. Following this the field improved somewhat but the tension in the left eye rose to 30 mm. Hg and remained at that level in spite of the continued use of miotics, also the blindspot increased in size. Consequently in October, 1947, an iridencleisis was done on the left eye followed by two additional weeks on dicumarol. In November, one month after operation, the tension was 19 mm. Hg in each eye and has remained at that level since, while at the same time the field showed considerable improvement. In January, 1948, the field was almost normal in all meridians and the Bjerrum scotoma has shown some improvement but the central vision has not been improved.

Case 9. Mrs. C. B. J., aged 36 years, white, was first seen on April 21, 1947. She stated that she had been born blind in the right eye and that, while she was still an infant, it had begun to enlarge. It had been enucleated because of pain by Dr. Louis S. Greene 10 years before I had seen her. She said that Dr. Greene had prescribed drops for the left eye and had cautioned her about constant observation of it but she had not seen him for eight years and had not used the drops for six years. There had been no pain nor inflammation in the left eye. Left vision was 20/40—, unimproved by refraction; the media were clear and the fundus normal with the exception of the disc which showed a wide and deep cup with marked pallor. The cor-

nea measured 12.5 mm. in diameter and the intraocular pressure was 52 mm. Hg. The peripheral field showed a marked upper nasal defect and the central field a large Bjerrum scotoma below.

On the following day a flap sclerotomy after the method of Cruise was done and the patient placed on dicumarol for 10 days. One month after operation the tension had been reduced to 17 mm. Hg. and has remained in that vicinity since. There was no improvement in the field a month after the surgical procedure, but on June 28th an improvement had begun. The peripheral field showed continued improvement on September 24, 1947, but the blindspot had not responded and consequently in early October she was again hospitalized for two weeks of dicumarol therapy. By November 7, 1947, the field and blindspot showed marked improvement and when last seen on January 13, 1948, no further changes were noted. The central vision has improved to 20/20—.

COMMENT

Until recently there has been no alarming increase in the prothrombin time of any patients undergoing treatment with dicumarol. However, there are two recent patients who have been taking the drug at home with weekly checks of the prothrombin time, after it was thought that their maintenance dosage had been adequately determined, and who have suddenly developed hematuria with all the symptoms of renal calculus.

Upon examination by a urologist, nothing of note was found except a marked increase in the prothrombin time. Because of the experience of these two patients, I feel that it probably will be safer in using the drug to have daily checks of the prothrombin time for some weeks rather than let the patient be checked weekly after a supposed stabilization of the blood level during a 1-week or 2-week period of frequent observation.

Of the 9 cases reported in this preliminary report, 6 had dicumarol with benefit some months or years after the tension had been reduced by surgery but, in spite of the reduction of tension, the field changes showed continued progression. One patient had dicumarol immediately following operation and five months later had a second course following which there was marked

improvement in the fields. The remaining 2 patients had dicumarol immediately following operation with improvement in the visual fields. Therefore, it is impossible to say whether dicumarol was the effective agent in the gain in field or that surgery played the important role. However, it has generally been assumed in the past that the field that was lost in glaucoma was not restorable by any means except in very rare instances.

There are many questions that come to mind in relation to this problem which I cannot answer at this time. This report is presented because it has seemed to offer some hope in what has formerly been an almost hopeless condition and, while the work that has been done is purely preliminary, it would seem to warrant further investigation by many more ophthalmologists.

105 North Braddock Street.

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HISTORICAL MINIATURE

Egyptian Ophthalmology

Concretion of the meibomian glands and white corneal scars were recognized by the Egyptians. For the latter they applied turtle brain in honey. Their use of the aqueous of pigs' eyes as a vehicle for drugs, the brain of the turtle and man, to say nothing of blood, milk, and dung points to a faith in organotherapy which has again been advocated in our time.

Hirschberg, *Graefe-Saemisch Handbuch.*

THERAPY OF SOME OCULAR INFLAMMATIONS BASED ON IMMUNOLOGIC PRINCIPLES*

F. HERBERT HAESSLER, M.D., AND HERMAN A. HEISE,† M.D.

Milwaukee, Wisconsin

It is our purpose to call attention to the great value of bacterial antigens in the treatment of some ocular inflammations. Its successful use depends on an understanding of a process that involves two factors: antigen and antibody. The remainder of this paper —after a few introductory remarks—will exhibit the process as simply as is consistent with adequate understanding and without violence to the truth. It will also elucidate the practical application of the principles.

Abundant clinical experience has convinced us that vaccine therapy is a great help in many situations and indispensable in some. We base our belief on our clinical experience with several dozen patients in whom resistant inflammations of the conjunctiva and of the iris were successfully treated. We will not describe this clinical material. It is too small for statistical analysis and the details of the observations on an individual patient could only illustrate a principle, not give proof of its validity. We have found it so useful in some inflammations that failed to respond to therapy with drugs or antibiotics that we want to communicate our faith in its efficacy.

The successful use of vaccine therapy depends on an understanding of immunologic principles which are not new, and which are accessible in the more comprehensive textbooks of bacteriology, such as that of Topley and Wilson.

Our purpose is to select the data which are essential to an understanding of vaccine therapy. The ophthalmologist need not have at his fingers' ends a grasp of the entire subject which constitutes the full-time occupation of the immunologist. He needs only a few principles which are easily outlined. We present such an outline which, to the immunologist, may seem oversimplified, but we believe that this outline is not only a safe guide in the treatment of patients but a true description of one of the important processes of resistance to infection.

It has the same relationship to the therapy of inflammations that a road map has to travel. The road map is not a drawing of the countryside, but a series of symbols that are easily understood and if properly applied lead the traveler to his destination without danger or detours. Similarly, our scheme is a simplified diagram which is a symbol for the essential reactions that take place in the resistance to infection. It is not only a safe guide to therapy but also to an understanding of fundamental processes in infection, tuberculin therapy, and allergy.

THE IMMUNOLOGIC PRINCIPLES

The fundamental mechanism of the tissue injury that results from the introduction of all organisms except the few that are primarily toxic—diphtheria, tetanus, gas bacillus, and botulinus—and also from the nonliving agents in allergic individuals, is the reaction between antigen and antibody. Most antigens are protein and in infections they are protein from the protoplasm of the invading organisms. The tissues of the host react to the invasion of antigen by the production of antibody. Antibody is doubtlessly not a single simple substance but all the reactions in which it is involved can be understood by conceiving of it as a single reacting unit. In this discussion it will be referred to as a substance.

Antigen alone is harmless to all tissues. As time goes on, antibodies develop in response to its presence. Antibodies alone are also harmless but when antigen reacts with
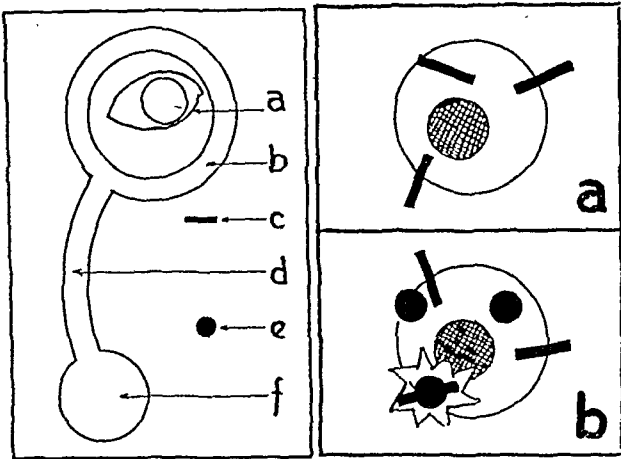
FIG. 1   FIG. 2

Fig. 1 (Haessler and Heise). Identification of symbols in the other figures: (a) Eye. (b) Circulation of fluids in tissues in and about the eye. (c) Antigen. (d) Blood stream. (e) Antibody. (f) Skin.

Fig. 2 (Haessler and Heise). Fundamental characteristics of antigen and antibody: (a) Antigen alone is harmless to a cell. (b) Antigen combined with antibody that is attached to a cell is destructive.

antibody that is attached to a tissue cell, the reaction is destructive. It is the immunity, not the antigen, that causes the trouble. Antigen increases because of multiplication of the invading organism. Antibody increases in response to the increased antigen. When enough of both substances is present to involve many cells in a tissue, clinical signs of inflammation become manifest.

The interval of time between the first introduction of antigen and visible signs of inflammation is the incubation period of the disease. It is the proliferation of antibody, not the supposed accumulation of enough antigen to injure tissue cells that marks the end of the incubation period. This was pointed out by von Pirquet years ago and still is not clear to everyone. Antibodies may be elaborated at a much greater rate than antigen. When they are, 1 or more of 3 events will take place:

1. The antibody destroys the antigen at the site of invasion.

2. The antibody enters the body fluids. Antigen-antibody reactions that take place here—humeral reactions—are harmless to the primarily inflamed tissue.

3. The antibody may become concentrated in a secondary focus in some other tissue. When it does, this tissue will become inflamed immediately if antigen is introduced into it. This is the probable process of focal infection.

The first 2 of these 3 reactions lead to healing at the original site of inflammation but leave the tissue "sensitive" to reintroduction of the same antigen. The word "immune" may be substituted for "sensitive" in this sentence. It is identical in meaning. In the course of time, however, the supply of antibodies gradually decreases and the tissue loses its sensitivity but, if a similar antigen should be introduced anew, the production of antibodies will proceed much more rapidly.

The essential processes of acute inflammation and spontaneous recovery have just been described. However, antibody is not always developed in adequate quantities to deplete the invaded tissue of antigen. It may develop just rapidly enough to keep the antigen in check, and yet not rapidly enough to wipe it out completely. In this event a long-continued smouldering inflammation results—the situation for which vaccine therapy is indicated.

Vaccine therapy is essentially the introduction of an antigen similar to the invading one into tissues of another organ—not the infected one. In practice, this other tissue is almost always the skin and the process has unfortunately been named "desensitization." Actually we are not desensitizing the skin but rather sensitizing or immunizing it. We are inducing it to become the site of origin of an adequate supply of antibody. When treating an eye, we strive to inject antigen into the skin in such quantity that local antigen-antibody reactions will take place in the skin and humeral antigen-antibody reactions which are harmless to the eye will deplete the eye of antigen. The essential point in understanding vaccine therapy is that we are not desensitizing any tissue; on the contrary, we are sensitizing another tissue—the skin. We are shifting the site of the harmful
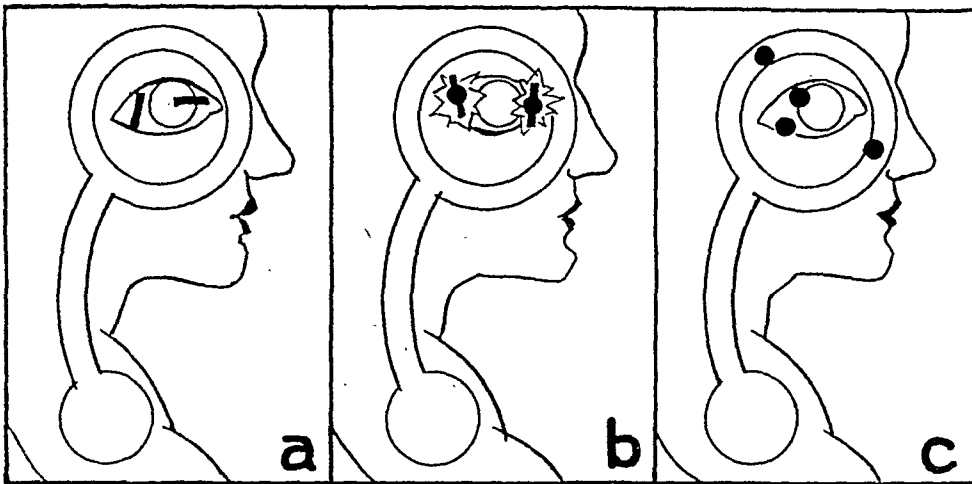
Fig. 3 (Haessler and Heise). Infection, incubation period, and spontaneous recovery: (a) Antigen alone, derived from invading organism, produces no inflammation. Antibodies gradually develop. This is the incubation period. (b) Antigen and antibody react in tissues of eye and cause inflammation. (c) Antibodies have destroyed antigen. Eye has recovered.
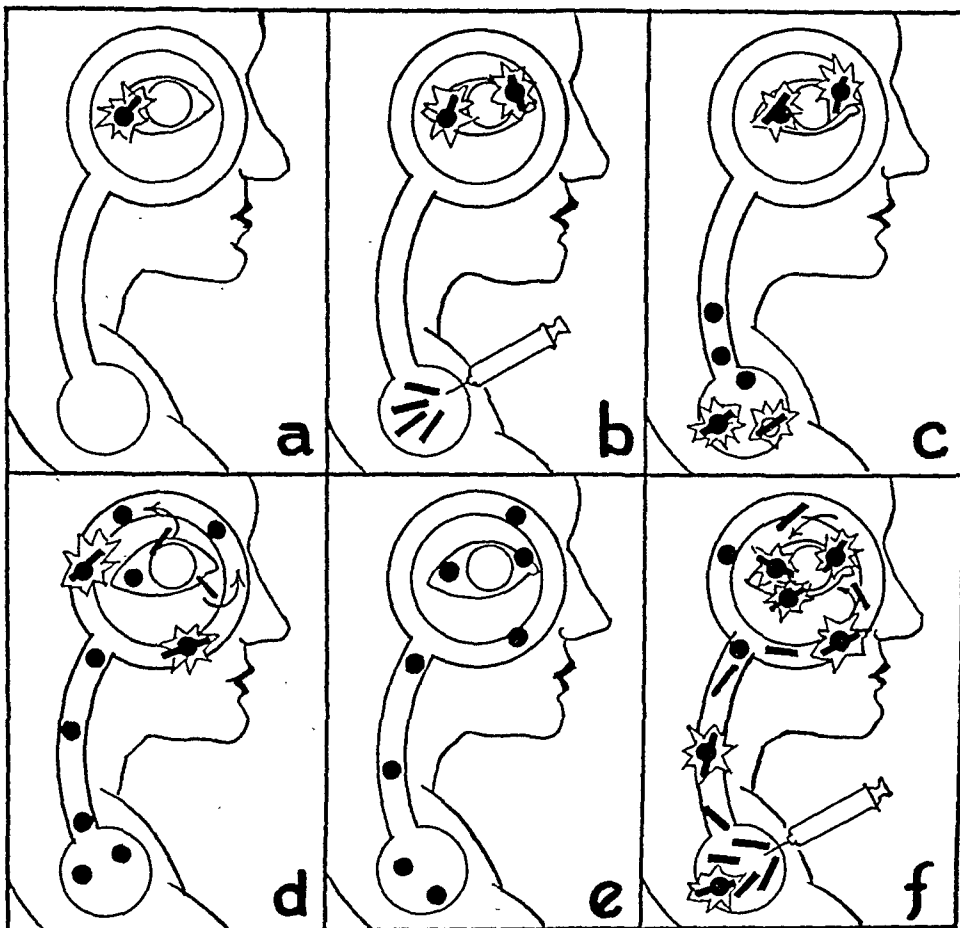
Fig. 4 (Haessler and Heise). Treatment. (a) Eye is inflamed. Antigen-antibody reactions in eye. (b) Antigen is introduced into skin. (c) Skin elaborates antibodies. Excess antibodies enter blood stream. (d) Antigen enters circulating fluids from eye. Humeral reactions destroy antigen. Eye recovers. (e) Antibodies only in skin, blood stream, and eye. No inflammation. All tissues immune; that is, sensitive to further introduction of the same antigen. (f) Overdose of vaccine. Excess antigen enters blood stream and eye, where it reacts with antibody and produces inflammation.

antigen-antibody reaction from the eye to the much less vulnerable skin. The essence of the treatment is the shifting of the shock organ.

The danger of vaccine therapy is overdosage. If we give too large a dose, we introduce a quantity of antigen that is large enough to produce a harmless local reaction in the skin, a harmless humeral reaction, and to leave an excess of antigen that will reach the eye and produce a dangerous focal reaction there. A proper dose inadvertently injected into a vein produces the same deleterious effect as an overdose.

These reactions take place with all nontoxic antigenic substances, living or dead, of whatever source. The principles of treating allergic lesions are precisely similar.

DETAILS OF VACCINE THERAPY

The practical corollaries of the reactions are these: One must have a vaccine which contains the antigen which is the cause of the inflammation. In conjunctival inflammations a suspension of a 24-hour heat-killed culture of the invading organism is the surest and most convenient source of antigen. When the causative organism gives rise to a soluble antigen, the filtrate of a 4-day veal brain broth culture diluted to 1:10,000 is efficacious. In iritis a similar culture from the tissue of primary infection, for example, nose, throat, or prostate, is often available. If it is not, stock cultures of the common etiologic factors, usually streptococcus, pneumococcus, and staphylococcus, can be used. In probable tuberculous lesions a tuberculin or P.P.D. are readily available antigens.

The important factors to emphasize about dosage are size and interval. The dose must never be large enough to produce a focal reaction. We use extremely small doses with success. We start with the intracutaneous injection of 0.01 cc. of a suspension of organisms from a 24-hour culture (not over 10 million organisms) and gradually increase the dosage in succeeding injections until we note clinical improvement of the lesion. After that we no longer increase the dose. There is no theoretical reason for doing so and our practical experience encourages us to be guided by reasoning based on the theory we have outlined.

This is probably as true of tuberculin as of other antigens but we do not, as yet, have adequate clinical data on the basis of which we could affirm or deny this statement with confidence.

The interval between injections may be 3 to 5 days in the beginning of treatment when the dose is small. Later the interval may be increased but not to an extent that there is a falling off in the production of antibodies. The patient's observations are of use in determining this interval. Frequently we have been told by a patient who had been asked to return in 2 weeks that he felt well for 6 days and then gradually became vaguely uncomfortable.

The illustrations in the text represent crucial moments in the diagrammatic motion picture that accompanied the presentation of this essay.

SUMMARY

When the tissue of a host is invaded by antigen, it responds with the development of antibody. Neither the antigen nor the antibody is harmful to the tissue. The reaction of antigen with antibody that is attached to a tissue cell is destructive to the cell. If the number of antibodies exceeds the antigen, spontaneous healing takes place. When it does not, one strives in rational therapy to have this antigen-antibody reaction take place in the body fluids or in a less vulnerable organ, the skin. Injection of antigen into skin in minute quantities accomplishes this object without danger. An excessive injection is dangerous because the excess of antigen can reach the diseased organ and increase the inflammatory process.

561 North 15th Street (3).
425 East Wisconsin Avenue (2).

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SCLERAL STAPHYLOMA AND RETINAL DETACHMENT*

DERRICK VAIL, M.D.
Chicago, Illinois

In 1940, before this society, I reported a case of equatorial scleral staphyloma and retinal detachment successfully cured by excision of the staphyloma. In 1945, the second eye of this patient developed scleral staphyloma and retinal detachment. The staphyloma was excised and the retina became reattached. The latest report from this patient indicated that she had no further disturbance in either eye and the corrected vision has remained useful (20/30+ in the right eye, 20/40+ in the left).

Since then, in a recent series of 34 retinal detachment cases, 8 additional cases, all more or less similar, of scleral staphyloma and retinal detachment have been operated upon by me. The series is too small to draw any conclusions regarding the frequency of this finding, but is significant in indicating that the combination of staphyloma and detached retina is perhaps not infrequent.

So far as could be determined no other author, surprisingly enough, has reported this association. It is incredible, when one considers the enormous amount of time and work devoted in the past to studies of the pathogenesis and pathology of retinal separation, that this circumstance was not encountered and remarked. It is therefore entirely possible that somewhere in the vast literature on retinal detachment, a note of this combination and its significance is to be found.

PATHOGENESIS

The pathogenesis of scleral staphyloma has had little study and attention. Considered as a part of the terminal stage in absolute glaucoma or the result of obvious injury or inflammation of the sclera plus increased intraocular pressure, it has been lightly dismissed in our systems of ophthalmology and textbooks, except in that of Fuchs's. Mention is made of the three types, classified for many years as intercalary, ciliary, and equatorial staphylomas, depending on their location.

Birnbacher and Czermak, in 1886, were the first authors to discuss the evolution and progression of scleral staphyloma. According to Mattice, from whom I have freely borrowed, these authors assumed that a weakened spot in the sclera begins to yield before a normal or increased intraocular pressure. Since the sclera is relatively inelastic, the inner fibers cannot stretch sufficiently to preserve their integrity, and finally break off short, the broken ends retracting somewhat. Successive layers of scleral fibers are thus exposed to the disintegrating process and are broken through. The scleral wall becomes thinner and yields altogether to the force of the intraocular pressure, thus forming an ectasia.

The histologic findings of these authors revealed that the edges of the excavation on the inner surface of a large and old staphyloma are slanting and that it presents a roughened surface due to the irregularly broken ends of the scleral fibers. Only the deepest (that is most superficial) fibers that form the floor of the excavation are intact. These fibers, however, may later rupture until eventually the scleral wall is broken entirely through.

The relation which the uvea bears to such staphylomas was found to depend upon the degree of inflammation in the sclera and uvea. In cases where very little inflammation has occurred, the uvea retains its normal position and bridges across the mouth of the excavation. However, in cases with more extensive inflammatory changes and exudation, the uvea is found firmly attached to

Fig. 1 (Vail). Scleral staphyloma, showing the torn fibers of its inner third.

the sclera as a thin atrophic layer lining the walls and floor of the excavation.

If scar tissue has been found in the uvea prior to the beginning of the staphyloma, the uvea is found ruptured since stretching is impossible. A normal uvea, however, may also rupture if the mouth of the excavation becomes too wide. In most of their cases, Birnbacher and Czermak found the choroid adherent to the walls and floor of the excavation. As a result of their studies, these authors laid down two general rules which govern the formation of staphylomas:

1. Inflammatory changes can always be demonstrated in the sclera.

2. The staphyloma always develops at a point' of least resistance in the sclera, for example, where it is perforated by blood vessels.

Mattice, in 1913, described the histologic findings in a case of equatorial staphyloma that had no connection whatever with the point of entrance of blood vessels, nor with inflammatory changes that could be observed in either retina, choroid, or sclera. The choroid was not pressed against the floor of

the excavation but loosely filled out the space between the floor and the lamina vitrea, bridging over the mouth of the excavation, indicating that intraocular pressure alone was not responsible for the ectasia. The floor of the excavation was covered by a ciliary artery and nerve and Mattice thought that this relationship had a direct bearing on the origin of the excavation. He compared this finding to the gradual grooving of bone by arteries with age and considered that the continued action of blood pressure within the walls of the ciliary artery, particularly if sclerotic or calcified, would form a groove in the sclera, especially if the latter were weakened by disease or injury.

Fuchs mentioned the diminished resistance of the sclera as an infrequent cause of ectasia of the sclera even in the presence of normal intraocular pressure. It is found in cases of deep scleritis, tumors (malignant neoplasms, gummatous or tuberculous nodules), and injuries, especially ruptures of the sclera. He said, "Scleral ectasiae arising in this way lead subsequently to elevation of the intraocular pressure, which then, however, must be regarded not as the cause, but as the result of ectasiae, even though, just as in the case of ectasiae of the cornea, it does contribute to make the latter larger still."

A study of two specimens of scleral staphyloma found in the pathologic laboratory of the Eye Department, Northwestern University, brings out several very interesting points in support of the work of Birnbacher and Czermak.

Figure 1 is an illustration of a section of an eye removed from a patient, aged 77 years, for a suspicious intraocular tumor and secondary glaucoma. The histologic diagnosis in addition to the staphyloma was an occlusion of the central vein. A staphyloma the size of a globe, with smooth surface, was found beneath the internal rectus muscle, measuring 25 by 21.5 by 22 mm.

There is marked thinning of the nasal sclera from the ora serrata backward to

well beyond the equator. Just in front of the equator there is a circumscribed scleral staphyloma within which the inner third of the scleral fibers are torn, while the outer two thirds bulge sharply outward. Between the frayed ends of the torn fibers, filling the staphyloma, there is a loose areolar tissue which contains a few round cells and many fibroblasts. The choroid and retina in this and the immediately adjoining region are reduced to a thin, partly fibrous, partly glial membrane, which does not follow the outline of the staphyloma but crosses or bridges it. Anterior to this region the retina shows excessive cystoid degeneration. The nasal sclera in general shows poor stain of its nuclei. Several small, thin-walled vessels course through the staphylomatous portion of the sclera. There is marked retinal and choroidal vascular sclerosis throughout.

The second specimen is that from a patient, aged 75 years, (fig. 2). No history is obtainable. The histologic diagnosis is secondary glaucoma. The globe measures 30 by 24 by 24 mm. (high myopia). There is a circumscribed staphyloma in the diffusely

Fig. 3 (Vail). Adjacent to the staphyloma which shows a cystic degeneration of the retina with bands of glial fibrous strands across the cyst.

thinning sclera of the posterior polar region. The inner two thirds of the scleral fibers are torn, leaving frayed edges, the outer third bulges in an ampulliform fashion. Its inner surface is lined by extremely atrophic choroid and the thin outer wall of a large retinal cyst. There is a detachment of the posterior vitreous. The subhyaloid region and the retinal cysts are filled with the same pink coagulum. Anterior to the staphyloma is to be found an enormous area of cystic degeneration of the retina. The outer wall has prolapsed into the scleral staphyloma.

These two specimens are, I believe pertinent to the discussion since they reveal the method of the development of the staphyloma of the sclera supporting the previous histologic studies of this condition by other authors and also indicate that even in the presence of increased intraocular pressure, the retina may bridge over the staphylomatous area. In addition, Figure 3 reveals the mechanics of the development of a retinal

Fig. 2 (Vail). Scleral staphyloma, showing ruptured scleral fibers and containing a retinal cyst.

tear as a result of contraction of glial fibrous bands in a retinal cyst.

We see, therefore, that a staphyloma of the sclera can arise in different ways. Scleritis and episcleritis are not unusual ocular diseases. Other factors besides inflammation of the sclera may play a role in weakening its inner wall, factors such as choroiditis, cyclitis, endarteritis, phlebitis, or perhaps some nutritional condition of the sclera comparable to scleromalacia or senile hyaline scleral plaques.

It is easy to conceive of the development of a tear in the inelastic retina bridging over a diseased area in the sclera that is stretching and yielding to intraocular pressure. This is particularly likely when one considers that the retina in this area is probably diseased and cystic as is seen histologically. Such a tear was found in almost all of the cases about to be described.

CASE REPORTS

Case 1. A woman, aged 57 years, had a large balloon detachment of the retina in the upper temporal portion of the left eye. No tear was observed. The ocular tension was subnormal; transillumination was negative for shadow. On exposure of the scleral operative field, a scleral staphyloma occupying the area between the tendons of the superior and external rectus muscles was found. It measured 12 by 16 mm. and began abruptly at a point 6 or 7 mm. from the limbus. The staphyloma was excised more or less according to Müller's technique. A cure of the retinal detachment resulted and the patient has retained useful vision in the left eye since then. (Case reported in 1940.)

Case 2. The same patient described in Case 1. In 1945, she developed a similar detachment in the upper temporal portion of the right eye. No tear was seen and the ocular tension was subnormal. A staphyloma of the sclera in the area of the detachment was observed. On exposure it was found to arise abruptly about 10 mm. from the limbus and measured approximately 20 by 7 mm., between the 8- and 10-o'clock positions. This was excised in a fashion similar to the operation done on her left eye. A cure of the detachment resulted and the vision in this eye has likewise remained good to date. (Case reported in 1946.) The refraction changed as the result of the operation from, R.E., —0.5D. sph. ⊃ —0.75D. cyl. ax. 175° to +1.25D. sph. ⊃ +4.5D. cyl. ax. 175°; L.E., from —1.0D. sph. ⊃ +1.75D. cyl. ax. 115° to +3.5D. sph. ⊃ +3.25D. cyl. ax. 25°.

Case 3. A man, aged 60 years, was examined on November 11, 1946. Four weeks before he noticed a veil descending over the vision of the left eye. A large dark balloon detachment of the retina was found in the upper temporal portion. A very large horseshoe-shaped tear was observed 18 mm. from the limbus at the 1-o'clock position. Ocular tension was subnormal (14 mm. Hg, Schiøtz). Transillumination was negative.

At operation on November 23, 1946, an irregularly shaped staphyloma of the sclera was found. It measured 8 by 10 mm. and arose abruptly 10 mm. from the limbus. There was some question for a moment if this could be a melanoma of the choroid. However, light shone through it readily and the sclera was obviously thinned and dented easily on palpation with the tip of a muscle hook. Instead of excision, a series of ignipunctures in and around the area was performed and some yellowish subretinal fluid was evacuated. On the tenth postoperative day a massive vitreous hemorrhage occurred which began to clear shortly before his discharge from the hospital on December 14, 1946.

On his return three weeks later, the retina at the site of the operation was found to be in place and showed the usual postoperative pigment action. However, in the floor the retina was detached in a trilobular fashion. On February 1, 1947, the involved area was operated on with diathermy coagulation, without a completely successful reapposition of the retina. Final vision on May 21, 1947, was counting fingers at 10 feet. Tension was 22 mm. Hg (Schiøtz).

Case 4. A woman, aged 59 years, was examined on March 12, 1947. Five days before she had noticed blurred vision in the left eye. An extensive detachment of the retina in the temporal area of the left eye from the 2- to 7-o'clock positions was seen. The retina was in folds with the area of greatest detachment at the 4-o'clock position. No tears were seen and transillumination was negative for shadows. The ocular tension was subnormal.

At operation, a staphyloma of the sclera arising 9 mm. from the limbus and measuring 8 by 6 mm. at the 3-o'clock position was seen. It was excised according to the modified Müller technique. Nonperforating ignipunctures were made on each side of the scleral excision. The result was a failure. The retina remained detached from the 4- to 8-o'clock positions.

Case 5. A man, aged 46 years, was examined on April 2, 1947. He had a detachment of the retina in the right eye of two weeks' duration. A balloon, dark detachment was seen beginning at the 10-o'clock position and extending to 3 o'clock. There was a large horseshoe-shaped tear at the 12-o'clock position and 16 mm. from the limbus. Another fishhook vertical tear, not connecting with the first one, at the 1-o'clock position, extended to 18 mm. from the limbus. The ocular tension was low, 10 mm. Hg (Schiøtz).

At operation, a large staphyloma of the sclera extending from the 10- to 1-o'clock positions, arising 10 mm. from the limbus and extending to the equator, was found. The area was extensively treated

with diathermy ignipunctures, most of which were perforating, and particularly heavy in the area of all tears. The sclera shriveled under the treatment. At the first dressing, 48 hours later, the interior of the eye was found filled with blood and there was a severe ocular reaction. The blood gradually absorbed, but traces of it were still present three months later, and the posterior surface of the lens above was blood-stained. This has persisted.

The retina was reattached and the field of vision became full. Ocular tension on September 27, 1947, was 16 mm. Hg (Schiøtz). Preoperative refraction was: −0.5D. sph. ⊃ −2.5D. cyl. ax. 90° (vision, 20/20. Postoperative refraction on September 27, 1947, was: −0.5D. sph. ⊃ 3.0D. cyl. ax. 110° (vision, 20/30.)

As a result of, the extensive diathermy of the sclera beneath the superior rectus tendon, severe scarring resulted and there remained 25 degrees exotropia and 14 degrees right hypertopia in the primary position, necessitating later freeing of the adhesions and recession of the external and superior rectus tendons with considerable improvement, but still marked limitation of movement downward and outward. An annoying diplopia is therefore still present, although the patient is learning to suppress the vision in the right eye.

Case 6. A man, aged 22 years, was examined on April 18, 1947. The upper temple part of the retina in the left eye had become detached in 1941 and was operated upon successfully with diathermy coagulation. No staphyloma of the sclera in that eye was noted. In October, 1946, the patient noticed blurring of vision in his right eye. Examination on April 18, 1947, showed what was considered to be a large cystic detachment of the retina involving the temporal zone from the 5- to 11-o'clock positions with multiple small tears in a disinsertion zone at 9 o'clock particularly. Tension was 15 mm. Hg (Schiøtz).

At operation on April 21, 1947, a bluish rectangular staphyloma of the sclera was observed beneath the tendon of the lateral rectus muscle and extending about equally above and below the edges of the tendon. It measured 12 by 20 mm. and began about 8 mm. from the limbus. A scleral resection of the staphyloma, 10 by 16 mm., was performed and the area around the wound was treated with perforating ignipunctures. The retina did not become reattached and the result was a failure. Postoperative tension was 12 mm. Hg (Schiøtz).

Case 7. A woman, aged 43 years, was examined on April 18, 1947. The left eye had had a retinal detachment seven years before and was operated on elsewhere with failure. A funnel-shaped detachment was now present. About March 15, 1947, she noticed blurred vision in the right eye. A large balloon detachment of the retina was found in the temporal portion of the right eye, extending from the 7- to 11-o'clock positions. It was of dark color and encroached onto the macular area. At the 8-o'clock position could be seen a series of small round holes in the cystic (shagreen) retina, 16 to 18 mm. from the limbus. Tension was 12 mm. Hg (Schiøtz).

At operation a bluish discoloration was noticed beneath the tendon of the lateral rectus. It measured 12 by 12 mm. and was roughly triangular in shape. It dented easily on pressure and transillumination of the area revealed a thin sclera. A 12 by 8 mm. strip of sclera was excised. The underlying choroid was present and not adherent to the sclera. It was obviously atrophic. A small amount of vitreous was lost. The lips of the wound were treated with diathermy coagulation (nonperforating) after the sutures were tied. A successful result ensued. Preoperative refraction was: −1.5D. sph. ⊃ 1.0D. cyl. ax. 35° (vision, 20/100). Postoperative refraction was: −1.5D. cyl. ax. 60° (vision, 20/40+).

Case 8. A man, aged 76 years, was examined on December 12, 1947. His right eye had been lost as the result of an accident at the age of 21 years. An extracapsular cataract extraction was done in the left eye on July 27, 1946, followed at intervals by two needlings and a capsulotomy (October 26, 1947). On November 11, 1947, his vision became blurred and a detachment of the retina developed in the temple side of the eye.

At operation a staphyloma of the sclera was observed. It resembled a leaf, the inferior portion lying largely under the lateral rectus muscle, measuring 9 by 8 mm., and a superior portion extending vertically and laterally, measuring 4 by 6 mm. There was a connecting isthmus between the two leaves. A piece of sclera from the 2- to 4-o'clock positions, 5 mm. wide and 12 mm. from the limbus, running through as much of the staphyloma as possible, was excised. No diathermy was used. A considerable amount of fluid vitreous escaped, and the eye became very soft. Failure resulted.

Case 9. A woman, aged 62 years, was examined on January 30, 1948. Two months before she had noticed sudden partial loss of vision in the left eye, and three days after onset she awakened to find the sight in the left eye "gone." Examination on January 30, 1948, revealed an extensive detachment of the lateral part of the retina of the left eye from the 11- to 5-o'clock positions, with the area of greatest elevation at 2 o'clock. Here could be seen a large horseshoe-shaped tear 18 mm. from the limbus. The retina was dark in color. Tension was 10 mm. Hg (Schiøtz) and transillumination was negative for shadows. There was an incipient cataract present in each eye.

At operation a staphyloma of the sclera was discovered. It was situated between the tendons of the superior and lateral rectus muscles. It consisted of three radial bluish pigmented areas about 1 to 2 mm. wide, each one beginning at 8 mm. from the limbus. The entire area involved was approximately 8 mm. wide and extended just beneath the upper edge of the lateral rectus tendon.

An elliptical area, 14 by 5 mm., of the sclera, 8 mm. concentric to the limbus, was outlined with a knife. Four double-armed (cutting-edge needles) 4-0 black silk sutures were placed in mattress fashion from sound sclera to sound sclera and tightly tied. There resulted a tuck of the staphyloma. Loss of subretinal fluid occurred around the

sutures, softening the eyeball, and thus increasing the ease of tying them. The tucked portion of the staphyloma was excised, and several gaps were closed with single black silk sutures. About 25 diathermy punctures were placed around the wound. Healing was uneventful in spite of the difficulty of keeping this patient quiet.

Preoperative refraction was: +1.0D. sph. ⊃ —2.0D. cyl. ax. 45° (vision, light perception). Postoperative refraction (April 1, 1948) was: +0.5D. sph. ⊃ +1.75D. cyl. ax. 120° (vision, 20/50). The postoperative field was full; there were some vitreous opacities and the tension was 16 mm. Hg (Schiøtz).

Case 10. A man, aged 59 years, was examined on February 10, 1948. One week before, the vision in his left eye suddenly blurred. Examination of the left eye showed some lens spicules, a few floating opacities and a large balloon-shaped retinal detachment extending from the 11- to 5-o'clock positions as far as the optic nervehead. The outline was sharply defined. There was a large horseshoe-shaped tear at the 2-o'clock position, 16 mm. from the limbus and a second round tear at 3 o'clock, 19 mm. from the limbus. The color of the detachment was dark. Transillumination revealed no shadow. The ocular tension was 14 mm. Hg (Schiøtz).

At operation (February 18, 1948) a staphyloma of the sclera was found extending from the 12- to 5-o'clock positions. The posterior border was 18 mm. from the limbus and the staphyloma measured 11 mm. by 30 mm. It arose about 7 mm. from the limbus. There were radial lines and areas in the staphyloma, reflecting the bluish color of the choroid. It was darkest at the 2-o'clock position and lightest at 10 o'clock.

Four mattress sutures of 4-0 silk were inserted in the staphyloma from 12 to 17 mm. from the limbus from 1 to 4 o'clock. A tucking of the sclera was therefore made and a piece of sclera, roughly 5 by 11 mm., was excised. The closure of the wound was further secured by placing of several single-armed silk sutures in gaping areas. A large amount of fluid vitreous, and a bead of solid vitreous was lost.

A row of perforating ignipunctures was made with the diathermy, 12 and 18 mm. from the limbus from the 12- to 5-o'clock positions. Another series of nonperforating diathermy punctures was made on either side of the scleral wound. The conjunctiva was closed with continuous black silk sutures. Inspection of the retina at the close of the operation revealed many folds in the area of the resection. The media was clear.

There was considerable postoperative reaction, as manifested by edema and chemosis of the lids and bulbar conjunctiva. For three weeks there was no red reflex obtainable; the retina in places could be seen with oblique illumination. Although the patient had good light perception, the prognosis was considered hopeless. At the end of three weeks the edema and chemosis had cleared and a red reflex became apparent, first on the nasal and later on the temple side.

On April 22, 1948 (two months after the opera-

tion), the ocular congestion was clearing. The peripheral field of vision was full except for a small notch up and out. There was a small central scotoma. The red reflex was bright. A large scar of the retina, with pigmented edge, occupied the temple portion of the eyeball, with some blood-staining of the retina in the floor extending into the macular area. The tension was 12 mm. Hg (Schiøtz).

Preoperative refraction was: +1.5D. cyl. ax. 75° (fingers at 10 feet). The postoperative refraction two months later was: —1.0D. sph. ⊃ +4.5D. cyl. ax. 180° (20/100+).

COMMENT

Two of the described cases were treated with diathermy alone. One was a failure. The successful one, however, had had so much coagulation, some of it involving the ciliary zone, that a severe intraocular hemorrhage and cyclitis resulted, leading to a long convalescence and resultant and perhaps permanent blood-staining of the posterior surface of the lens and vitreous. In addition, so much scar tissue bound down the superior rectus muscle, and to some extent the external rectus muscle, that a marked muscle imbalance occurred, requiring further surgery in an effort to overcome a very annoying diplopia.

The rest of the patients were operated upon by scleral resection combined with some diathermy coagulation. The last two patients were treated surgically by mattress sutures passed through the staphyloma which, on being tied, resulted in a tuck of the sclera that was then excised without too much difficulty. This idea was obtained from Gayer Morgan who, in 1943, successfully excised a ciliary staphyloma in this fashion. It is apparently safer and easier to perform than is the more tedious excision hitherto described by Müller, Lindner, Pischel, and myself.

The placing of a row of perforating ignipunctures near to the wound further enhances the chances of success and the avoidance of hemorrhage. Of the 8 cases of scleral resection, 4 were total failures; 3 can be considered successful and 1 a partial success. The operations were all performed under sodium pentothal intravenous anesthesia, and the usual method of exposure of the field of operation was performed.

CONCLUSIONS

This small series of cases permits one to draw the following conclusions:

1. Retinal detachment may occur subsequent to a scleral staphyloma in the affected area.

2. In most of the cases the detachment was dark and ballooned. There was usually to be found a large horseshoe-shaped tear in the area of greatest detachment.

3. Most of the staphylomas occurred in the lateral portion of the eyeball.

4. Unless the staphyloma is small, diathermy alone offers the least chance of successful surgery.

5. Excision of the staphyloma, after first tucking the affected sclera, appears to be relatively simple to perform. Diathermy ignipunctures can be placed around the scleral wound, thus increasing the chance of success and reducing the hazard of intraocular hemorrhage.

6. Scleral staphyloma and retinal detachment occur perhaps more frequently than has hitherto been realized, and the presence of a staphyloma is more common than suspected.

7. The diagnosis is made by the bluish, bulging appearance of the affected sclera, the easy indentation of its surface, and its increased transparency on transillumination.

700 North Michigan Avenue (11).

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THE USE OF PROCAINE INTRAVENOUSLY IN OPHTHALMOLOGY*

A PRELIMINARY REPORT

ISADORE GIVNER, M.D., AND DAVID J. GRAUBARD, M.D.
New York

The recent introduction of intravenous procaine infusion in the management of pain in trauma and inflammatory conditions, as well as in the pruritus of jaundice, the treatment of burns, as a substitute for morphine in postoperative care, and for serum sickness, has suggested the need for an investigation as to its possible value in ocular disorders.

In reviewing the literature on the use of

intravenous novocaine in ocular disorders, the following are worth recording:

Lutton, Roumer, Giroud, and Ferron were able to combat eclamptic amaurosis by the intravenous administration of recorcoin. Esente[1] used it in painful glaucomas where the results mostly were satisfactory (no statistics). Pain was relieved and intraocular pressure was reduced for much longer than the time during which the drug was administered. He noted that the simultaneous use of miotics may enhance these effects. The doses

given varied between 10 and 100 centigrams.

Mme. S. Schiff-Wertheimer and Mlle. Gaillard[2] used intravenous novocaine (1:100) in the treatment of thrombosis of the retinal veins. Uncertain results were had in central retinal-vein occlusion but satisfactory results were had in branch obstructions if they were treated early enough.

Lorofi[3] used intravenous novocaine in the treatment of visual difficulties caused by arsenical trypanocides. He had only 2 failures, with 7 successes and 2 ameliorations. When blindness was complete, 3 cases were successful and 2 were improved of the 7 cases observed.

Rouher[4] used intravenous novocaine in the treatment of retinal edema and found quicker absorption and lessening of visual disturbances that could be attributed to the injections.

CHEMISTRY

Procaine is para-aminobenzoldiethylaminoethanol, soluble in one part of water in which its reaction is neutral. It is stable and does not decompose at temperatures as high as 100°C. When injected intravenously in sublethal doses, two processes are initiated: (1) Hydrolyzation of procaine by an enzyme into para-aminobenzoic acid (PABA) and diethylaminoethanol (DEA); (2) acetylation of para-aminobenzoic acid.

Nearly 95 percent of the injected procaine can be found in the urine either as PABA, para-aminohippuric acid, para-aminobenzylglycuronate and DEA, or even as traces of procaine. Procaine or one of its hydrolytic products, PABA, has been shown to be removed from the blood stream in 20 minutes. It is thought that, in inflamed areas, procaine administered by the intravenous route has a two-fold action: (1) Direct action in the irritated nerve fibers; (2) indirect action of DEA on the endothelium of blood vessels. The basic structural similarity between DEA, benadryl, and choline must be noted. The mode of action, as with benadryl at the capillary bed, may be considered as a competition between histamine and DEA for a

given site of action or receptive substance; or the action might be explained from the clinical observations on a cholinergic type response—*DEA* has an *anticholinesterase* action.

DIETHYLAMINOETHANOL

$$C_2H_5 \diagdown N-CH_2-CH_2-O-C-O \diagup C_2H_5$$

BENADRYL

$$CH_3 \diagdown N-CH_2-CH_2-O-CH \diagup CH_3$$

CHOLINE

$$CH_3 \diagdown \\ CH_3-N-CH_2\cdot CH_2OH \diagup \\ CH_3 \quad OH$$
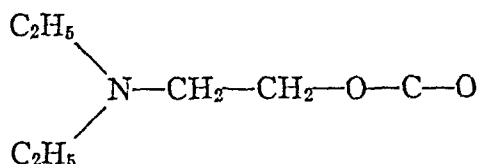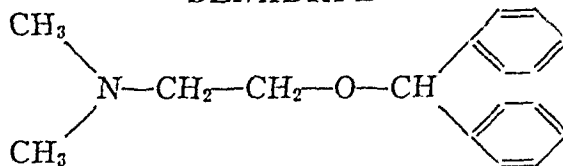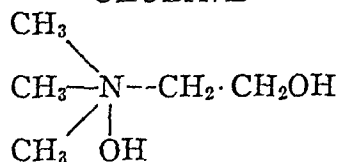
STRUCTURAL RELATIONSHIP OF DEA-BENADRYL AND CHOLINE

PHYSIOLOGIC ACTION

In order to simplify the giving of the procaine, "procaine unit" was devised which is the amount of procaine calculated at 4 mg. per kg. body weight to be given in 20 minutes in a 0.1-percent isotonic saline solution. One gm. of vitamin C is added to 1,000 cc. of isotonic saline solution containing 1 gm. of procaine hydrochloride.

During the administration—after about 5 minutes the patient usually describes a sensation of warmth over the entire body—a dryness of the mouth may be experienced.

In order to see what changes occurred in the normal eyes during and after its administration, 12 cases were studied as tabulated in Table 1. Although tearing of the eyes and dilation of the pupils has been reported with larger and more concentrated doses, neither reaction was observed in this series.

The pupils remained the same size and

TABLE 1

CHANGES OCCURRING IN NORMAL EYES DURING AND AFTER PROCAINE ADMINISTRATION

No.	Date	Name and No. of Injections	Chart No.	Age (years)	Condition for Which Procaine Administered	Weight and Dosage	Tension Before and 30 Minutes After Administration (mm. Hg Schiøtz)
1	1/11/48	M.O.	38478	58	Herniated disc	90 Kg.–360 mg.	O.D. 18; O.S. 18 O.D. 18; O.S. 18
2	1/11/48	J.D. (20)	38469	48	Dest. Arthritis of hips	70 Kg.–280 mg.	O.D. 18; O.S. 18 O.D. 18; O.S. 18
3	1/25/48	E H. (7)	38502	61	Arthritis of knee	80 Kg.–320 mg.	O.D. 23; O.S. 23 O.D. 23; O.S. 23
4	1/25/48	R.K. (24)	38464	30	Arthralgia	58 Kg.–232 mg.	O.D. 22; O.S. 20 O.D. 20; O.S. 20 Aniridia, O.U. Nystagmus O.U. Post. polar cataracts O.U.
5	1/18/48	S.S. (10)	37042	56	Incipient gangrene	75 Kg.–300 mg.	O.D. 20; O.S. 20 O.D. 18; O.S. 20
6	1/18/48	I.B. (21)	37051	52	Scalenus anticus syndrome	48 Kg.–192 mg.	O.D. 20; O.S. 20 O.D. 18; O.S. 18
7	1/18/48	R.F. (9)	39023	52	Arthritis of hips	75 Kg.–300 mg.	O.D. 12; O.S. 12 O.D. 12; O.S. 12
8	1/18/48	S.Y.	37907	53	Rheumatic arthritis	70 Kg.–280 mg.	O.D. 15; O.S. 18 O.D. 12; O.S. 16
9	1/25/48	J.L. (2)	38492	30	Arthritis	100 Kg.–400 mg.	O.D. 18; O.S. 16 O.D. 17; O.S. 17
10	1/25/48	J.B. (3)	38512	58	Fractured fibula	90 Kg.–360 mg.	O.D. 12; O.S. 12 O.D. 12; O.S. 12
11	1/25/48	M.D. (7)	39022	43	Traumatic arthritis	85 Kg.–340 mg.	O.D. 17; O.S. 16 O.D. 15; O.S. 16
12	1/25/48	J.S.	38435	48	Concussion with paralysis of right lateral rectus	70 Kg.–280 mg.	O.D. 10; O.S. 12 O.D. 10; O.S. 12

continued to react normally consensually and to light and accommodation. There was no change in the size of the retinal vessels or other evidences of caliber variation. The tension showed no appreciable fluctuation, either during the administration or 30 minutes after.

From its physiologic action and chemical nature, on theoretical grounds, it seemed that in conditions in which vasodilation would be of value, procaine intravenously might be of ocular aid (figs. 1, 2, and 3). Accordingly, several cases of occluded retinal vessels were studied including one case of Buerger's disease with an occlusion of a superotemporal artery. No change was noted after treatment that could in any way be interpreted as related to the treatment. In like fashion, no improvement that could be attributed to the medication was noted in the treatment of five cases of branch thrombosis. Several cases of diabetic retinopathy were likewise treated with no effect whatsoever.

USE IN GLAUCOMA

In view of the anticholinesterase action of procaine, a reduction of intraocular pressure in some forms of glaucoma might theoretically be expected. Accordingly, 10
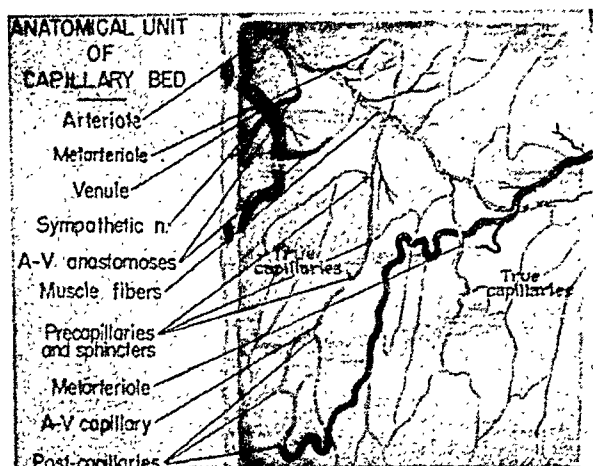
Fig. 1 (Givner and Graubard). Anatomy of capillary bed.
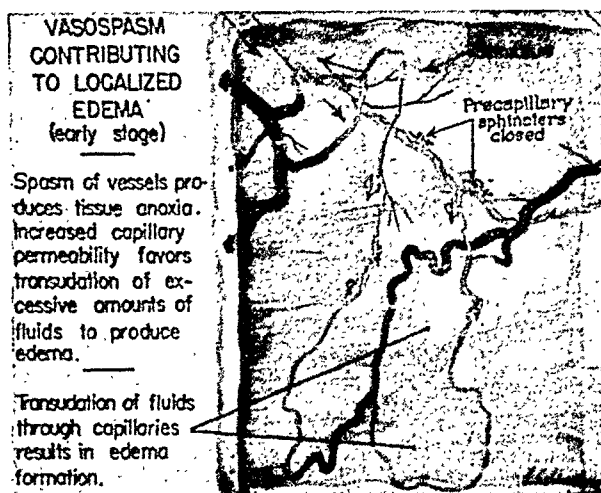
Fig. 2 (Givner and Graubard). Formation of edema.
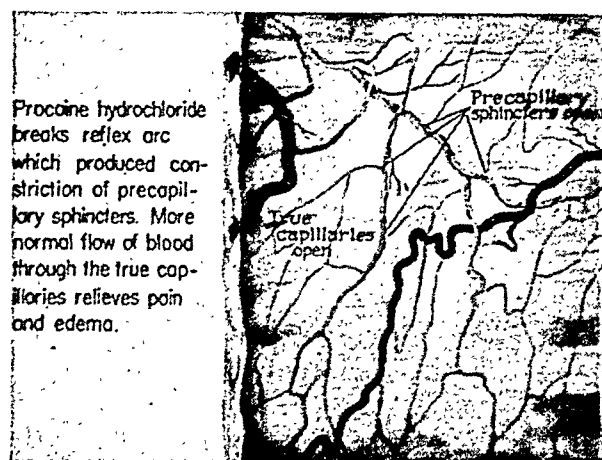
Fig. 3 (Givner and Graubard). Mode of action of procaine.

cases of glaucoma (table 2) were investigated. Realizing that the drop in tension might not be noticeable until more than 30 minutes had elapsed, tensions were taken at 30-minute intervals for 2 hours after the administration of the procaine.

One might thus conclude that to date there seems to be no indication for the use of procaine intravenously in the treatment of glaucoma. Two cases of painful absolute glaucoma are, however, worthy of note. In these cases, there was marked relief of pain after intravenous procaine.

Case 1. H. S., a woman, aged 75 years, was a diabetic who had absolute glaucoma of the left eye. Vision was light perception and the unbearable pain could be controlled only little by the use of opiates. A cycloelectrolysis was done, as well as a retrobulbar alcohol injection, but the pain continued. After several weeks, enucleation was decided on but intravenous procaine was attempted as the last palliative. Pain was promptly controlled and, after three injections, no further injections were needed even though the tension remained high and no visible difference was seen by the examiner.

Case 2. N. Mc., a woman, aged 63 years, had a thrombosis of the central retinal vein of the right eye (incomplete) with secondary glaucoma. An iridencleisis had been performed, and the pain and tension were temporarily reduced. After sulfonamides were administered systemically for an infection not related to the operation, the tension rose again, hemorrhage appeared in the anterior chamber, and pain recurred and could not be controlled. The patient was given an intravenous procaine injection and experienced complete relief of pain. One other injection was given three days later, as a prophylactic measure against the recurrence of pain. The pain has not recurred (8 months). The patient had been using miotics previous to the onset of the pain and has used them subsequently. Following procaine administration, the tension was lowered to normal with miotics and has remained this way.

In one other condition, herpes zoster ophthalmicus, there was relief of pain after

TABLE 2
GLAUCOMA CASES TREATED WITH INTRAVENOUS PROCAINE

Date	Name	Sex	Condition	Initial Tension	Tension after Procaine		
					30 min.	1 hr.	2 hr.
2/4/48	M.A.	M.	Iritis with secondary glaucoma, O.D.	O.D. 18 O.S. 60	18 60	18 60	18 60
2/4/48	H.B.	M.	Aphakia with glaucoma, O.D.	O.D. 65 O.S. 18	65 18	65 18	65 18
2/19/48	M. Del.	F.	Chronic simple glaucoma (Irido-Corneosclerectomy had been done, O.U.	O.D. 30 O.S. 40	30 40	30 40	30 40
2/19/48	T.D.	M.	Chronic simple glaucoma, O.D.	O.D. 65 O.S. 23	60 20	65 23	65 23
3/4/48	H.L.	M.	Chronic simple glaucoma, O.D.	O.D. 40 O.S. 20	40 20	40 20	40 20
3/4/48	P.P.	M.	Chronic simple glaucoma, O.U.	O.D. 35 O.S. 40	37 42	35 48	35 45
3/18/48	F.D.	F.	Chronic simple glaucoma, O.U. O.D. absolute glaucoma	O.D. 55 O.S. 30	55 30	55 30	55 30
4/5/48	A.M.	F.	Incomplete thrombosis of central ret. vein., congested glaucoma, O.D.	O.D. 45 O.S. 20	45 20	40 20	40 20
4/6/48	F.S.	F.	Diabetic Absolute glaucoma, O.S.	O.D. 20 O.S. 50	20 50	20 50	20 50
4/6/48	M.M.	F.	Aphakic, O.D. Chronic simple glaucoma, O.D.	O.D. 30 O.S. 20	30 20	30. 20	30 20

the administration of procaine intravenously (2 cases). The injection had to be repeated, since the beneficial effect was only temporary (lasting two days after one injection). However, this type of therapy can be safely added to our armamentarium in the handling of the pain in this condition.

SUMMARY

1. Administration of procaine intravenously has no effect on the intraocular pressure either in normal individuals or in patients with chronic glaucoma.

2. No beneficial effect followed the use of procaine intravenously in occlusion of retinal arteries, in diabetic retinopathy, or in five cases of thrombosis of retinal vein branches.

3. Some relief of pain followed the administration of procaine intravenously in the treatment of herpes zoster ophthalmicus. The relief was not permanent.

4. Marked continued relief of pain was experienced in one case of absolute glaucoma and one case of hemorrhagic glaucoma.

5. Further studies will be made to see if there are other indications for its use in ophthalmology.

108 East 66th Street (21).

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LOCAL USE OF ANTISTINE IN NODULAR EPISCLERITIS*

Erwin E. Grossmann, M.D., and Milton J. Loring, M.D.

Milwaukee, Wisconsin

According to Duke-Elder,[1] "Nodular episcleritis is a disease of obscure origin, of recurring but benign habit, characterized by the appearance of a localized nodular inflammatory focus in the episcleral tissues. The nodule seems to appear suddenly, and is always surrounded by an area of hyperemia and vascular dilatation. The entire globe may show some generalized hyperemia, but it is never as marked as the region about the nodule."

ETIOLOGY

The etiology has never been satisfactorily explained, but the texts and the literature of the present and past persist in incriminating the famous triad—rheumatism, gout, and focal infection. On this basis the treatment has been directed to the alleviation of pain in which the use of salicylates has been the most popular.

The condition called episcleritis periodica fugax has undoubtedly been frequently confused with the nodular type. Here, too, Fuchs,[2] father of its name, listed rheumatism, gout, and so forth as the etiologic agents. Although a great similarity may exist, the clinical differentiation between the two conditions is characterized by the transient character of the latter and its marked tendency to recur with great regularity.

It is noteworthy that, in this periodic type, the role of allergy has long been suspected. The most prominent view implicates hypersensitivity to the tuberculoprotein. Cases have been reported that appear strongly suggestive of allergy, although their authors did not always bring this out too clearly.

Balyeat[3] reported a single case in 1932 occurring in a physician, who was "apparently" cured by avoidance of certain foods. These authors quote the work of Edward Jackson, who after a period of several years of study felt strongly concerning the possibility of allergy as the etiologic factor.

Shoemaker[4] reported two cases of episcleritis caused by the excessive use of carbohydrates. However, instead of suspecting allergy, the author concluded that the condition was caused by poisons formed in the gastrointestinal tract, due to faulty digestion and carbohydrate metabolism.

Sinskey[5] and his co-workers also reported a case of episcleritis due to faulty carbohydrate metabolism, and they concluded that dietetic factors should be considered in each case.

In the recent literature Shepherd[6] reports five cases of episcleritis wherein the pain was relieved by the local instillation of histamine diphosphate. No attempt at etiologic correlation was made.

USE OF ANTISTINE

Because of the gratifying results obtained with the use of Antistine (Ciba) locally in a large series of known allergic eye disorders, it was deemed worthwhile to examine the effects of this drug.* The chemical known as Antistine hydrochloride† is the trade name for phenazoline hydrochloride, which is a synthetic preparation. It is made up in ophthalmic solution to a 0.5-percent concentration bearing a pH of 6.94.

Antistine was apparently first used internally at the University of Basel, and was found to be a useful antihistaminic in the

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treatment of allergic diseases by Schindler[7] and Brack.[8] The ophthalmic solution was apparently first used by Bourquin,[9] who reported its use in 37 cases, many of which were nonallergic. As far as is known there is no specific report concerning its use in the treatment of nodular episcleritis.

IN EPISCLERITIS

A total of 22 patients whose conditions were diagnosed as episcleritis were treated by topical instillations of Antistine. In each case the clinical picture was characterized by a sudden onset of deep injection of a quadrant or more of the globe and with well-marked pain. There was a definite, elevated yellowish or grayish yellow nodule surrounded by intense redness and hyperemic blood vessels.

In the series of cases treated, only 3 patients admitted to having had a previous attack, 2 cases of which were in the opposite eye and were treated by this method; the other 19 patients were positive in their assertions that the present episode was the initial one. Two of these 3 are known tubercular patients.

Patients were instructed to instill the solution into the affected eye by eye dropper every three hours, and were told to return daily for further observation.

RESULTS

Of the total treated, 17 were men and 5 were women. The ages varied from 20 to 57 years. The apparent disproportion in sex distribution is accounted for by the unusually high proportions of men patients seen at this institution.

TABLE 1

SUBJECTIVE RELIEF OBTAINED WITH ANTISTINE THERAPY IN NODULAR EPISCLERITIS

Symptomatic Relief (Time)	Number of Patients
24 hours	3
24–72 hours	11
3 to 7 days	7
No relief	1

Noticeable relief in symptoms were obtained in all patients except one, as shown in Table 1. The patients were thoroughly questioned concerning this subjective relief, and there seemed no doubt that the element of pain had disappeared. Clinically the cure was noticeably less dramatic; yet the redness and the nodular elevation subsided within a few days after symptomatic relief (table 2).

Of the 22 cases, 7 were diagnosed as

TABLE 2

OBJECTIVE IMPROVEMENT OBTAINED WITH ANTISTINE THERAPY IN NODULAR EPISCLERITIS

Objective Improvement	Number of Patients
1 to 3 days	8
3 to 5 days	4
5 to 7 days	7
7 or more days	2
No improvement	1

pulmonary tuberculosis (the one failure occurred in this group), 1 had an associated rosacea keratitis, 1 had an undiagnosed skin disease, and 13 had no associated disease.

CONCLUSIONS

The use of the antihistaminic known as Antistine has shown to be highly efficacious in the treatment of nodular episcleritis. Of a total of 22 cases, 14 obtained dramatic relief from pain within 3 days, and 21 of the 22 were relieved in 7 days. Objective improvement was noted to be somewhat slower, the greatest improvement occurring in from 5 to 7 days after treatment.

The use of the antihistaminic was suggested by the inferences in the past literature concerning the possibly allergic etiologic factor in nodular episcleritis.

The local use of the drug was deemed to be the best method of application in view of the work by Friedlaender and Feinberg[10] suggesting that failure of relief when antihistaminics were used was due to insufficient drug reaching the site of action.

238 *West Wisconsin Avenue.*

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CIRCINATE DEGENERATION OF THE RETINA*

WITH REPORT OF A CASE

R. H. HENDERSON, M.D.
Wilmette, Illinois

Circinate degeneration of the retina is the term preferred by Duke-Elder for the disease originally described by Hutchinson, in 1876, as retinitis circinata. It was thoroughly reviewed by Edgerton in 1936 and another case reported by him.[1]

Since Edgerton's review, reports on seven more cases can be found in the literature. J. Margenot,[2] in 1936, reviewed the pathogenesis in two cases. M. Handmann,[3] in 1937, reported a case in a woman, aged 49 years, which he had observed for five years, from its incipient stage until the development of the white, degenerated area.

Two cases reported by Jules François[4] showed a retinal degeneration which began following thrombosis of the macular veins. The thrombosis preceded by several months the development of the retinal degeneration.

Holden[5] presented the case of a woman, aged 58 years, who had diabetes and high blood pressure. There were both old and new hemorrhages in the involved areas of the retina. S. Holm,[6] in 1941, reported the case of a woman, aged 82 years, in whom the eye was enucleated, but the suspected neoplasm was not found. In this case, the principal microscopic changes found were: increase in pigmented cells, some in massed formation and others scattered throughout the degenerating tissue; changes in the arrangement of rods and cones in some places, and, in others, the entire loss of rods and cones; round-cell infiltration of the retinal vessels.

Rebelo,[7] in 1943, reported a case in which there were discreet hemorrhagic areas within the ring of degenerating retinal tissue. His observation of normal appearing retinal vessels coursing uninterruptedly over the white areas of degeneration is in accord with the observation of most authors on this point.

One case in a child has been reported since Edgerton's review in 1936. This was reported by Morgan in 1944.[8] This case was in a boy, aged 8 years, in whom the chief complaint was reading difficulty. He had vision of 6/18 in the right eye and 6/5 in the left. There was a history of concussion at seven years of age with bruises over right side of head, so that the right eye was closed. No definite etiology could be established in this case and the concussion could only be referred to as a possible cause.

CASE REPORT

History. The case to be reported here occurred in a man, aged 57 years. He came to me first in May, 1947, on account of an acute blepharitis and conjunctivitis. He also complained of poor vision in his right eye. He had had his eyes tested for glasses one year previously but no mention was made by the examiner of any visual defect.

Vision was: R.E., counts fingers at 15 inches; L.E., 6/6—3. He gave a history of some prostatic involvement, but his general physical examination was otherwise essentially normal. Blood pressure was 165/85 mm. Hg, with urine negative for albumin and sugar, and Kahn test negative.

External eye examination. Mild, acute blepharitis of both eyes and a small chalazion in the left upper lid were present. There was acute conjunctivitis of both eyes. The pupils were regular, 3 mm. in diameter, and reacted normally to light and accommodation. The corneas were clear. Tension was normal in both eyes.

The ophthalmoscopic examination of the right eye was as follows: The cornea, lens, and vitreous were clear. The optic disc was sharply outlined and of normal appearance. There was marked tortuosity of some of the smaller veins and along the superior temporal vein were tortuous, dilated small veins, resembling clusters of grapes and occasionally punctate hemorrhages from these clusters. The retinal tissue immediately surrounding the macula was cloudy, with several punctate hemorrhages in the macular area. The macula was girdled by two semicircular arcs with open spaces at the nasal and upper temporal ends. The lower arc was wider in its middle portion, approximately 1½ times the diameter of the optic disc, and tapering somewhat toward both ends. This lower arc was yellowish white in color throughout its entire extent and had numerous small, rounded, discreet spots of a silvery sheen scattered over its surface. Its borders were irregular in outline, as though numerous smaller white spots had coalesced.

In the upper arc, the temporal half was yellowish white in color, but more narrow than the lower arc. The nasal half was a mottled slate gray in color and composed of numerous rounded, discreet patches which had not yet coalesced and were evidently of more recent origin. Coursing over this entire degenerated area, retinal vessels could be seen clearly outlined. There were numerous punctate hemorrhages, especially along the superior temporal vessels and in the region of the gray inner end of the upper arc.

In the left eye, the media were all clear, except for a few small vitreous opacities. The retinal vessels also showed some sclerotic changes. The fields of vision in both eyes showed a normal peripheral field. In the right eye, there was a large central scotoma.

This retinal degeneration occurred in a man in whom no general physical condition could be found as a possible etiologic factor.

The inner, upper portion of the degenerating retina was evidently the most recent part to be affected and it was in this region where most of the punctate hemorrhages were noted and in which the tortuosity of the veins was most marked.

Comment. Many other reports have noted the occurrence of hemorrhage as the probable beginning of the circinate degeneration, and it is probable that some degree of arteriosclerosis occurs in the majority of the cases occurring in elderly people. The fact that an occasional case is seen in children and young adults would indicate that, at times, factors other than arteriosclerosis are responsible.

In the case here reported, hemorrhage and sclerotic changes in the retinal vessels are the predominant findings, and it seems reasonable to assume that they were the prime factors in producing the degeneration noted.

Course. This patient was seen again in

May, 1948, approximately one year following the original examination. The only change to be noted in the period of one year was an increase in the density of the white portion of the upper arc of the degenerating area. This change is further evidence that the upper arc is the portion of the retina most recently involved. Also that
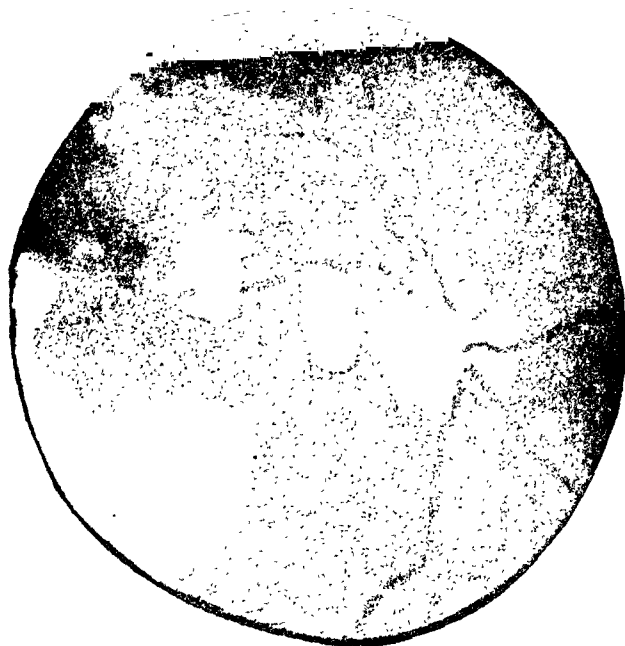
Fig. 1 (Henderson). The white, degenerated area is not elevated above the surrounding retina but retinal vessels course evenly across its surface.

hemorrhage was of prime importance in the etiology, since it was in the proximity of this area in which most of the punctate hemorrhagic spots were noted.

DISCUSSION

In making a diagnosis in this case, it is necessary to rule out the possibility of angiomatosis retinae, which may be found in a great variety of retinal manifestations and which is sometimes accompanied by a circinate degeneration.

The appearance of the upper temporal vessels (fig. 1), which were described as resembling clusters of grapes, leads one to a careful inspection of the fundus periphery for other evidence of angiomatosis.

There are no sacculations or aneurysmal dilatations, such as described by Duke-Elder and others.

The white, degenerated area is not elevated above the surrounding retina but, as can be seen from the photograph, retinal vessels course evenly across its surface. The retinal vessels, other than those seen in the upper temporal area, while considerably dilated, show no evidence of aneurysmal dilation and none of them end in a sacculation.

The preponderance of reports of angiomatosis are in young adults, the preference being in the third decade.

In the present case, there is definitely a lack of the extensive and marked vascular changes, or evidence of tumor formation or massive retinal exudate, which are more characteristic of angiomatosis.

1200 Central Avenue.

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SILVER NITRATE CAUSING DACRYOCYSTITIS

Peter Sykowski, M.D.
Schenectady, New York

For the prophylaxis of ophthalmia neonatorum, silver nitrate instillation is a routine procedure. In ophthalmic textbooks, old and new, no mention is made of silver nitrate solution as an etiologic factor in the production of dacryocystitis in cases of nasolacrimal duct obstruction. That such a factor exists is suggested by several observed cases.

REPORT OF CASES

CASE 1

Bilateral nasolacrimal duct obstruction. T. R. was seen at the age of 5½ weeks. Silver nitrate, 1 percent, was instilled following birth. On the fifth day, acute purulent discharge in the right eye occurred, followed by a similar involvement of the left eye. In both eyes there was lid edema, marked conjunctival injection, profuse purulent discharge, purulent expression from the puncti, and an extensive superficial central keratitis. Bilaterally, the ducts were obstructed. Dilatation of the puncti, irrigation with penicillin, and probing of both ducts established drainage. The course thereafter was uneventful.

CASE 2

Unilateral nasolacrimal duct obstruction. P. M. was seen at the age of 7 days. Silver nitrate, 1 percent, was instilled after birth. On the fifth day following birth, the left eye became involved. Lid edema, marked purulent discharge, purulent expression from the punctum, and several small corneal punctate staining areas were observed. The nasolacrimal duct was not patent. The course after probing of the duct was unremarkable.

Ten additional unilateral cases were observed within seven days after birth. Except for the absence of corneal involvement, all were similar in severity with uneventful courses following reëstablishment of duct patency.

CASE 3

Unilateral duct obstruction. P. A. was seen at the age of 7 months. Epiphora of the right eye was present shortly after birth. Signs of duct inflammation were at no time present. Irrigation of the duct system revealed complete obstruction.

Following the irrigation, experimentally, one drop of 1-percent silver nitrate solution was instilled. On the third day, a moderate amount of silver catarrh was present, the cornea being clear. Upon irrigation of the sac, considerable white, stringy, clumpy debris was obtained through the puncti.

After probing of the duct, the course became uneventful.

COMMENT

The coincident occurrence of dacryocystitis in nasolacrimal duct obstructions alerts one to the likely implication of the nitrate of silver solution. Normally, silver nitrate solution is said to be neutralized rapidly by the chlorides in tears. A deficiency factor, influencing considerably the pathologic process —a deficiency in the defense against bacterial invasion—is the absence of tears at birth. Inadvertent instillation of strong silver solution into the eyes of newborn infants, or failure in the neutralization of the instilled drops, may form the basis of the complication.

Prophylactically, to minimize the danger to the nasolacrimal duct system, neutralization by and generous irrigation with normal saline solution should follow nitrate of silver instillation. This neutralization and irrigation would be especially desirable after use of those solutions which, unknown to the user, have increased in concentration.

It seems possible that the dacryocystitis observed in newborn infants with nasolacrimal duct obstruction may be the result of nondrainage through of the silver nitrate solution and its subsequent caustic action on the mucous membrane of the lacrimal system.

1330 Union Street.

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A SIMPLIFIED ASTIGMOMETER*

JAMES E. LEBENSOHN, M.D.
Chicago, Illinois

Precision in refraction requires that the axis and value of any cylinder needed be known before dealing with the spherical correction. The reverse routine, by which the sphere that gives the best vision is first determined and the weakest acceptable cylinder then added, does not assure an exact correction even under cycloplegia. The final result of such technique is not infrequently an undesigned spherical equivalent. To attain the sharpest possible focus, the correct cylinder, regardless of power or axis, must be prescribed. Toleration will ensue if compensation is provided for associated factors, such as the differential prismatic action of the lenses or persisting accommodative tone, though, or course, the patient may require some days to reinterpret the new type of imagery and "get used to the glasses."

All methods of cylinder determination have their place but one of the most generally useful is the astigmatic chart. It is invaluable in noncycloplegic and postcycloplegic refraction, and likewise is a desirable check after cycloplegic retinoscopy. Moreover, when adequate objective refraction is impossible, as in opacities of the cornea, conical cornea, and incipient cataract, the astigmatic chart often gives helpful results.[†]

The ideal astigmatic chart should be a single unit of simple design, easily handled, unsoilable, and need no computation. The projectochart cross dial, although excellent otherwise, fails in the last qualification. The correct use thereof is also rather complicated. After proper fogging, the cross is set at axes 90° and 180°. If the lines look alike either no astigmatism is present or the axis is 45° or 135°. If the vertical line is clearest, as will be assumed, the axis may be 90° or within 45° to either side. The cross is then rotated 45°. If the line at 45° is clearest, the 45° meridian must be closer to the true axis than that at 135°. As the clearer line is rotated step by step away from 90°, the difference between the two lines lessens until at a certain point both lines have the same appearance. If this position is 30°, the true axis is 45° therefrom or at 75°.

ASTIGMOMETER OF NEW DESIGN

All this computation is avoided in the dial of my design which I appropriately term "a simplified astigmometer" (fig. 1). Incidentally, the word astigmometer, though perchance unfamiliar, is in the unabridged dictionaries, the definition being "an ap-

† Illustrative cases: (a) Woman, aged 31 years. Paracentral scars left cornea. Glasses from oculist, one month old: L.E., +1.25D. sph. ⊃ —3.0D. cyl. ax. 95° = 20/30. Prescription after astigmometer test (postcycloplegic)): L.E., +0.25D. sph. ⊃ —4.0D. cyl. ax. 95° = 20/20. (b) Girl, aged 12 years. Bilateral conical cornea. Oculist reported after cycloplegic refraction uncorrectible amblyopia: R.E., —0.5D. sph. ⊃ +5.0D. cyl. ax. 10° = 20/70; L.E., —0.50D. sph. ⊃ +4.50D. cyl. ax. 170° = 20/100—1. After the astigmometer test the indicated prescription was: R.E., —1.0D. sph. ⊃ +8.0D. cyl. ax. 5° = 20/30; L.E., —5.75D. sph. ⊃ +7.0D. cyl. ax. 175° with 4.5ᐃ slab-off, 20/40. Although this would have given serviceable vision, contact glasses were advised, and an excellent result was reported. (c) Man, aged 70 years. Immature cataract, left eye. Glasses from oculist, six weeks old: L.E., +0.75D. sph. ⊃ +0.75D. cyl. ax. 180° = 20/200. After astigmometer test prescribed: L.E., +2.0D. sph. ⊃ +2.0D. cyl. ax. 10° = 20/30.

paratus for measuring the degree of astigmatism."

This new chart is durably made of vinylite plastic and hence maintains permanently its cleanliness and contrast. The axes are indicated with dual numbering completely around the dial. The outer figures are read when the dial is seen in the mirror while, with direct vision, the inner figures in parentheses are noted. The use of the dial with a mirror facilitates considerably the examination, and is highly recommended. If the convenient roller acuity chart is used, a nail at the top of the box can serve when needed to hold the astigmatic dial. In a lightly decorated examining room the general illumination is usually adequate enough for the astigmatic test. Additional local illumination when required on account of poor discrimination can be provided by the Sphero-Lux or similar examining lamp. Clinical experience has shown that the single-line cross is most suitable for the determination of cylindrical power. For the location of the axis the rotating Maddox V is more efficient since the astigmatic eye can distinguish best a difference between two lines at an angle of 60° (Verhoeff). By placing an inverted V as an arrowhead over one line the two designs are neatly combined and the astigmometric procedure is greatly simplified. The arrowhead is used to indicate the cylindrical axis; the cross to determine the cylindrical power. The chart design thus consists simply of two long lines making the cross and two short lines forming the arrowhead, all of an even 5-mm. width.

USE OF DIAL

In using this dial, the eye is properly fogged and the cross lines are presented at axes 90° and 180°. If the lines look alike and the wings also match, no astigmatism is present. But if the wings do not match the axis is 45° away on the side of the lighter wing. On shifting the arrow to this position, the arrow-line will be the blacker of the two principal lines. If, in the primary position of

the cross, the clearest line is vertical, the arrow is pointed to 90°; if horizontal, to 180°.

The attention is now directed to the arrowhead. If the wings match, the axis, as indicated by the shaft, is correct. If one wing is blacker, the arrow is rotated *away* from the blacker wing until matching ensues.
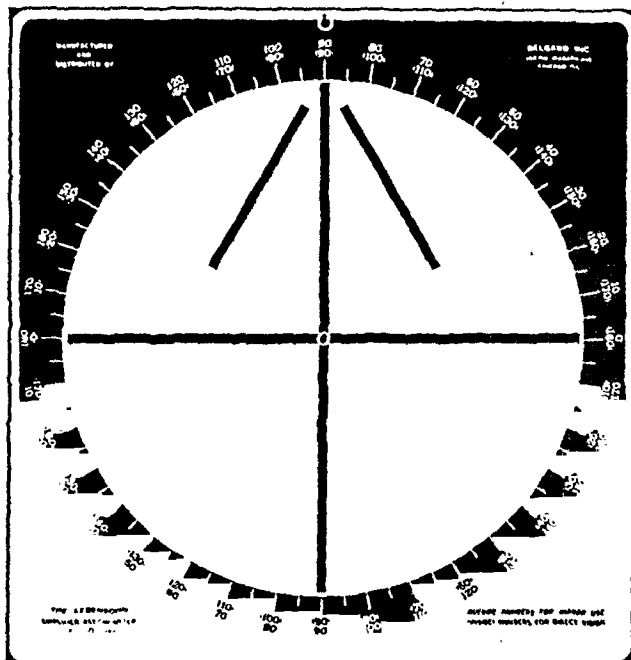
Fig. 1 (Lebensohn). A simplified astigmometer.

Where this occurs, the arrowshaft is at the *correct axis and no further computation is* necessary. To illustrate: if the clearest line is horizontal and the lower wing blacker, the arrow is moved upward until the wings look alike. Should the arrow be rotated beyond the neutral point, the upper wing will be clearer, an indication that the movement must be reversed somewhat.*

After the axes are located, the cylindrical power is next determined. The arrowhead now serves as a distinguishing mark by which the arrow-line or the other can be identified. Minus cylinders are placed at right angles to the arrow-line until this line,

* When the astigmatism is of such high degree that the wings of the arrow cannot be distinguished, the position of greatest clarity of the one line seen can still be determined. The patient usually notes a change in blackness and sharpness as this line is rotated in steps of five degrees in one or other direction.

at first the clearest, is matched by the other. If the fogging is adequate the next 0.25D. stronger cylinder should reverse the contrast.

With the cylindrical correction worn, the fog is gradually reduced in turn from each eye until no further visual improvement occurs. The position of the axis is then checked by the effect of the cross-cylinder on the Snellen letters, using the 0.12D. instrument for a corrected acuity of 20/20 or better, the 0.25D. model for a correction of 20/25 or less. If this test indicates a divergence from the axis found with the astigmatic dial, the exact axis direction can be decided by the Crisp-Stine test for which the arrow-line is ideally adapted.

CRISP-STINE TEST

The use of the Crisp-Stine test can be explained best by an illustrative case. Assume that the provisional correction is: R.E., +1.0D. cyl. ax. 15°, 20/20. With the letter chart, the cross-cylinder indicates apparently an axis of 30°. The eye is fogged 0.25D. and both the trial cylinder and the arrow-line are placed at 15°. The 0.12D. cross-cylinder is applied in the test for axis and the query is whether the wings look more alike before or after the turn of the cross-cylinder.

If the wings seem alike with the plus mark of the cross-cylinder up, *both* the arrow-line and the trial cylinder are moved to 25°, and the test reapplied. If now the wings appear matched with the plus mark of the cross-

cylinder down, the correct axis is 20°. When both the arrow-line and the trial cylinder are moved to this position, application of the cross-cylinder test will show a contrast in the wings that is reversed on rotation of the instrument.

The average fog should be about 0.75D. For cycloplegic cases the proper fog is attained by algebraic addition of the sphere and cylinder found in retinoscopy at one meter. When the arrow-line is placed in the axis of the plus cylinder, the appearance of the arrowhead will signal what change in axis position is required. In presbyopic cases, the glasses worn should be measured and the corrected acuity noted. Then a slip-on occluder is placed over one lens. The desirable fog is determined by placing over the other a plus sphere from the trial case of 1.0D. or more as indicated. In postcycloplegic testing +0.5D. sph. is added to the previous cycloplegic findings before the check for cylindrical power. Subsequently, after the fog is adequately reduced, +0.25D. sph. is added and the accuracy of the axis is checked by the Crisp-Stine test.

It is sincerely hoped that the simplified use of the astigmatic chart which I have described will help to extend the popularity that this technique deserves.

4010 West Madison Street (24).

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

November 1, 1948

DR. BENJAMIN ESTERMAN, *president*

CORRELATIONS BETWEEN OPHTHALMOSCOPY AND HISTOPATHOLOGY

DR. BERTHA A. KLIEN, Northwestern University Medical School, Chicago, discussed this subject during the instruction period.

RECURRENT UNILATERAL GLAUCOMA WITH CYCLITIC SYMPTOMS (case of the month)

DR. ISADORE GIVNER presented the case of a man, aged 43 years, whose right eye had been painful and red for 10 days. Past history showed recurrent attacks of similar nature. A diagnosis of glaucoma had been made and the patient had used pilocarpine during the previous attacks. The patient stated that for many years he had had a fever in the afternoon, fatigue not related to exercise, and attacks of diarrhea. He had spent time on a farm many years ago where unpasteurized milk was drunk. X-ray studies of the chest and the Wassermann test were negative.

Examination of his eyes revealed that the right pupil was larger than the left, and there were many keratic precipitates on the posterior surface of the cornea of the right eye. The intraocular pressure was 37 mm. Hg (Schiøtz) in the right eye and 20 mm. Hg in the left. The peripheral fields were normal and the blindspot of the right eye was enlarged. Six days later, after using pilocarpine (2 percent) 3 times a day, the tension was 25 mm. Hg in the right eye. Following skin testing for brucellosis, 8 days previously, all keratic precipitates disappeared. The tension of the right eye was 18 mm. Hg with and without pilocarpine. The patient discontinued drops and the tension remained at 18 mm. Hg, and vision was 20/15, with no symptoms.

Dr. Givner said that he wished to submit the following questions for discussion:

1. He asked Dr. Conrad Berens, what is the relationship, if any, of systemic disease to primary glaucoma?

2. He asked Dr. Harold Harris whether the evidence cited was sufficient to establish a diagnosis of brucellosis?

3. He asked Dr. Adolph Posner if he felt that this was a case of glaucomatocyclitic crisis described by Posner and Schlossman; if so, what is its position in the classification of glaucoma?

Discussion. DR. CONRAD BERENS replied to the question that undulant fever has been regarded as a cause of chronic uveitis by many investigators, notably by Orloff, who reported two cases of undulant fever with extensive ocular complications, and produced experimental keratitis, uveitis, and neuro-retinitis in guinea pigs by inoculations with Brucella abortus. Green also observed 4 cases of undulant fever, and collected from the literature 28 additional cases with such ocular conditions as keratitis, uveitis, retinitis, and optic atrophy.

In studies at Cornell University, agglutination and skin tests for undulant fever were carried out on 57 patients. Because it is often difficult to make a clinical diagnosis in the subacute or chronic forms of undulant fever by the isolation of brucella organisms, immunologic procedures, such as agglutination, intradermal or complement fixation tests, and opsonocytophagic reactions are used. The interpretation of these tests were clarified in 1933 by Huddleson, Johnson, and Hammann and more recently by Harris. Since the intradermal and agglutination tests were considered to be the most reliable

tests for determining the existence of brucella infections, these tests were used at Cornell University.

Agglutination and intracutaneous tests were made on 25 patients with uveitis, 32 with other inflammatory eye diseases, and 6 with noninflammatory ocular lesions. Only one patient with chronic conjunctivitis had a positive agglutinin titer of 1:40; the intracutaneous reaction, however, was negative.

Of 57 patients, 3 had positive skin tests —2 with uveitis, and 1 with endophthalmitis. These patients were known to have used raw milk in their diet. The fact that the large majority of the tests were negative indicates that Malta fever did not play a significant role in this group of patients. However, most of the group were residents of a metropolitan area where only pasteurized dairy products were used.

Since these studies were made, Dr. Harris has examined many patients and, although some have apparently benefited from treatment with brucella antigen, only two have had severe ocular reactions. Dr. Berens said he believed that these two cases were quite certainly caused by brucellosis.

The last patient, who had bilateral uveitis, had a very severe ocular reaction. The vision was reduced to hand movements in the right eye and 10/200 in the left eye two days after a small dose of brucella antigen. This patient's condition did not respond to 25 gm. of dihydrostreptomycin. Dihydrostreptomycin is considered to be one fourth as toxic for the eighth nerve as the ordinary streptomycin and the patient has had no unpleasant symptoms or reactions.

After giving this treatment over a period of 10 days, combined with three intravenous injections of typhoid-H antigen, the anterior chambers of both eyes were aspirated and, two days following this treatment, there was considerable improvement in the left eye but the right eye gained little, if any, in vision or field. Following two blood transfusions, both the right and left eyes improved.

In spite of the fact that there was no specific proof that the treatment with brucella antigen was specific in any particular case, there were patients who had marked improvement after receiving brucella antigen. Therefore, for patients who show positive tests for brucellosis by experienced observers, the treatment with brucella antigen certainly is to be considered a worthwhile addition to our armamentarium in treating this disease.

What effect the intradermal testing had in apparently curing Dr. Givner's patient is difficult to say. However, Dr. Berens said that, in his experience, the cure of chronic uveitis by a single treatment with any antigen or by any other method has never occurred, although the first or second intradermal injections often cause a marked improvement. Dr. Berens asked Dr. Givner whether he thinks that this patient may have had so-called primary glaucoma for several years and that this attack was merely a subacute attack of uveitis from some cause other than brucellosis in a patient who had had recurrent attacks of glaucoma.

However, the fact that in 38 of 437 eyes the pathologic diagnosis was uveitis and the clinical diagnosis was chronic primary glaucoma makes one suspect that we often fail to recognize glaucoma as secondary to uveitis. The history and Dr. Harris's tests seem to be highly suggestive of the correctness of the diagnosis, but as in many cases it is difficult to say whether nature or our treatment was responsible for affecting a cure.

Another point in this case is unusual and that it is the almost immediate control of the tension with a 2-percent pilocarpine solution. Dr. Berens said that he usually has to try homatropine and cocaine and alternate these drugs with pilocarpine and the use of neosynephrin. In chronic or recurrent cases it is usually necessary to inject nonspecific protein and follow aspiration with atropine before tension is controlled. This seems to be another point in favor of the possibility

of a subacute attack of uveitis, not necessarily due to brucellosis.

DR. HAROLD HARRIS said that this man had an ocular condition which could be caused by a Brucella allergy. There was a history of ingestion of raw milk prior to 1915. About 1927 he began to have afternoon fever of unknown origin, accompanied by fatigue. In May, 1948, tests for brucellosis showed the following significant findings: Slight relative lymphocytosis with a total white count of 6,800, a so-called positive opsonocytophagic reaction, and a very weakly positive skin test. All other tests were negative. Eight days after skin testing all intraocular signs had disappeared. Seventeen days after the first opsonocytophagic test, a second test showed a moderate increase in phagocytosis of Brucella.

The evidence was insufficient to establish or rule out a diagnosis of brucellosis. However, it is not uncommon for pathologic processes of various types to clear up rapidly following the desensitizing effect of intradermal Brucella antigens, as may well have happened in this patient. Prolonged observation would be necessary, in view of the equivocal nature of the laboratory data, in order to clarify the diagnosis.

DR. ADOLPH POSNER said that this case is interesting because it opens to discussion the basic question: What is the nature of glaucoma, on one hand, and of cyclitis, on the other.

Glaucoma is generally classified into primary and secondary. Clinically such a classification is of little use and serves to stifle further thinking and research. To revert to the case presented, Dr. Posner posed three questions to be discussed:

1. Is brucellosis an etiologic factor?
2. Is the glaucoma primary or secondary?
3. How is the cyclitis related to the glaucoma?

Dr. Posner said that there was little he could add to the discussion given previously on this question except to mention that he had observed very similar clinical cases who gave negative results to brucellosis tests as well as to all others.

The second question loses much of its significance when it is realized that we have adopted arbitrary criteria in classifying glaucoma into primary and secondary. It is only by maintaining an open mind and by carefully observing and analyzing all the delicate nuances of each individual case that we can hope to learn more about the many different diseases which we include under the generic term of "glaucoma." By such a discriminating study, we may ultimately break down this heterogeneous group into several clinical entities.

One such entity, represented by only a small number of cases, appears to have been isolated by Barkan, Sugar, and Kronfeld as "narrow-angle glaucoma." The acceptance of "narrow-angle glaucoma" as an entity does not imply that glaucoma should be classified into narrow- and wide-angle glaucoma.

Wide-angle glaucoma still remains a heterogeneous group of diseases of unknown etiology and the term is therefore meaningless.

In May, 1947, Dr. Posner said that he and Dr. Schlossman presented a group of 9 cases similar to the one described by Dr. Givner. This was believed to be another clinical entity and was called "the syndrome of recurrent glaucomatocyclitic crises." Dr. Posner said that he felt that the case presented belongs to this group.

The third question, that of the relation between the glaucoma and the cyclitis, has not been fully elucidated. That a relationship does exist is apparent from the fact that the keratitic precipitates disappear soon after the subsidence of the ocular hypertension. Both the glaucoma and the hypertension may be a result of an increased permeability of the capillaries in the ciliary body, or to a change in the ciliary epithelium itself. It may be related to an allergic response, although local and systemic administration of the antiallergic or antihistaminic drugs have thus far failed to produce a significant response.

Dr. Posner said that he agreed with Dr. Berens that pilocarpine does not always help, and other drugs may have to be tried. He said that he has never had to resort to paracentesis or other forms of surgery.

In these cases it is possible for keratitic precipitates to appear occasionally without a concomitant rise in ocular tension. In some of the cases, individual attacks of glaucoma have been noted in which cells and keratitic precipitates have remained absent. Such attacks assume all the earmarks of primary glaucoma and have been treated as such without bad effects.

This entity thus takes on an importance out of proportion to its actual incidence. It may well be that certain cases of primary glaucoma are related to this syndrome, so that it may be regarded as an intermediate link between primary and secondary glaucoma.

General discussion. Dr. Ludwig von Sallmann said that he felt that this case belonged to the group of cases known as recurrent glaucomatocyclitic crises. He suggested that the use of antihistaminics or pituitrinlike drugs might be beneficial. He said that Dr. Givner did not mention whether this case had attacks of cyclitis with cells in the anterior chamber without increased tension and at other times had a rise in tension without appearance of cells in the anterior chamber. He said that he agreed with Dr. Posner's views on the classification of primary and secondary glaucoma.

Dr. Frank Vesey asked why the investigation of this case was limited to brucellosis and whether any tests had been done for tuberculosis.

Dr. Arthur A. Knapp asked whether there was any systemic disturbance, whether an ear, nose, and throat examination was done, and whether the sphenoids had been irrigated.

Dr. Benjamin Esterman asked whether this case could be one of simple glaucoma with coincidental uveitis, and whether any provocative tests were done.

Dr. Adolph Posner replied that to determine whether it is primary glaucoma it is necessary to observe the case over future attacks. The provocative tests, water tests, and Lambert-Bloomfield tests give only positive results in simple glaucoma. Homatropine and dark-adaptation tests give positive results in narrow-angle glaucoma. This does not seem to be a case of narrow-angle glaucoma.

Dr. Isadore Givner said that he had presented only the positive findings in describing this case. X-ray studies of the sinuses and teeth were negative, and there was no infection of any kind found. X-ray studies of the chest to eliminate the possibility of tuberculosis were made and proved to be negative. The sphenoids were not washed since there was no indication for such a procedure, and the angle was perfectly normal.

CLINICAL AND HISTOPATHOLOGIC ASPECTS OF ANGIOID STREAKS

DR. BERTHA A. KLIEN, Northwestern University Medical School, Chicago, (by invitation) said that the main fascination of histopathologic studies lies in the ultimate possibility of finding explanations for all clinical manisfestations of disease. No other condition lends itself more readily to the correlation of a great variety of clinical and histologic phenomena than angioid-streak formation, mainly because of two circumstances. First, the clinical picture is characteristic and the clinical diagnosis definite from the earliest stage of just a few streaks around the optic disc to the advanced lesion with loss of central vision due to the disciform macular degeneration. Second, the course of the disease is very chronic, lacking the incidental tissue reactions of acute and subacute processes, every phenomenon being inherent in the pathogenesis of the disease.

The various phenomena occurring with angioid-streak formations are most easily discussed under two headings: (1) Find-

ings, which underlie clinically visible streak formation; (2) findings that underlie the peculiar appearance of the remaining fundus which is present in all advanced cases of angioid streaks and which consists of diffuse yellowish and diffuse opaque grayish discolorations.

Clinically, the earliest streaks are reddish brown with sharp, ragged outlines. Choroidal details are often visible within the broadest portions. Histologically, they are simple breaks in Bruch's membrane, rendered visible by the opacification of this membrane through elastic degeneration and calcification. Pigment epithelium and choroid are intact.

Old streaks often appear more yellowish or have yellowish-white accompanying lines. Histologically, many of the old defects of Bruch's membrane are filled with fibroblastic granulomas, which have formed around displaced, calcified fragments of Bruch's membrane. Other breaks are accompanied by linear crests of new tissue, which often undergoes hyalin degeneration. Injury of capillaries by sharp, calcified fragments of the membrane often leads to hemorrhages.

The pathologic process underlying the diffuse opaque yellowish or grayish areas consists in extensive new formation of a cuticular substance similar to the cuticular portion of Bruch's membrane but many times thicker. These cuticular deposits are often found over multiple breaks of the membrane, as if nature had attempted to preserve its continuity, so necessary to a normal pigment epithelium. The absence, presence, or hypertrophy of the pigment epithelium over these cuticular deposits produce their varied clinical appearance.

In the late stages of the disease the macular area is invariably occupied by a lesion, which has the typical clinical and histologic appearance of a disciform degeneration. The causes for the breaks in Bruch's membrane, however, are obvious, while they are still obscure in the Kuhnt-Junius type.

The pathogenesis of angioid streaks is based upon an abnormal fragility and opacification of Bruch's membrane. The fully developed picture, however, represents not only the visible ruptures of this membrane but also the multiform end results of irritation of pigment epithelium and choriocapillaris by the sharp, calcified edges and fragments of the broken membrane.

Discussion. Dr. A. L. Kornzweig asked about the various types of degeneration of the macula, and whether the pathology is the same.

Dr. Klien replied that the pathology was the same except for the appearance of Bruch's membrane. In angioid streaks the membrane stains black.

OCULAR PATHOLOGY IN DIABETES

DR. SAMUEL GARTNER said that diabetes is an important cause of visual impairment and blindness. The survival of more old people has increased the numbers suffering from this disease and insulin has prolonged their lives, so that we now see many more diabetics with eye lesions. The incidence of diabetic retinopathy increases with duration and severity of the disease regardless of the best modern care with diet and insulin, which does not prevent its onset and extension. A formula has been made to forecast the development of retinopathy.

Dr. Gartner described the pathology of diabetic retinopathy. There are hemorrhages, exudates, and cysts associated with extensive vascular damage.

All the cases examined showed some sclerosis of the arteries. Endothelial proliferation with canalization was found frequently in arteries and veins. Capillary disease was manifest by the formation of capillary aneurysms and capillary occlusions by endothelial proliferation. Rubeosis iridis probably follows the slow occlusion of the central retinal vein by phlebosclerosis.

Bernard Kronenberg,
Recording Secretary.

LOS ANGELES OPHTHALMOLOGICAL SOCIETY

September 2, 1948

Dr. William Endres, *chairman*

ALLERGY IN OPHTHALMOLOGY

Dr. Charles Petitt (by invitation) gave a comprehensive presentation of allergy as related to ophthalmology. The causes of inflammation are numerous and variable and depend on the rate of development of the reaction, its duration, and the release of substances such as histamine by the agent.

The histologic classification of lesions in allergy may be divided into two groups. The first necrotizing, in which there is some degree of necrosis. Parenchymal cells are present and eosinophilia is rare. Cincophen poisoning is an example of acute allergic necrosis. There may be either organ specificity or cell specificity such as anaphylaxis.

The second group are anaphylactoid or exudative reactions of which urticaria is an example. These are characterized by rapid onset, short course, and rapid regression. Secondary changes, as seen following any inflammation, are present. Cellular exudates, usually neutrophilic, are present but, if the condition is prolonged, eosinophilia predominates.

Eosinophilia is not pathognomonic of allergic states. Fibrinoid necrosis, which is focal and sharply delimited, such as periarteritis nodosa, may be present. This may or may not be on an allergic basis. Anaphylactoid reactions may follow injection of foreign serum. Rheumatic fever, which is a colloid disease, may be on an allergic basis since it is well known that the Ashoff nodule can be experimentally produced.

Granulomatous diseases in which tumorlike nodules are present are the result of inflammation. Examples of this are foreign-body reactions and sarcoidosis. There is no necrosis present in these conditions.

Allergic granulomas are characterized by central necrosis. These may be divided into two types: (1) The tuberculoid group which is caused by well-known agents such as tuberculosis, tularemia, mycosis, and brucellosis. These show positive skin tests to the causative agent. (2) Rheumatoid diseases of which there is no known etiology or positive skin test. Most rheumatoid diseases can be experimentally produced.

In vernal catarrh the diagnostic criteria are plaques in the conjunctiva especially superiorly. These plaques are usually pale and are not red and injected. The fornix is not usually involved and, on section, lymphocytic and fibrous tissue are seen. Eosinophilia are present in conjunctival secretions and the bacteriologic findings are the usual conjunctival inhabitants.

The disease follows a seasonal incidence usually occurring in the warm months—more often in children and especially boys. It is interesting to note that the seasonal incidence does not correspond with the seasonal incidence of pollens. Food sensitization has not been established and the picture, histologically, is not consistent with allergic manifestations. These patients rarely show positive skin tests and there is no greater incident in allergic than in nonallergic individuals.

The speaker did not believe that vernal catarrh is due to allergy nor did he believe that it was due to infection. Vaccine therapy has been of no help whatever. There are many types of conjunctivitis which are allergic and are due to dust, yeast, foods, and so forth.

In treatment, radium will alter the inflammatory states. If the allergen is given properly, a desensitization usually occurs and the condition is at least temporarily controlled.

Daniel B. Esterly,
Secretary.

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ELECTROPHYSIOLOGY

In 1849, Emil du Bois-Reymond placed the anterior and posterior poles of a vertebrate eye between two electrodes connected to a galvanometer and found that, independent of illumination, a current passed from the cornea to the fundus of the order of 6 millivolts. Since this demonstration of an electrical response from the eye, a century of zealous study has been devoted to the phenomenon.

Du Bois-Reymond, although of Swiss-French extraction, was born and educated in Berlin. Like his fast friend, Helmholtz, he was inspired by the illustrious teacher, Johannes Müller. Humbolt, in 1841, read a report of some simple experiments in animal electricity and suggested to Müller exploration of this field. Müller handed the problem to du Bois-Reymond, whose investigations continued for the next 40 years. After seven years, then aged 30 years, he published the first of his celebrated volumes on "Researches in Animal Electricity." At the death of Müller, 10 years later, he was awarded the Chair of Physiology at the University of Berlin.

The action current of the retina, now

called the electroretinogram, was discovered in 1866 by Holmgren, and simultaneously by Dewar and McKendrick of Scotland whose paper was actually in print when Holmgren's article was published. The Scotch investigators later observed, in 1873, that the invertebrate eye with its erect retina has a resting potential of the opposite sign to that of the vertebrate eye, signifying that the electric response of the eye, at rest as well as in action, is maintained by the visual cells.

The sensitive capillary electrometer enabled the Englishman Gotch to obtain, in 1904, the first electroretinogram that embodied all the features now known. The technique of valve amplification, which is now standard practice, was introduced by the Americans, Chaffee, Bovie, and Hampson, in 1923, and the retina was the first sense organ to be thus studied. By its means, Adrian demonstrated, in 1928, that an optic-nerve fiber responds to increased stimulus by increased rate of discharge, the size of the impulse remaining constant.

The analysis of the polyphasic response of the retina to light was initiated by Granit in 1932. His experiments with selectively acting agents proved that the vertebrate electroretinogram is built from at least three distinguishable components.

In 1938, Hartline isolated single fibers of a vertebrate optic nerve and demonstrated that all do not respond to light in the same way, and that a large number of visual units evidently respond only to changes in intensity. Shortly thereafter, Granit advanced Hartline's work by placing micro-electrodes directly on the retina, and so determined the color sensitivity of small groups of retinal elements—experiments which resulted in his modulator-dominator theory of color vision.

The electroretinogram affords a sensitive objective expression for the effects of light upon the retina. Even the luminosity curve is quantitatively reflected by the electrical response, as Granit revealed in 1943.

Among the contributors to the study of human electroretinograms are Karpe of Sweden, Spellberg of Russia, Amsler of Switzerland, and Adrian of England. Adrian has been his own subject in most of his work, operating the instruments by strings led into the dark room. The clinical application is illustrated by a case of Amsler's with variable concentric contraction of the visual field following trauma. Since the electric responses corresponded to a normal field he concluded that the contraction was due to a functional block at the cortical level.

The variation of the resting potential that occurs in the eye movements of reading can be recorded through electrodes placed at the external canthus of each eye. The graph closely duplicates the photographic record, but the electro-oculogram has the advantage of requiring no restraint nor the presence of a glare light. This method, perfected by Miles in 1939, was recently utilized by Carmichael and Dearborn in the most comprehensive study of reading and visual fatigue yet made. James E. Lebensohn.

THE FRENCH OPHTHALMOLOGICAL SOCIETY

The French Ophthalmological Society opened its 56th annual congress in 2,000-year-old Paris, at 8:30 a.m., on Sunday, May 22, 1949. The meeting lasted the customary six days. The mornings were devoted to papers and discussions and the afternoons to visiting hospitals.

Some 400 members attended, out of a total membership of 1,200. Strange to say, the French are far in the minority, numbering only 500, the other 700 members being foreigners. It is never possible for all to be present at any one meeting.

Twenty-three countries were represented: France, England, Ireland, Belgium, Switzerland, Italy, Holland, Spain, Portugal, Yugoslavia, Turkey, Greece, Syria, Lebanon, Iran, Poland, Denmark, Sweden, Luxemburg, United States, Colombia, Brazil, Argentina, and the town of Gibraltar.

The symposium of the congress, on uveitis with hypertension, was opened by Marcel Kalt. The discussers were J. François who spoke on gonioscopy in hypertensive uveitis; J. D. Blum and S. Forni on results of cyclodiathermy coagulation on the surface in secondary hypertensions; Hambresin on what collyria should be employed in hypertensive uveitis; Florian Verry on the aqueous humor in the hypertensive syndrome of uveitis; and Nectoux on the action of metamethylarmine (M.M.P.) on the eye and its employment in hypertensive uveitis.

The masterly review of the entire subject by Kalt and the gracious manner in which he replied to the discussers created a most favorable impression.

J. Q. Barraquer read a paper on postoperative complications of keratoplasty and Arruga one on the mechanical role played by retrobulbar injection in operations for strabismus. (It was during the meeting that Arruga was awarded the Gonin medal by the International Council of Ophthalmology then in session in Paris.) Valiere-Vialeux's paper on liquefaction of the vitreous and the loss of it in cataract extraction causing collapse of the globe was particularly instructive. Kirby's demonstration (using films and projection) of his technique for intracapsular extraction was excellent.

In the more than 60 presentations, almost every field of ophthalmology was touched on, surgery predominating. The proceedings were so efficiently conducted that no precious moment was lost. As a rule each discusser was already on the steps to the platform or actually on it before the speaker had concluded his last sentence. Nothing could be more stimulating and educational than to attend a session of the French Ophthalmological Society.

For the afternoons some 15 hospitals had prepared special operative and clinical programs which had all been posted the first day of the congress.

All through the week, in a large room under the meeting hall, there was held an exhibit, surprisingly fine for the times, of surgical instruments and various appliances gathered from many countries of Europe.

The afternoon for the traditional outing in the country fell on the third day. This time it was by bus to Malmaison and its lovely gardens, so reminiscent of the glorious days of the Consulate and the sad hours of the Emperor's abdication. On the way back to Paris a rarely enjoyable hour was passed in Villenes at Dr. Gabriel Renard's country place, hidden away from the roadside, in its lovely grounds, by trees and shrubs.

The banquet took place in the evening. Two hundred and eighty-two guests sat down at table. Paris still shows scars from bullets and fires of the recent conflict, especially around the Place de la Concorde, but gastronomically the recovery has been complete, as was borne out by the delicious dinner and the food everywhere. Prendront la parole à la fin du dîner, the president of the banquet, Sir Stewart Duke-Elder, made a most appropriate speech, as did Dr. Appelmans, Dr. Alvara, Dr. Streiff, and Dr. Rossi who sat at his table. The secretary general, Dr. Edward Hartmann, on whose shoulders had fallen the brunt of the whole congress, replied in the name of the society. His speech was on a very felicitous note that brought into the scene, one by one, each country that was represented.

Concerning the beginning of an organization that has met with well-nigh unprecedented success and world renown it will be informative to turn the pages of ophthalmology back to the year 1857 when the first International Ophthalmological Congress was held. Because it met at long intervals and at great distances and because the evolution of ophthalmology was proceeding so rapidly, the desirability of forming national societies for more convenient discussions arose which in turn have led to local societies. The German Ophthalmological Society of Heidelberg came into existence in

1863, the American Ophthalmological Society in 1865 and the Ophthalmological Society of the United Kingdom in 1880. The French Ophthalmological Society, at its foundation in 1883, was patterned after the Heidelberg society. However, it was to be an organization composed exclusively of French-speaking oculists. The Germans, when they heard of the new society, in sending their congratulations, made it known that, although their mother tongue was different from the Latin, they nevertheless hoped that the French would extend to them the hospitality of their meetings.

The granting of this desire was destined to have a far-reaching effect. At the second congress, in 1884, no less personages than Art and Hirschberg of Berlin, Bowman of London, Becker of Heidelberg, Donders of Utrecht, Horner of Zurich, Pflüger of Berne, and Reymond of Turin were numbered among the 112 members present. Today, among those from afar, are 21 members from the United States.

The society, like so many others, is but the lengthening shadow of one man, Chibret, of Clermont-Ferrand, whose initiative created it and who sent out the call for its first meeting. It always sits in Paris. Only twice has it gone elsewhere. In 1923, it met in Strasbourg at the centenary of Pasteur and, in 1925, in Brussels where at its opening session it was honored by the presence of her Majesty the Queen.

The society is governed by a committee of 12—5 members from Paris, 6 from the French provinces, and 1 from a foreign country. There is no president but instead a secretary general. It is often called the most international of all the national societies.   Bernard Samuels.

ACTA OPHTALMOLOGICA POLONICA

A Polish journal of ophthalmology has been launched. It is a quarterly publication called *Klinika Oczna, Acta Ophtalmologica Polonica,* and is a most promising journal. The paper is not nearly so good as that which we use and the half tones, although adequate, are certainly less crisp than they might be. But the intellectual content, on the other hand, has great merit. The scholarly articles in Polish are also presented in a very extensive abstract in English or French. The first articles in the first of the two issues that have been received report the work of Wilczck Marian on the lamina cribrosa which also appeared in the *British Journal of Ophthalmology.* There are also articles on refraction, physiologic optics, glaucoma, streptococcus, and on lesions of the cornea and retina.

The new journal is a welcome addition to ophthalmologic literature. We congratulate our Polish colleagues and wish them success in this fine venture.   F. H. Haessler.

OBITUARIES
ROBERT J. CURDY
(1868-1948)

Robert J. Curdy was born January 25, 1868, at Humbolt, Kansas. He was the son of William Wilson Curdy and Helen Sackett Curdy. There were two brothers and one sister. He received his early education in the public schools of Humbolt, Kansas, and then attended the College of Liberal Arts and Sciences at the University of Kansas, 1883 to 1886. He received the degree of Doctor of Medicine from Washington University in 1895, and completed the postgraduate course in 1896 (*cum laude*). He then entered the office of Dr. John Green, Sr., and was his assistant for three years. The following year he spent in study and in working in several leading European clinics. On his return to the states, Dr. Curdy opened his office in Kansas City, Missouri, for the practice of ophthalmology and remained in active practice to the day of his death, December 15, 1948.

Dr. Curdy became a member of the

American Ophthalmological Society in 1906 and was made emeritus member in 1938. He was a past president of the Kansas City Society of Ophthalmology and Otolaryngology. He was also a fellow of the American College of Surgeons and the American Academy of Ophthalmology and Otolaryngology. He was a member of the staffs of St. Luke's, Research, Municipal, St. Margaret's, and Children's Mercy Hospital and remained active in the clinic of the latter until 1946.

Dr. Curdy published many scientific articles and was the first to advocate equal recession and resection in horizontal strabismus. He was also first to advocate the external approach in narrow-angle glaucoma, and designed a special knife for the purpose of performing the Lagrange sclerectomy by the external approach.

He was married to Ann Richardson Hall on November 3, 1906. Two daughters, Helen and Isabel, and Mrs. Curdy, survive.

Robert Curdy was a keen clinician and was unsurpassed in presenting and discussing the differential diagnosis in an obscure case. He was one of those rare individuals who knew no enemies, either in or out of the profession, and never once was he known to have said an unkind word of anyone. Robert Curdy has died but his memory and ideals will live on in the minds of us who have been privileged to have known him intimately. Albert N. Lemoine.

DAVID L. TILDERQUIST
(1872-1948)

With the passing of David Tilderquist on September 26, 1948, the medical profession lost one of its most unassuming but devoted ophthalmologists and the people of the Northwest lost a well-beloved friend and skilled physician, who had served them for 44 of his 76 years. Dr. Tilderquist will always be remembered for his humble and kindly manner, his generosity, his unswerving loyalty to all that was good, and for an integrity of character which endeared him to everyone who knew him.

He was born in Vasa (Goodhue County), Minnesota, on October 22, 1872. He lived and worked on the parental farm, attending the local public schools and then Gustavus Adolphus College in St. Peter, from which institution he was graduated in 1894. After teaching in the public and parochial schools in Goodhue County and at Hope Academy in Moorehead, Minnesota, for six years, he entered the University of Minnesota with a keen desire to become a chemist. His brother, William, a mining engineer, prevailed upon him to continue his studies in medicine rather than chemistry and, in 1903, after he was graduated from the University of Minnesota, he spent a year interning at Swedish Hospital in Minneapolis—in the days when many medical students entered practice without benefit of internship. Dr. Tilderquist spent much time in the pathologic laboratory doing independent study.

He established a general practice in Duluth, in 1904, which, from the early days, taxed even his great capacity for long hours of work. He studied abroad first from 1910 to 1911, when he specialized in ophthalmology and otolaryngology, and then again in 1924, when he took further work in Vienna.

Dr. Tilderquist held a number of hospital staff appointments during his long years of service in Duluth, including that of chief of staff at St. Luke's Hospital, and chief of the Eye, Ear, Nose, and Throat Service at St. Mary's Hospital. During the past 25 years he had taught the nurses' classes in ophthalmology at St. Luke's Hospital and annually offered awards for scholarship in therapy and bedside nursing. He was instrumental in establishing and running the ophthalmologic service of the Methodist Dispensary for many years and later assumed more than his share in the ophthalmic work of the Miller Memorial Hospital Dispensary, when younger men were not available to carry on the service.

In 1926, Dr. Tilderquist was president of the Minnesota Academy of Ophthalmology and Otolaryngology; at the time of his death he was serving as its vice-president. He was a member of the American Academy of Ophthalmology and Otolaryngology, a member of the American Medical Association, the American College of Surgeons, the Minnesota State Medical Association, and the St. Louis County Medical Society. He was a diplomate of the American Board of Ophthalmology and the American Board of Otolaryngology.

He was an ardent student and followed the ophthalmic literature closely. His mind was a scholarly one and his reading was not aimless. In addition to following the current literature, he always pursued one or more definite lines of study. He wrote few articles, largely because of his extreme modesty. For many years he found time to abstract Scandinavian ophthalmic literature for the AMERICAN JOURNAL OF OPHTHALMOLOGY, whose editor was his close friend, Edward Jackson. He developed a few surgical instruments, which are on the market, but of which he never spoke.

This quiet scholar encouraged studious habits in others; his was the moving spirit in the small local organization of ophthalmologists and he it was who stimulated the members to study and to make reports. He always faithfully attended the meetings of the local county society, the weekly pathologic conference, the Minnesota Academy of Ophthalmology, and the American Academy of Ophthalmology. He was always most kindly and generous to younger men, several of whom, it has been learned, he helped through medical school. He established a scholarship at his alma mater, Gustavus Adolphus, for freshmen who give promise in scientific study. In 1946, this college honored him with a special award as one of the outstanding alumni who had been of great service.

His generosity and unselfishness are typified in the letter, accompanying a research grant given to the writer, which reads in part:

"Enclosed herewith please find a gift in the interest of research. . . . You may use this fund in any way you see fit, or you may even reimburse yourself from it for expenses incurred or for losses sustained or compensate yourself for time spent on account of research done in the past.

"This fund is meant to be a help and not a burden. Therefore it does not carry with it the implication that any research must be carried out that would not otherwise have been undertaken without the fund.

"Wishing you many dividends in the form of new knowledge and much enjoyment and satisfaction. . . ."

Dr. Tilderquist gave unstintingly of himself to his patients; no matter how late the hour or how great his own fatigue, he worked patiently and carefully with each one. Colleagues, who sought his consultations frequently, did so because they felt assured an exhaustive and conscientious study would follow.

Dr. Tilderquist had the rare good fortune to experience, while he was still alive, hundreds of expressions of love and admiration, which so often go unsaid. His measure, indeed, was overflowing with the admiration, respect, and love of his colleagues and his thousands of grateful patients and friends.

A. C. Hilding.

CORRESPONDENCE

BETA IRRADIATION OF THE EYE

Editor,
American Journal of Ophthalmology:

In a recent pamphlet distributed by Dr. Harold Swanberg describing his radium-D applicator, produced by the Canadian Radium and Uranium Corporation, quotations were made from the article by Hughes and Iliff, "Beta irradiation of the eye," AMERICAN JOURNAL OF OPHTHALMOLOGY, 32:351 (March) 1949.

The results of beta radiation reported in

this article were obtained by using radon (not radium-D) applicators. The experiments and clinical results from the use of a Swanberg radium-D applicator at the University of Illinois have been reported by Dr. Fred M. Wilson at the 1949 meeting of the Association for Research in Ophthalmology.

Dr. Wilson found important differences between the effects of radium D and radon, the former showing about 40-percent effective beta output and less penetrating power. These differences are important in the practical aspects of treatment; for example, duration of treatment and ability to eliminate corneal vascularization and other pathologic processes situated more deeply in the lids, cornea, and sclera.

(Signed) William F. Hughes, Jr.,
Chicago, Illinois.

STAINING TECHNIQUE FOR
TRACHOMA INCLUSIONS

Editor,
American Journal of Ophthalmology:

In the May, 1949, issue of the JOURNAL, page 702, Lieut. V. O. Eareckson brings forward Wright's staining method as "a rapid staining technique for the demonstration of trachoma inclusions." Forty years ago I brought forward the same method for the same purpose—"A rapid method of staining the trachoma bodies of Halberstaedter and Prowazek," *Ophthalmic Record*, October, 1909. Probably the reason it did not come into general use was that it requires more careful attention to detail than does the Giemsa method.

(Signed) F. H. Verhoeff,
Boston, Massachusetts.

BOOK REVIEWS

TOXIC EYE HAZARDS. A manual prepared by the Joint Committee on Industrial Ophthalmology of the A.M.A. and the American Academy of Ophthalmology and Otolaryngology. Publication No. 494. New York, The National Society for the Prevention of Blindness, 1949. 34 pages, 10 illustrations, bibliography. Price, $1.00.

The preparation of this manual and the extensive work that went into its background excites profound admiration for all who had a part in its formation and assisted in its publication.

It is a factual, practical, and inexpensive masterpiece of great use to industry and ophthalmologists working with industrial eye problems.

Chapter I has to do with standards and tests for eye-protection equipment. It describes, as an example, a well-organized eye-protection program. Part II of the first chapter gives tables of toxic compounds and the ocular signs and symptoms they produced.

Chapter III contains an excellent description of standard emergency and first-aid procedures in chemical eye injuries, based upon the completely satisfactory results obtained from practical experience.

The manual should be read and studied by every ophthalmologist, whether interested in industrial ophthalmology or not, and by every physician employed by industry. Derrick Vail.

UEBER WERTUNG ANGEBORENER FEHLER DES FARBENSEHENS. By Georg Wilhelm Keyser, M.D. Oslo, Norway, A. W. Brøgger Press, 1943. Paper covers. 174 pages, bibliography, 2 colored plates. Price, not listed.

The problems of color vision have excited a marked recrudescence of interest in the past decade. Keyser, as a practicing ophthalmologist, is primarily concerned with the color capacity requisite for the performance of various tasks. The introductory chapters review both critically and comprehensively the contributions to our knowledge of color deficiency, from the original discovery by Dalton of his own color blindness in 1794 to the present.

Then follows a detailed analysis of the signals used in railroading, navigation, aviation, and military maneuvers. Keyser objects to the Nagel anomaloscope because it tests only foveal function, whereas he maintains that the parafoveal area, because of irradiation and dispersion, should be of principal importance in signal discrimination.

Keyser prepared a strip of color film that recorded a blinking red light in Oslo harbor. With this strip he tested men from 11 to 77 years of age, classified by the standard tests as normal or having various types and degrees of color deficiency. Only deuteranopes failed consistently in the test, calling the red light green. The anomalous trichromats named the color correctly.

He asserts that modern signal devices largely eliminate the danger of wrong interpretation by the color deficient. However, he would consider any form of color weakness as a serious handicap in medical practice, as the undue color contrast characteristic of anomalous trichromats may induce false judgments on tissues and bacterial slides.

The book is highly stimulating and suggests the need of further studies on the practical problems of color deficiency in connection with the conditions of the assigned tasks. It is to be hoped that Keyser will soon complete the English version of this work according to his original intention.

James E. Lebensohn.

How to Become a Doctor. By George R. Moon, A.B., M.A. Philadelphia, The Blakiston Company, 1949. 130 pages. Price, $2.00.

The boy or girl interested in a medical career is often at a loss for where to turn for advice on where to go for his medical education, for information about the courses given, and how to qualify to take them.

Moon has performed a much-needed task in giving this information in a compact form that is highly successful in its aims. It is a "complete guide to the study of medicine, dentistry, pharmacy, veterinary medicine, occupational therapy, chiropody and foot surgery, optometry, hospital administration, medical illustration, and the sciences."

It should be in the hands of anyone who is preparing to "become a doctor."

Derrick Vail.

Gli Antibiotici in Oftalmologia. By Antonio Grignolo. Torino, Minerva Medico Press. 321 pages, 21 figures. Price, not listed.

This thorough monographic treatment of the antibiotics is to be highly recommended to Italian readers. The author has not favored us with summaries in another European language, as have some of his countrymen, but it is arrogant to expect this from one who writes in a language which was used by perhaps the only poet who is the equal of Shakespeare. The date of publication is not stated but the bibliography contains reference to publications in 1948.

The entire subject is adequately treated. After a brief introductory statement on the nature of the antibiotics, the work on penicillin and streptomycin is extensively described and many other antibiotics are given shorter but adequate review. The preparation, titration, biologic properties, tolerance, and dosage are discussed from personal experience and on the basis of a thorough review of the literature.

Even more, extensive treatment is accorded the specifically ophthalmic experience. Diseases of each ocular tissue are discussed in detail and the merits, as well as inadequacies, of antibiotic therapy are evaluated. Each section has an extensive list of references.

F. H. Haessler.

ABSTRACT DEPARTMENT

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

2
GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Buschke, W. **Morphologic changes in cells of corneal epithelium in wound healing.** Arch. Ophth. 41:306-316, March, 1949.

The authors report their experiments with corneal injuries in rats and frogs. Pseudopodial extensions of the cytoplasm directed into the denuded area are seen in the basal layers of the epithelium in the early stages of healing of pinprick injuries. These pseudopods are observed particularly in pockets of the wound margin during the healing of larger injuries. Spreading and flattening of the epithelial cells, which lead to sealing off of the wound margin, occur in linear and larger lesions in the early stages. This sealing off is seen also in the healing of small injuries in the superficial layers of the epithelium.   Ralph W. Danielson.

3
VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Agrest, A., Roncoroni, A. J., García Badaracco, J. E., and Vidal, F. **Carbam-**inoylcholine in rabbits with partial parathyroidectomy. Arch. de oft. de Buenos Aires 23:294-297, Oct., 1948.

The authors feel that the tetany of hypoparathyroid states occurs because the hypocalcemia modifies the sensitivity of acetylcholine. Partial parathyroidectomy was performed on rabbits and carbaminoylcholine was used as an index of the activity of acetylcholine. In some hypocalcemic animals observed, the ocular tension did rise as the body contractions increased, and when calcium was administered intravenously the tetany diminished and the tension was lowered. However, as yet, it is not possible to draw any satisfactory conclusions. (4 graphs.)   Edward Saskin.

Baumann, Adamo. **First report on experimental researches in electroretinography.** Ann. di ottal. e clin. ocul. 74:375-380, May, 1948.

A suitable subject for electroretinography was found in a woman with craniofacial dysostosis whose eyeball could be dislocated so far forward that an electrode could be applied to the posterior pole of the globe. Baumann found that as the intensity of the luminous

stimulus is increased the retinal action current likewise increases up to a point beyond which further increase in the stimulus results in decrease in the action current. (References.)

Harry K. Messenger.

Cristini, G., **The vascular action of pilocarpine, eserine, adrenalin and atropine, and their influence in primary chronic glaucoma.** Brit. J. Ophth. 33:228-242, April, 1949.

Pilocarpine and eserine do not dilate the large vessels of the iris and ciliary body but dilate the capillary bed and open new capillary districts. Although this produces an increase of the sum of resistances in the circulation, the total result is reduction of the mean capillary hydrostatic pressure and, therefore, of the ocular tension. Atropine dilates the large vessels, but does not open new capillary beds. This decreases the sum of resistances and, therefore, increases the mean hydrostatic pressure whenever the capillary bed is already impaired, as in chronic glaucoma. Adrenalin dilates both the large vessels and the capillaries and increases the circulatory bed. The result is an increase in the sum of resistances, and a decrease of the mean capillary hydrostatic pressure and of ocular tension. In acute glaucoma, however, the excessive permeability in the capillaries for plasma proteins may produce elevation of intraocular pressure.　　Orwyn H. Ellis.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Swan, K. C. **Pharmacology and toxicology of the cornea.** Arch. Ophth. 41:253-275, March, 1949.

This article combines literature, original research, and practical suggestions in therapy so admirably that it should be read in full.　　R. W. Danielson.

Vidal, F., García Badaracco, J., Agrest, A., and Roncoroni, A. J. **Neurocapillary test in rabbits.** Arch de oft. de Buenos Aires 23:292-293, Oct., 1948.

Carbaminoylcholine solution, 0.33 percent, was instilled into rabbits' eyes with these results: increased lacrymal and salivary secretion within three minutes, increased intestinal motility and diarrhea within five minutes, increased pulse rate, conjunctival vasodilatation, and miosis. Influence on ocular tension was equivocal. (2 graphs.)　　Edward Saskin.

Woods, A. C. **Experimental studies on the pathogenesis and treatment of ocular tuberculosis.** Brit. J. Ophth. 33:197-228, April, 1949.

The author reports on 12 years of investigation in which human strains of the tubercle bacillus were injected into the anterior chamber of rabbits. In the study of pathogenesis the influence of the number and virulence of organisms was determined. Small doses of virulent bacilli in a normal animal produce a slowly-spreading infection. A larger dose accelerates the reaction. In the immune-allergic rabbit the propagation and spread of the organisms is restrained. With a large dose the immunity is overwhelmed and the animals develop an acute destructive inflammation. In both the normal and immune-allergic animals the ocular inflammation resulting from infection approximates the degree of ocular sensitivity. Desensitization before inoculation abolishes the primary ocular reaction to tuberculoprotein, and the ocular inflammation is of low degree when the desensitization is maintained. The resistance to reinoculation was totally undisturbed by complete densensitization before inoculation. With high cutaneous sensitivity the ocular sensitivity is also high; however, ocular disease may produce great ocular sensitivity without affecting a normally low cutaneous sensitivity. The transient

immunity to re-inoculation shown by eyes that have recently recovered from tuberculosis is due to the presence of persisting macrophagic cells. Desensitization with tuberculin is accompanied by a marked decrease in manifestations of the disease. It removes the destructive factor. If tuberculin treatment is stopped the tissue sensitivity, and in many animals the ocular lesion, recur. The relatively nontoxic sulphone, promizole, has a deterrent action on the local tuberculous lesion in the immune-allergic rabbit, and when combined with streptomycin eradicates the bacilli from the infected tissue of most of the animals, and curtails their growth and virulence in the others.

Orwyn H. Ellis.

5

DIAGNOSIS AND THERAPY

Bunge, E. **A new method for quick determination of the dominating eye.** Klin. Monatsbl. f. Augenh. 114:69-71, 1949.

An observer looking into two mirrors joined by a stick at a right angle will note double images. The image in the dominating eye is the more disturbing. The author discusses his method and compares it with others. Max Hirschfelder.

Dattner, B., Distelheim, I. H., and Maltzer, L. **BAL in arsenical optic neuritis.** New York State J. M. 49:190-192, Jan. 15, 1949.

BAL has been found to be of value in removing arsenicals and heavy metals from living tissue. Pentavalent arsenic was used for pemphigus vulgaris and toxic optic neuritis secondary to the treatment was relieved by the intramuscular use of BAL. The dosage used was 0.5 cc. intramuscularly, increased by 0.5 cc. every three hours until 2 cc. is reached. Ephedrine sulphate 0.24 gm. is given orally one half hour before each dose and at the time of injection of BAL it is re-

peated. BAL must be used with caution. It produced a toxic psychosis in this patient during the course of treatment.

H. Weinberg.

García Notico, F. **New technique for the inclusion of muscles on a spike, in enucleations.** Arch. de oft. de Buenos Aires 23:216-219, Sept., 1948.

The plastic prosthesis has a central cone behind, which extends back into the muscle cone. The anterior portion consists of a hemisphere, from which a spike projects forward. Near the circumference are four slits, through which the muscles are drawn forward and impaled on the spike. They are then sutured together. Tenon's capsule is sutured over the muscle ends, and the conjunctival covering is closed. A conformer is placed in the conjunctival sac, which has a hole in the center to receive the tip of the spike. Iced compresses are used during the first twenty-four hours and pressure bandages for five days. A. G. Wilde.

Goldman, H. **Slit-lamp examination of the vitreous and the fundus.** Brit. J. Ophth. 33:242-247, April, 1949.

Inflammations, detachments, cysts, degenerations and tumors can usually be definitely diagnosed by fundus biomicroscopy, with the help of a fundus lens and the author's own prism for reducing the angle between the illuminating beam and the corneal microscope.

Orwyn H. Ellis.

Jaeger, A. **An addition to the nyctometer of Comberg.** Klin. Monatsbl. f. Augenh. 114:82-84, 1949.

In order to avoid variation in illumination of the Comberg nyctometer it is necessary to test the incandescent lamp more exactly than is possible by the use of a simple ampere or volt meter. The author describes a photometer for this purpose. (1 figure.) Max Hirschfelder.

Toennis, W. **Indications for surgical treatment of tumors in the sella turcica.** Klin. Monatsbl. f. Augenh. 114:1-18, 1949.

In a postgraduate lecture the author surveys tumors in the region of the sella turcica, which are about one fifth of all intracranial tumors. The pathologic findings associated with various tumors of this region (pituitary tumors, craniopharyngiomas, meningiomas, gliomas, aneurysm, epidermoids, arachnoiditis, tumors of the cranial base) are discussed briefly. (9 figures, references.)

Max Hirschfelder.

6

OCULAR MOTILITY

Abbate, Vincenzo. **A case of paresis of the elevator of the left upper lid and of the left external rectus, treated with injections of irradiated maternal blood.** Ann. di ottal. e clin. ocul. 74:369-374, May, 1948.

The nine-year-old patient received daily for eight days an injection of 4 cc. of her mother's blood which had been exposed for five minutes to ultraviolet radiation. Complete recovery ensued in about three weeks. The efficacy of irradiated maternal blood is ascribed not only to its physical properties but also to imponderable spiritual factors which transferred only from a mother to her child.

Harry K. Messenger.

Bruens, E. **Sutures used in resection for strabismus.** Klin. Monatsbl. f. Augenh. 114:62-69, 1949.

The author describes a modification of Blaskovics' two U-shaped sutures for his resection. (20 figures, references.)

Max Hirschfelder.

Bursaux, M. O. **Orthoptic treatment for strabismus.** Ann. d'ocul. 182:128-132, Feb., 1949.

The author compares the newer principles, methods and instruments used in orthoptic treatment with those of the older French masters such as Javal, Rémy and Landolt. Several French ophthalmologists studied orthoptics in the United States and Great Britain during and after the war. In their writings they have introduced the newer instruments, methods and principles to French ophthalmologists. An orthoptic clinic has been established in the Lariboissiere Hospital in Paris. The newer methods are but slightly improved adaptations of the fundamentals laid down largely by French ophthalmologists several generations ago. In many cases the results have been no better than those obtained with the older orthoptic methods.

Chas. A. Bahn.

Gartner, S., and Billet, E. **Progressive muscular dystrophy involving the extraocular muscles.** Arch. Ophth. 41:334-340, March, 1949.

A lesion of the nerve supply is so commonly the cause of palsy of an extraocular muscle that there is a great tendency to forget the rarer occurrence of a primary muscular disorder. Progressive muscular dystrophy was the cause of ptosis and divergent squint in a case presented. This case is the second in which histologic study of the extraocular muscles has been reported and the first in which involvement of the extraocular muscles has been demonstrated in a case of generalized progressive muscular dystrophy. The differentiation of primary muscular dystrophy and secondary muscular atrophy is discussed.

Ralph W. Danielson.

Gasteiger, H. **Some rarely performed muscle operations.** Klin. Monatsbl. f. Augenh. 114:49-54, 1949.

In four patients a high degree of paralytic strabismus was corrected by the method of Vogt. Three had extreme convergence. The medial rectus was completely tenotomized and severed from all its connections. Double-armed sutures were then laid through the superior and

through the inferior rectus and conducted laterally, subconjunctivally, and through the skin to a point lateral to the outer canthus. They pulled the eyeball straight and were removed after ten days. A similar method was used for a contraction of the superior rectus in the fourth patient. Muscle transplantation was done in three patients with paralytic strabismus. This method is of advantage when strong secondary contracture of the antagonist is lacking. (9 figures, references.)

Max Hirschfelder.

Kunz, E. **A method for exact dosage of strabismus surgery.** Klin. Monatsbl. f. Augenh. 114:55-62, 1949.

The effect of surgery in horizontal strabismus is mathematically analyzed. The rotation of the eye after unilateral surgery corresponds to the actual amount of advancement or recession multiplied by an undetermined factor. This factor is a fraction, the numerator of which is the elastic power of the antagonist, and the elastic powers of both muscles is the denominator. If equal amounts of recession and advancement are done on the two horizontal muscles at the same time, this factor can be disregarded. The article shows mathematically why this is the case. A schedule indicating the necessary amounts of recession and resection for all degrees of horizontal strabismus is displayed. (References.)

Max Hirschfelder.

Lienau, R., and Alvarez Montalván, E. **Bilateral congenital paralysis of the facial muscles and the lateral rotators.** Arch. de oft. de Buenos Aires 23:272-275, Oct., 1948.

A 20-year-old man was unable, from birth, to move his eyes outward, had bilateral facial paralysis, and a deformity of the feet. He had a moderate loss of visual acuity and normal fundi. The oculomotor apparatus was defective in associated lateral version. He could converge and at times force a bilateral diversion. There was only elementary fusion. (13 figures.)

Edward Saskin.

Loutfallah, M. **Surgery of the inferior oblique.** Ann. d'ocul. 182:81-121, Feb., 1949.

The muscles primarily and secondarily involved in paralyses of the vertical ocular rotation are discussed in detail. After a primary paralysis of the right superior rectus, a hyperfunction of the right inferior rectus and left inferior oblique may follow within a short time. Later a hyperfunction of the right inferior rectus and right inferior oblique with hypofunction of the left superior oblique may occur. The author presents the surgical anatomy and clinical physiology of the inferior oblique muscles at some length. Their proximity to the optic nerve and vorticose veins is important. Their torsional function is analysed. The indications for surgical weakening operations of the obliques include some forms of unilateral and bilateral hypophorias and tropias which may primarily involve the contralateral superior rectus; also disassociated vertical deviations with or without faulty insertion of the internal rectus. Methods for weakening include recession (White), myectomy with lid incision (Bonnet) and with conjunctival incision (Parker). Strengthening or reinforcing procedures include: resection (Berens), tucking (White), and advancement (Wheeler). Transplantation of the inferior oblique (Weiner) is seldom considered of value. Among the contraindications to inferior oblique surgery are slight and transient disassociated deviations, and faulty insertions. Operations and postoperative complications are discussed. Finally, an analysis of 38 operations performed by the author is presented in detail. The author prefers recessions and resections near the sclera to myectomy. (52 references.)

Chas. A. Bahn.

Piper, H. **The etiology of infantile ocular muscle disturbances.** Klin. Monatsbl. f. Augenh. 114:42-49, 1949.

The author describes nine children who had strabismus with secondary underaction of certain muscles. The first of three groups comprises cases of concomitant squint, in which lack of function during an important stage of development led to an underaction of a muscle. The second group involves supranuclear disturbances. In the third group isolated muscle paralysis with degenerative changes (shortening) lead to an underaction of the antagonist. The retraction syndrome belongs in this group. (13 figures, references.) Max Hirschfelder.

7

CONJUNCTIVA, CORNEA, SCLERA

Appelbaum, H. B., and Hale, A. S. **Aureomycin in dendritic keratitis.** J. Michigan St. M. Soc. 48:352, March, 1949.

The authors review the properties of aureomycin and its toxicity. A patient who had dendritic keratitis for over four years with frequent exacerbations was given two drops of aureomycin ophthalmic solution (0.5 percent) every two hours and was well in two days. There has been no recurrence. H. Weinberg.

Delaney, J. H. **Treatment of dendritic keratitis.** Pennsylvania M. J. 52:845-847, Sept. 25, 1949.

Dendritic keratitis is caused by a virus. Iodine therapy is still the best method of treatment. Streptomycin seems to inhibit the progress of the virus and aureomycin may well be an effective drug.
F. H. Haessler.

Houet, R., and Weekers, R. **Xerophthalmia of the newborn and hepatic insufficiency.** Arch. d'opht. 9:39-43, 1949.

The authors note that xerophthalmia in the newborn due to deficient intake of vitamin A is extremely rare, whereas xerophthalmia resulting from poor absorption of vitamin A due to various diseases, particularly of the intestinal tract, is more common. They describe two cases in which there was disturbance in the transformation of carotene into vitamin A in the liver. The first baby had a sudden attack of jaundice at the age of two months which recurred at intervals. At three months a corneal ulcer developed simultaneously with the onset of xerophthalmia. Following daily injections of 60,000 units of vitamin A, the xerophthalmia disappeared rapidly but the infant progressively lost weight and died. The lesion was a serious disturbance of the liver parenchyma. The second infant, premature at 7½ months, developed normally until the age of 3½ months when it developed bilateral corneal opacification with perforating ulcers of each eye. There appeared to be normal absorption of vitamin A and the diet had not been deficient. The child was placed on a daily dosage of 60,000 units of vitamin A and slowly improved, but the corneas healed with extensive scars.

The authors comment on the mechanism of vitamin A absorption and on the double role of the liver in vitamin A metabolism. It produces bile which emulsifies the fats, permitting absorption of vitamin A, and its parenchyma is concerned in the transformation of carotene into vitamin A. Phillips Thygeson.

Muller, P. **Mosaic degeneration of Bowman's membrane.** Ann d'ocul. 182:122-127, Feb., 1949.

This rare condition which Vogt has named "crocodile chagrain" is essentially a degeneration of Bowman's membrane which seems to be composed of round or polygonal cells. An illustrative case in a 51-year-old man is described. After slight injury to the left eye by a twig, hypopyon keratitis developed. Later, a transplantation operation was performed. The ex-

cised cornea showed breaks in Bowman's membrane, which were replaced by cicatricial tissue.   Chas. A. Bahn.

Paraipan, C. **Severe corneal ulcer cured by intraocular penicillin in 48 hours.** Ann. d'ocul. 182:133-134, Feb., 1949.

A 68-year-old man developed a severe corneal ulcer after injury. A solution of 10,000 units of penicillin to the cc. was injected into the anterior chamber and two subconjunctival injections of 10,000 units of penicillin were also made. The ultimate vision was 20/50.

Chas. A. Bahn.

Sená, J. A., and Cerboni, F. C. **Scleral excavations.** Arch. de oft. de Buenos Aires 23:313-325, Oct., 1948.

After a discussion of the history and pathology of such common afflictions of the sclera as senile hyaline plaques, inflammatory processes, and scleromalacia perforans a case is presented in which there were bilateral excavations of the sclerae, temporally, with typical senile hyaline plaques. (8 figures, references.)

Edward Saskin.

Trovati, E. **The bacterial flora of the conjunctiva in certain exanthematous diseases of infancy.** Ann. di ottal. e clin. ocul. 74:358-368, May, 1948.

The conjunctiva was not inflamed in scarlet fever and chickenpox; the conjunctival flora was normal in chickenpox, but in scarlet fever streptococci and staphylococci were isolated. Conjunctivitis is a usual accompaniment of measles, in which the flora is normal except for an increase in sarcinae, to which the conjunctivitis is attributed.

Harry K. Messenger.

Wenda, L. **The syndrome of blue sclerotics.** Arch. d'opht. 9:44-47, 1949.

The syndrome is a constitutional one with numerous complications in different organs and tissues of the body although the principal manifestation is blue scleras. The blue coloration of the scleras is not due to pigmentation but to the thinness of the structures which reflects a disturbance of the tissues of mesenchymal origin throughout the body. The disturbance is particularly marked in the bones, and repeated fractures are the rule. The ligaments are the next most seriously involved and dislocations of the joints and prolapses of various organs are common. Hemorrhages are frequent due to faulty connective tissue in the blood vessels. Visual disturbances due to cataract and deafness due to otosclerosis are common. Myopia with staphyloma has been reported. Wenda reports two cases, one a young girl of 16 years, the other a woman of 60, both with the classical syndrome. He notes, however, that whereas cases of the complete syndrome are rare, many instances of the incomplete syndrome have been reported. He states that women are more subject to the syndrome than men and urges that persons with this disease marry only individuals who are strong and vigorous.

Phillips Thygeson.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Kapuscinski, W. J., Jr. **Pyretotherapy as a diagnostic provocative in uveitis.** Arch. d'opht. 9:27-30, 1949.

Kapuscinski uses typhoid vaccine intravenously in a technique devised by him which consists of a series of small doses increased gradually from .01 cc. to 1.0 cc. By this method he obtains a fever curve comparable to that of tertian malaria. He has found that in uveitis of tuberculous origin subjected to fever therapy there is usually an aggravation of the local eye lesion, an increase in the sedimentation rate, and sometimes a manifest oscillation of the daily tempera-

ture curve. In nontuberculous uveitis the fever therapy usually results in an acceleration of the sedimentation rate but does not change the daily temperature curve and affects the eye lesion favorably. In a series of 40 cases only four could be considered tuberculous. Fifteen cases are described in detail. The most frequent cause of uveitis is a streptococcal granuloma in a dead tooth or in the tonsils.

Phillips Thygeson.

Malbrán, J. L., and Rebay, C. A. **Rubeosis iridis and anterior glaucoma of Contino and Favaloro.** Arch. de oft. de Buenos Aires 23:276-291, Oct., 1948.

Rubeosis iridis is characerically seen in many diabetics on the anterior surface of the iris, from the root to the pupillary zone, as many radially arranged thin vessels that do not invade the pigmentary pupillary epithelium nor quite reach the angle of the anterior chamber, which description coincides with Salus' original observations. The ocular tension is often elevated. This syndrome may be more completely described as follows: painful glaucoma, deep anterior chamber, iris turbidity with new-vessel formation as described above, dilated pupil, with or without anterior chamber hemorrhage, and venous hyperemia. The authors point out that rubeosis may or may not exist with or without glaucoma and that the glaucoma may appear in patients without diabetes as well as in diabetics. Thirteen cases are described in detail and the important findings are tabulated. (4 figures, 1 table, 25 references.)

Edward Saskin.

Tower, P. **Traumatic choroiditis.** Arch. Ophth. 41:341-352, March, 1949.

Ten cases of so-called rupture of the choroid are reported. The etiology and pathology of these lesions are discussed. Discontinuity of the choroid following indirect injury to the eyeball is shown to

be due to necrotic changes of trophic character. A more precise terminology is proposed; "arciform traumatic choroiditis" is suggested for crescentic lesions and "diffuse traumatic choroiditis" for those of irregular outline.

Ralph W. Danielson.

9

GLAUCOMA AND OCULAR TENSION

Bloomfield, Sylvan. **The lability test: a new procedure for the diagnosis of chronic simple glaucoma.** New York State J. Med. 49:659-662, March 15, 1949.

The test combines the cold presser test of Hines and Brown and the jugular compression test described by Schoenberg. The patient lies flat on the table and one hand is immersed to the wrist in ice water. A blood pressure cuff around the neck is inflated to a pressure of 50 to 60 mm. Hg so that both jugular veins are compressed simultaneously. After one minute the tension is recorded. A rise of more than 9 mm. Hg (Schiøtz) above the ocular tension taken just before the patient immerses his hand in the ice water is a reliable aid in making a diagnosis of chronic simple glaucoma in that eye. This test compares very favorably with the other provocative tests now in use. The responses are greater and more easily recognized than those from the other tests in use. (4 figures.)

H. Weinberg.

Bonavolontà, Aldo. **Ophthalmoscopic examination with red-free light in glaucoma.** Ann. di ottal. e clin. ocul. 74:459-478, Aug., 1948.

In prodromal and incipient glaucoma slight fading of the macular yellow and diminution of the foveal reflex may be noticed, but nothing is found that might not be expected in the eyes of any elderly person. In more advanced cases the nerve fibers become attenuated and undergo fragmentation, and ultimately the pattern

of the nerve fiber layer is lost altogether and replaced by a marbled appearance, and likewise the foveal reflex becomes irregular in form, luminosity, and direction of movement, and may completely disappear. The macular yellow is also reduced or absent. Chronic simple and congestive glaucoma cannot be differentiated from each other by this means, but in the latter type the macula and the papillomacular bundle tend to be involved earlier and more extensively, whereas in chronic simple glaucoma the temporally situated nerve bundles may show the greater damage. The changes noted in glaucoma cannot be sharply distinguished from those found in atrophy of the optic nerve or macular degeneration due to other causes. (3 colored plates.)

Harry K. Messenger.

Raimondo, N. **Fuchs's heterochromia with glaucoma: pathogenetic considerations.** Ann di ottal. e clin. ocul. 74:423-435, July, 1948.

Raimondo reports two cases of Fuchs's heterochromia with glaucoma. The association of these two diseases is very rare. In one of his cases a bit of iris excised in trephining showed dystrophy of the stroma and rarefaction of pigment in the anterior limiting layer, conservation of the retinal pigment, thickening of the walls of the small vessels and capillaries, but no inflammatory changes. Raimondo's opinion is that both diseases are to be ascribed to congenital asymmetry in sympathetic innervation, which favors a vasomotor disequilibrium. (References.)

Harry K. Messenger.

10
CRYSTALLINE LENS

Barkan, Otto. **Operation for congenital cataract.** California Med. 70:274-277, April, 1949.

Refinements in linear cataract extrac-

tion are described in detail. The pupil is maximally dilated preoperatively with atropine and subconjunctival adrenalin. A flat corneal incision is made with a keratome, the lens is removed extracapsularly and saline solution or air is used to refill the anterior chamber.

Orwyn H. Ellis.

Meyer, F. **The origin of the X-ray cataract.** Klin. Monatsbl. f. Augenh. 114:33-36, 1949.

The author describes the development of cataract as a result of repeated exposure to small doses during the calibration of instruments. Summation of small amounts of X ray produced the lesion.

Max Hirschfelder.

Redl, T. **A family with partly presenile, partly infantile hereditary cataract.** Klin. Monatsbl. f. Augenh. 114:24-33, 1949.

The author reports the appearance of cataract in a family which he traced through seven generations. Intermarriage occurred on at least four occasions. Presenile cataract appeared in one member of the second generation and occurred in the third and fourth generation. Several members of the fifth, sixth and seventh generation sucered from congenital perinuclear (lamellar) cataract. The change in the type of cataract occurred in one generation, the fifth. The mode of inheritance is the "mixed form" of Groenouw. (Reference, 1 family tree.)

Max Hirschfelder.

11
RETINA AND VITREOUS

Cremona, A. C., and Manzitti, E. **Biogenic treatment of pigmentary retinosis.** Arch. de oft. de Buenos Aires 23:309-312, Oct., 1948.

When parts of the body are isolated from their usual vascular and nervous connections they are said to develop "biogenic stimulants." Pieces of tissue of the

cornea, choroid, retina, cerebrum or placenta may be removed from the newly-dead and refrigerated. These may then be implanted beneath the skin or conjunctiva, or may be administered as an intramuscular injection. Intramuscular injections of placental extract were given to 33 patients with pigmentary retinosis with improvement in 13. (2 tables.)

Edward Saskin.

Eross, S., and Tarjan, G. **Retinal blood pressure in gravidic intoxications.** Orvosi Hetilap 26:406, Sept. 26, 1948.

In 41 gravid women with disturbances of the kidney or cardiovascular system, discordant values between the diastolic pressure of the central retinal artery and the brachial were found. Among these, 13 had eclampsia, in 3 intrauterine death of the fetus occurred, and one had myodegeneration of the heart, and lues. Concordant values were found in two pregnant women with essential hypertonia. In 50 healthy pregnant women they found no discordant values. The proportional rise of diastolic blood pressure in a retinal artery in severe nephropathia is a warning sign. In patients who had proportional diastolic pressure in the retinal artery the nephropathy did not become worse during pregnancy or delivery. (2 figures.)

Gyula Lugossy.

Fleischer, Eberhard. **Four new cases of Aguchi's disease.** Klin. Monatsbl. f. Augenh. 110:296-302, May-June, 1944.

All patients were males between 9 and 25 years old. There was pronounced night blindness since early childhood. Vision, visual fields and color sense were always normal. There were areas of grayish discoloration in the fundus, especially in the periphery. Mizuo's color-change was positive. After one hour in the dark the fundus looked normal, but changed to the original appearance after exposure to daylight. The dark adaptation was

very much delayed, but after three hours or more the values were normal. The change of the gray to normal fundus and the dark adaptation do not take place at the same rate but the cause of both is probably an abnormal breakdown and regeneration of the visual purple. The transmission is recessive and not sex-linked.

George Brown.

Friedenwald, J. S. **A new approach to some problems in retinal vascular disease.** Tr. Am. Acad. Ophth. pp. 73-87, Nov.-Dec., 1948.

A new staining method (Hotchkiss) which demonstrates fixed carbohydrate is applied to ocular tissues. Any cellular structure containing carbohydrate stains red. Structures taking the stain include conjunctival goblet cells, Bruch's and Descemet's membranes, lens capsule, the subepithelial basement membrane of the ciliary processes, the internal limiting membrane of the retina, and, to a lesser extent, the peripheral portion of the rods and cones. The entire retinal vascular tree has a subendothelial membrane which is readily demonstrable. It is broadest in the arterioles, and less in the venules, and thinnest in the capillaries. Its breadth and stability vary with the age of the individual rather than that of the vessel. Two capillary systems are demonstrable in the peripapillary zone of the retina. One is in the nerve fiber layer and has a rectangular configuration; the other is an irregular network in the inner nuclear layer. Only the latter persists peripherally. Capillary aneurysmal dilatations occur most frequently at the posterior pole and in the inner nuclear layer. They are consistently found in diabetic retinopathy and only rarely in other retinopathies. The development of the aneurysms is briefly discussed, and an analysis drawn between the endothelial changes of Kimmelstiel-Wilson intercapillary glomerulosclerosis.

A histochemical investigation of the cot-cotton-wool patches frequently seen in malignant hypertension is briefly discussed. They occur at the posterior pole and in the nerve fiber layer. These lesions were shown to be globular cytoid structures and to represent minute ischemic infarcts in terminal arteriolar bifurcations. Resorption is the usual course. The Hotchkiss staining procedure and its adaptation to ophthalmic uses is described in detail. Preparation of the reagents employed is outlined.

<div align="right">Chas. A. Bahn.</div>

Grossmann, E. E., and Hitz, J. B. **Lipemia retinalis associated with essential hyperlipemia.** Arch. Ophth. 40: 570-573, Nov., 1948.

Since its first description, in 1880, about 60 cases of lipemia retinalis have been reported in the literature, and it is noteworthy that all have been in diabetic patients. The rare nondiabetic lipemia retinalis is associated with idiopathic hyperlipemia and is probably a familial anomaly of lipid metabolism that occurs in children. This case is the fifth recorded instance of lipemia retinalis in a nondiabetic person, and is probably the first in a nondiabetic adult.

<div align="right">Ralph W. Danielson.</div>

Guyton, J. S., and Reese, A. B. **Use of roentgen therapy for retinal diseases characterized by new-formed blood vessels (Eales' disease; retinitis proliferans): a preliminary report.** Arch. Ophth. 40: 389-412, Oct., 1948.

Intensive roentgen therapy to the posterior ocular segment was given in a series of patients with ocular diseases characterized by retinal and vitreous hemorrhages and by retinitis proliferans. Twenty-two eyes in 14 patients were treated. There was typical Eales' disease in 8 patients, atypical in 4, and diabetic retinitis proliferans in 2. The method de-vised by Martin and Reese for the treatment of retinoblastoma was used to avoid damage to the anterior ocular segment. A dose of 3,500 to 15,000 r was given each eye treated; doses of 6,000 r are probably optimal. There was moderate to complete collapse of new-formed vessels and variable regression of fibrosis. There has been only one recurrent hemorrhage since the treatment in the 8 cases of typical Eales' disease. In the patients with diabetic retinitis proliferans, hemorrhages have continued to appear.

<div align="right">John C. Long.</div>

Van Heuven, J. A. **Detachment of the retina following inflammation.** Tr. Ophth. Soc. U. Kingdom. 66:493-500, 1946.

A detachment of the retina about three months after an acute iritis showed a vitreous strand along the course of a vessel. No hole in the retina was visible for several days. Later a hole appeared and was cauterized. Beulah Cushman.

Hollenhorst, R. W., and Wagener, H. P. **The effect of rutin in the control of bleeding into the retina.** Am. J. M. Sc. 217:223-231, Feb., 1949.

The authors give a résumé of the work done on the treatment of retinal hemorrhages, especially those associated with increased fragility of the minute vessels of the skin, by such substances as citrin, hesperidin, and rutin. Rutin may decrease capillary fragility but it is not certain that increased fragility and permeability of the skin capillaries are accompanied by corresponding dysfunction of the retinal capillaries, especially in diabetic retinopathy. Some retinal hemorrhages may arise from a vitamin P deficiency. Evaluation of clinical improvement in the retina is most difficult. Superficial hemorrhages may be absorbed spontaneously in a short time, deeper ones may persist for a year or more, and all types frequently recur.

Rutin therapy in retinal complications of diabetes has been discouraging due to the deep location and the slow progress of the disease. In many other diseases the hemorrhages are more superficial and hence absorbed more rapidly. The value of rutin in retinal disease of diabetics is very doubtful.　　　　F. M. Crage.

Kinsey, V. E., and Zacharias, L. Retrolental fibroplasia. J.A.M.A. 139: 572-578, Feb. 26, 1949.

Since this disease was first associated with prematurity by Terry in 1942, there has been an increase in the number of cases reported which cannot be fully explained by the statement that the condition was formerly undiagnosed or missed, or that more premature infants survive now than before. Various factors were investigated which might have influenced this increase. The incidence of disease was higher in children born of multiparous women and in infants who remained in the nursery, incubator, and oxygen for longer than usual and also higher in the male. It might be of etiologic significance that the incidence was greatest during a time when there was increased use of vitamin in water-miscible form, and of iron. (14 tables.)
　　　　　　　　Bennett W. Muir.

Kreibig, W. Clinical demonstration of calcium deposits in retinoblastoma. Klin. Monatsbl. f. Augenh. 114:84-89, 1949.

Early necrosis of the gliomatous tissue often leads to calcium deposits in the intraocular part of the tumor. The author found these deposits in 16 of 20 eyes by histologic examination. No other intraocular tumor shows calcification, a fact which is of differential diagnostic significance. These calcium deposits form very soft shadows on the X-ray film. Positive findings remove all doubt. (7 figures, references.)
　　　　　　　　Max Hirschfelder.

Levitt, J. M. Occlusion of the cilioretinal artery. Arch. Ophth. 40:152-156, Aug., 1948.

Occlusion of the cilioretinal artery in a 19 year old woman is described. There was loss of central vision, a broad band of retinal edema between the optic nerve and macula and a large cecocentral scotoma. Intensive use of vasodilators was followed by almost complete recovery.　　　　John C. Long.

Lijó Pavía, J. Solar retinitis. Macular study with sodium light. Rev. oto-neuro-oftal. 23:71-78, Oct.-Dec., 1948.

In a previous paper the author established the fact that phototrauma of the eye results in a hole of the macula and central scotoma. Four cases of exposure to solar eclipse are presented now, each carefully studied with ordinary, red-free, and sodium light. The latter type of examination corroborated the findings with ordinary and red-free light, namely, mild optic neuritis, general retinal edema, alteration of the papillomacular fibers, marked central retinal edema, and a hole in the fovea. However, the pathologic picture was most readily appreciated in stereoretinography in yellow light. In all four cases visual acuity returned to normal in 20 to 68 days. (2 stereoretinographs.)　　　　Edward Saskin.

Lijó Pavía, J., and Cabrera, M. Vitreous humor substitution. Rev. oto-neuro-oftal. 24:13-17, Jan.-Feb., 1949.

The authors' surgical procedure is performed under pentothal and consists of an equatorial scleral incision through which 1.50 cc. of vitreous is removed by syringe and an 18 gauge needle. The syringe is then removed but the needle is left in situ, and 2 cc. of clear donor vitreous from an enucleated eye in another syringe is injected into the vitreous cavity through the same needle. The

scleral incision is then sutured. In an only eye with turbid vitreous visual acuity improved from perception of shadows to 20/200. Edward Saskin.

Linde, L. **Prophylactic surgery for potential retinal detachment.** Klin. Monatsbl. f. Augenh. 113:140-142, 1948.

The case histories of five patients in whom a prophylactic fixation of the retina was necessary are presented. The author recommends such surgery in all cases of retinal tears, whether detachment has occurred or not. It is imperative to investigate such an eye carefully for new tears even after seemingly successful surgery and the other eye as well. Prophylactic diathermy surgery also has a place in eyes that are inclined to retinal detachment. In a patient with Marfan's syndrome such prophylactic fixation was done and no detachment followed surgery for a dislocated lens. This type of surgery is harmless and obviates perforating procedures. Max Hirschfelder.

Loewenstein, A., Michaelson, J. C., and Hill, J. **Retinal vasculitis of the young: a pathological report.** Tr. Ophth. Soc. U. Kingdom 66:211-230, 1946.

The author reports the pathologic findings in two eyes with retinal vasculitis. The eyes had been enucleated in young people because of glaucoma. Histologic studies revealed numerous retinal hemorrhages, ectasia of the retinal vessels and venous stasis. Hemorrhages were present in the thickened vessel walls. There was extensive granulomatous infiltration of many venous walls. The choroid was normal. Numerous sections were stained with Ziehl-Neelsen's stain but no acid fast bacilli were found. Animal experiments suggest the presence of an infective agent in the retina. It is suggested that the use of retinal tissue for biological experiment may be a fruitful approach to the problem of causation. (19 figures.) Beulah Cushman.

Maggiore, L. **Histologic changes in retinal edema.** Ann. d'ocul. 181:681-691, Nov., 1949.

The most important factors in injury to the retina caused by edema are the intensity and duration of the edematous infiltration, its location, the coexistence of hemorrhage, and the coexistence of toxic or infectious disease. Variations in the degree of edema determine the degree of structural damage to the retina and whether vision is temporarily or permanently injured. Edematous infiltration of the fibers of Henle's layer may cause a hole in the fovea, an important factor in some cases of retinal detachment. The disposition of the fibers of Henle's layer in the macular region explains how intense edema can pull apart these fibers without causing rupture at the periphery of the fovea, whereas at the center, where the fibers are short and lie perpendicularly, stretching will tear them and produce a hole. If the edema is limited to the internal layers of the retina the hole will be superficial and the detachment intraretinal; if a massive edema infiltrates even the visual cells, the hole will penetrate the foveal retina throughout its thickness and will be complete, that is, a true retinal detachment. Chas. A. Bahn.

Malatesta, C. **Two cases of pigmentation of the disc after retinal detachment operation.** Boll. d'ocul. 32:722-733, Nov., 1948.

Two men, aged 49 and 57 years, had extensive dispersed pigmentation of the retina and the optic discs after diathermy coagulation for retinal detachment. The pigmentation appeared a few days after the operation and disappeared gradually in a month. (2 colored drawings.) K. W. Ascher.

Malbran, and Montalvan. **Pseudoforamina of the macula in disinsertions of the ora serrata.** Arch. de oft. de Buenos Aires 23:252-258, Sept., 1948.

There is little in the literature on the association of dialysis of the ora serrata with a pseudoforamen of the macula which was first described by Vogt in 1936, and is of interest in diagnosis, prognosis and therapy. Six cases are reported.

This is one of the forms of cystic degeneration of the macula. There is a reddish discoloration at the macula of variable size. The edges are clear-cut and surrounded by pale and edematous retina. The macular region is raised as if by a single or multiple tense vesicle of variable transparency. There is a foveal reflex because the internal limiting membrane is preserved. Fine striations extend outward from the macula. Differentiation from a traumatic or spontaneous hole at the macula is at times difficult. A. G. Wilde.

Marín Amat, M. **Spasm of a cilio-retinal vessel, and of the superior branch of the central retinal artery.** Arch. Soc. oftal. hispano-am. 9:91-93, Jan., 1949.

A woman had an ophthalmoscopically visible spasm of a cilioretinal artery with a total loss of the lower half of the visual field. After treatment with vasodilators vision was restored, and only slight pallor of the disc, and a slight constriction of the upper retinal vessels remained. Treatment must not be abandoned too early, persistence frequently leads to surprizing results. (3 visual fields.) Ray K. Daily.

Mariotti, Lorenzo. **Intravenous procaine and para-aminobenzoic acid in the treatment of thrombosis of the central retinal vein.** Ann. di ottal. e clin. ocul. 74:350-357, May, 1948.

Mariotti reports three cases of thrombosis of the main branch of the central retinal vein, and nine of thrombosis of a branch of the vein, in which 20 to 180 mg. of procaine were given in 2 to 18 intravenous injections of a 1- or 2-percent solution at intervals of a day or more. This therapy was ineffective in thrombosis of the trunk, but in the other cases the results were encouraging. The systemic systolic pressure, the retinal arterial pressure, and the ocular tension were always reduced. The efficacy of procaine in dislodging the thrombus seems to be due in great part to its vasodilator action. Presentation of the results obtained with para-aminobenzoic acid is reserved for another paper. Harry K. Messenger.

Moreu, Angel. **Observations on the pathogenesis and treatment of diabetic retinopathy.** Arch. Soc. oftal. hispano-am. 9:139-146, Feb., 1949.

The physiologic action of hyalouronic acid and hyalouronidase is reviewed. The development of diabetic retinopathy is attributed to variations in the sugar metabolism, caused by injudicious use of insulin. Hypoglycemia stimulates the production of hyalouronidase which destroys hyalouronic acid, and increased fragility of the vessel walls and hemorrhages follow. In the hyperglycemic phase an excess of hyalouronic acid stimulates the organization and proliferation of connective tissue. It is urged that insulin be used with great caution and that more attention be paid to capillary fragility. Agents that improve cellular respiration such as heparin are indicated.

Ray K. Daily.

Oravisto, T. **The ocular symptoms of arterial hypertension.** Ophthalmologica 117:161-168, March, 1949.

The author reports his examination of 70 patients under 50 years of age with pure essential hypertension and as little sclerosis as possible. The classification of hypertensive cardiovascular disease according to Keith-Wagener is recom-

mended as a basis for cooperation between the internist and ophthalmologist.

Peter C. Kronfeld.

Reese, A., and Blodi, F. **Retrolental fibroplasia.** Klin. Monatsbl. f. Augenh. 114:18-24, 1949.

Three groups of retrolental fibroplasia are discussed. Dysplasia of the retina is a bilateral malformation with persistence of the primary vitreous and lack of formation of the secondary vitreous. It is often associated with other malformations of the brain and the vascular system. Hyperplastic primary vitreous is usually unilateral and characterized by hyperplasia in the central retrolental region. True retrolental fibroplasia forms a third group which has increased in frequency during the past few years. Persistence of the primary vitreous leads to a dense grayish tissue formation behind the lens with its densest parts near the equator of the lens. The lens itself stays clear. Detachment of the retina is found in the final stages. The disease is always bilateral and prevalent among premature children. The theories of its etiology and the therapy are discussed. (References.)

Max Hirschfelder.

Schiff-Werthheimer, S., Jonquères, J., and Jarry, C. **Retinal detachment of young myopes.** Ann. d'ocul. 182:13-23, Jan., 1949.

The prognosis and symptomatology of 49 patients under 30 years of age with an average myopia of 12D are described. The prognosis is worse in the younger group. After operation, one third had a corrected vision of 0.1 or more and almost one half had no vision. Multiple tears are more frequent than in unselected cases and bilateral detachment is more frequent in the young.

Chas. A. Bahn.

Tirelli, G. **A case of macular hole following rapid lowering of atmospheric pressure.** Rassegna ital. d'ottal. 17:353-356, Nov.-Dec., 1948.

A 30-year-old man, a former aviator and Alpinist, suffered an epistaxis, rapidly followed by a sudden loss of vision while mountain climbing at an altitude of 4,000 meters and after passing through a severe storm. The ophthalmoscope disclosed a round hemorrhage at the macula of the left eye. In all other respects the eyes were healthy. Two months later, the hemorrhage was absorbed leaving a clear-cut, round hole, one half the disc diameter in size, exactly at the macula. The author assumes that the diminished atmospheric pressure and the low barometric pressure accompanying the storm and increased capillary fragility from severe fatigue caused the hemorrhage.

Eugene M. Blake.

Unsworth, A. C. **Retrolental fibroplasia.** Arch. Ophth. 40:341-346, Sept., 1948.

In observing the eyes of premature infants from birth, the author rarely saw remnants of the hyaloid artery but they appeared shortly. Of 30 premature infants none was born with a retrolental membrane. In two infants that he saw shortly after birth without evidence of ocular abnormality, retrolental fibroplasia has since developed. He believes that retrolental fibroplasia as it is usually known is not congenital. In one case, at least, the mechanism of its formation was seen to be leakage of blood from the retinal vessels into the vitreous, followed by vascularization of the hemorrhage in the vitreous from the retinal vessels. Remnants of the hyaloid artery were not persistent in any of these cases and certainly played no part in the formation of the angioplasia of the vitreous. He feels sure that this condition, if untreated, will become a typical retrolental fibroplasia by spreading over the posterior surface of the lens. This formation seems to be akin

to the formation of granulation tissue elsewhere in the body, to retinitis proliferans or to the syndrome of von Hippel's angiomatosis. The anemia of prematurity in itself may be a factor in the causation of retrolental fibroplasia. There seem to be two main types. The first develops from the proliferation of vascular tissue from the retinal vessels of the posterior portion of the fundus into abnormal vitreous. The second is the result of failure of development or condensation of the secondary vitreous at the anterior periphery, with proliferation into it of retinal vessels from the unattached peripheral portion of the retina.

Ralph W. Danielson.

Verhoeff, F. H. **Successful diathermy treatment of recurring retinal hemorrhage and retinitis proliferans.** Arch. Ophth. 40: 239-244, Sept., 1948.

Recurring retinal hemorrhage in the young is frequently associated with ophthalmoscopically recognizable periphlebitis. Usually there is a cutaneous reaction to tuberculin, and nodular foci of epithelioid cells along the veins have been observed. Histologically there is strong evidence that tuberculosis is the cause. The hemorrhage evidently results from engorgement of capillaries and small veins and when it is severe and persistent, new vessels are formed, which may extend into the vitreous. Hemorrhage into the vitreous usually occurs, and the blood becomes organized, thus producing typical retinitis proliferans. The author reports in detail the successful use of diathermy in such a case.

Ralph W. Danielson.

Wagner, E. **A late form of familial amaurotic idiocy in a brother and sister.** Klin. Monatsbl. f. Augenh. 114:37-42, 1949.

There was no sign of retinitis pigmen-tosa. The brother showed a secondary optic atrophy, concentric contraction of the field and colorblindness. Neurologic investigation by means of X ray, encephalograms and biopsy revealed increased intracranial pressure and the damage to the ganglion cells of the cortex characteristic of familial amaurotic idiocy. The sister who had a normal mind had a nystagmus, was colorblind and had a pituitary form of adiposity.

Max Hirschfelder.

13

NEURO-OPHTHALMOLOGY

Becker, F. Y. **Herpes zoster ophthalmicus: results of treatment with transfusions of convalescent blood.** Arch. Derm. and Syph. 58:265-275, Sept., 1948.

The author reports six cases of herpes zoster ophthalmicus treated successfully by the method of Gunderson, who gives 250 to 450 cc. of convalescent blood intravenously early in the disease, preferably before involvement of the eye. Herpes zoster is probably caused by a virus because recurrences are unusual, inclusion bodies are present in the vesicles, and there are antibodies in the serum of convalescent patients. However, because the agglutinins do not appear until the third week, convalescent serum should be given early. After transfusion, the temperature becomes normal, pain is alleviated, the edema and infiltration are decreased, the patient is less toxic, and the ophthalmic lesions begin to heal.

R. Grunfeld.

Bridges, T. J., Pool, J. L., and Riley, C. M. **Central autonomic dysfunction with defective lacrimation. II. Preliminary report of effect of neurosurgery in one case.** Pediatrics 3:479-481, April, 1949.

A division of the tentorium on the right side was performed on a 4-year-old boy

with defective lacrimation and central autonomic dysfunction. Lacrimation made its appearance on the sixth postoperative day and has persisted. The lability of blood pressure and the abnormal reactions disappeared immediately, only to return after a period of three weeks.

I. E. Gaynon.

Fonte Barcena, A., and Manzilli, E. **Ophthalmoplegic migraine.** Arch. de oft. de Buenos Aires 23:233-239, Sept., 1948.

Typical ophthalmoplegic migraine that occurred in a 51-year-old woman is described and our meager knowledge of the syndrome is discussed.   A. G. Wilde.

Freymann, M. W., and Bang, F. B. **Human conjunctivitis due to Newcastle virus in the U.S.A.** Bull. Johns Hopkins Hosp. 84:409-413, May, 1949.

Three laboratory workers developed conjunctivitis with preauricular adenitis due to the virus of Newcastle disease in chickens. Virus was isolated in two of the eyes. The course was brief, without complication, and lasted three to five days.   I. E. Gaynon.

Guthkelch, A. N. **Extradural hemorrhage as a cause of cortical blindness,** J. Neurosurg. 6:180-182, March, 1949.

A case of almost total cortical blindness due to bilateral occipital extradural hematoma is recorded.

Miss L. K., 67 years old, struck the back of her head. She was drowsy and irritable. Xrays revealed a fissured fracture. After four days her conscious level improved, but she complained of blindness. Ten days later she was garrulous, euphoric and devoid of insight. The discs showed acute papilledema with hemorrhages, but no exudate and the pupils were normal. A diagnosis of bilateral occipital subdural hematoma was made. At operation a huge black clot was re-

moved from the extradural space. Two days later the visual acuity improved and on the fourth day she could read a newspaper comfortably. When last seen one year later her health was excellent and she was able to do fine work as well as ever. Her visual fields remained full and the optic discs had returned to normal.

Theodore M. Shapira.

Jensen, Jens. **A case of herpes zoster ophthalmicus complicated with neuroretinitis.** Acta opth. 26:551-558, 1948.

Herpes zoster ophthalmicus occurred in a 9-year-old girl after she was exposed to varicella during an epidemic. The disease was complicated by optic neuritis, retinitis, internal ophthalmoplegia, optic atrophy and macular changes. The literature on similar complications of herpes zoster is reviewed.   Ray K. Daily.

Lijó Pavía, J. **Photographic documentation of nystagmus.** Rev. oto-neuro-oftal. 24:9-11, Jan.-Feb., 1949.

Three photographically documented cases of nystagmus are presented. A speed of 64 frames per second leaves much to be desired; 200 per second will yield a more revealing slow-motion analysis of the details of nystagmus.

Edward Saskin.

Paufique, Mayoux, Hugonnier, and Aubert. **Parinaud's syndrome associated with vertigo.** Ann. d'ocul. 182:1-12, Jan., 1949.

A man, aged 49 years, noted transient diplopia for about three hours. Subsequently he developed a bilateral paralysis of elevation and convergence with vertigo. Parinaud's syndrome is apparently due to a lesion in the posterior white commissure of the pons. The vertigo was believed due to a lesion in the vestibular nucleus, probably near the nuclei of Bechterew and Deiter. The cause was

probably a vascular disturbance. The blood supply of the pons includes rubo-pyramidal, oculo-nuclear and lateral sulcus arteries.   Chas. A. Bahn.

Riley, C. M., Day, R. L., Greeley, D. M., and Langford, W. S. **Central autonomic dysfunction with defective lacrimation. I. Report of five cases.** Pediatrics 3:468-478, April, 1949.

A syndrome consisting of diminished to absent lacrimation, hypertension, skin blotching, drooling, cold hands, cyclic vomiting, mental retardation and hyporeflexia in children is presented. The findings seem best interpreted as a central, possibly congenital, disturbance of autonomic function. (1 table.)

I. E. Gaynon.

Sitler, R., Cremona, A., and Manzitti, E. **Myasthenia of visual type.** Arch. de oft. de Buenos Aires 23:226-232, Sept., 1948.

A four-year-old boy had equal and progressive bilateral ptosis, since he was two and a half years old. He was able to open the eyes during the early morning hours, but this power decreased during the day. There was also an almost complete immobility of the eyes. The excursion of the gaze was about two millimeters. No other symptoms were demonstrable. The distinguishing feature of this disorder is a rapidly increasing fatigability of the involved muscles, which improves after variable periods of rest. It is necessary to differentiate myasthenia from congenital ophthalmoplegia and the chronic external type, which is progressive. A diagnostic aid is the dramatic improvement or even temporary disappearance of symptoms after prostigmin.   A. G. Wilde.

Spadavecchia, Vitangelo. **Nasociliary neuritis.** Ann. di ottal. e clin. ocul. 74: 321-338, May, 1948, 436-455, July, 1948.

The first installment of this monograph

was abstrated in Am. J. Ophth., Sept., 1942.

Four types of nasociliary neuritis are recognized: the simple irritative, the irritative-inflammatory, the atrophic, and the postinflammatory atrophic-degenerative. Our knowledge of the pathogenesis of this disease is much limited by the absence of histopathologic material and by our ignorance of the reciprocal influence between the central and the autonomic nerve fibers in the nasociliary region. Neuritic pain, photophobia and blepharospasm are referable to cerebrospinal elements, whereas vasomotor and secretory disturbances point to autonomic involvement. The symptoms are so typical that the diagnosis is easy, but in making a differential diagnosis it is necessary to eliminate neurosis, simple nasociliary irritation, lesions of the fifth cranial nerve, certain types of headache, and acute glaucoma. Symptomatic treatment of pain is indicated, and cocainization and adrenalization of the nasal fossa are of value. Intranasal foci or spurs causing irritation should be treated surgically, and in severe cases the injection of alcohol in the region of the nasociliary nerve is advised. (References.)

Harry K. Messenger.

14

EYEBALL, ORBIT, SINUSES

Belmonte-González, Manuel. **Hydatid cyst of the orbit.** Arch. Soc. oftal. hispano-am. 9:49-59, Jan., 1949.

A diagnosis of a hydatid cyst of the orbit was made in a woman 24 years old, with a rapid onset of exophthalmos, diplopia, displacement of the eyeball downwards, choked disc, and loss of vision and the absence of rhinologic and roentgenologic signs of paranasal sinusitis. The cyst was exposed through a canthotomy, punctured, evacuated and filled for a few minutes with a 1-percent solution

of formalin (its deep location precluded complete extirpation) and the wound was sutured and drained. The patient recovered with recession of the choked disc, restoration of vision but with restriction of lateral rotation, and diplopia. (3 figures.) Ray K. Daily.

Buesa, Lorente. **A case of thrombophlebitis of the cavernous sinus.** Arch. Soc. oftal. hispano-am. 9:34-48, Jan., 1949.

An acute fulminating case of thrombosis of the right cavernous sinus is reported in a man, 46 years old. The infection originated in the last right lower molar tooth and advanced through the inferior dental veins. It was complicated by an orbital abscess which drained spontaneously at the inner canthus. In addition to the classical symptoms there was myosis of the right eye which is attributed to a venous stasis in the iris and a paresis of the sympathetic fibers in the first branch of the trigeminal. The patient recovered under treatment with penicillin and sulfa drugs. Ray K. Daily.

Hughes, W. L. **Metallic implants and integrated artificial eyes.** Plast. and Reconstruct. Surg. 4:175-177, March, 1949.

The author has originated four types of Vitallium implants for use with integrated artificial eyes. They have a flat face with depression anteriorly to receive the peg on the posterior surface of the eye. No reaction has been noted from these implants. Few extrusions have occurred, and in them the usual buried implant was used. Alston Callahan.

Larsson, H., Lindblom, K., and Stenström, S. **Clinical and roentgenological view regarding the localization of foreign bodies in the orbit.** Acta ophth. 26:557-580, 1948.

This symposium consists of 3 papers. Stenström discusses the relation of varia-tions in the size and shape of the eye to the accuracy of roentgenographic localization. He reports graphically the data of measurements of the vertical diameter of the eyeball in 1,000 cases, and of the horizontal diameter in 766. The vertical diameter was determined by Rushton's method, and the horizontal measured with Berg's appliance. The charted data show that the size and form of the eyeball are subject to such marked variations that in cases requiring precise localization the determination of the length and equatorial diameter of the eyeball is indispensable.

Lindblom describes his method of bitangential roentgenographic localization without determination of the size of the eyeball. It consists in getting a shadow of the cornea on the film by surrounding it with air; the upper lid is elevated with a spring, and the lower lid fastened down with adhesive tape. The degree of magnification of the cornea in the radiographs is calculated from the focal film and focal eye distances. Outlines of normal eyeballs corresponding to the degree of magnification engraved on transparent film are placed on the radiograph and the distance of the foreign body from the coronal, sagittal, and horizontal midplanes of the eyeball measured. The relation of the foreign body to the cornea and sclera can be seen on the film.

Larsson's method of localization includes concurrent determination of the size of the eyeball. Various methods for determining the size of the eyeball are discussed, and preference expressed for a modification of Rushton's method. The modification consists in moving the eyeball forward to the X-ray beam, instead of moving the beam to the posterior pole of the eye. The shadow of the cornea is visualized on the same film which indicates the posterior pole of the eye with a dark streak; the axial length of the eye-

ball can thus be measured on the film. The apparatus and technique are described in detail. (12 figures.)   Ray K. Daily.

Lisch, K. **Familial occurrence of spontaneous pulsating exophthalmous.** Ophthalmologica 177:180-185, March, 1949.

Spontaneous (nontraumatic) pulsating exophthalmos was observed in a man, 23 years of age, and his sister, 45. In the latter the disease occurred bilaterally. The father of the two patients developed sudden unilateral proptosis at the age of 47 and died of apoplexy two years later. A hereditary predisposition to arterial rupture is assumed.

Peter C. Kronfeld.

Pallarés, J. **A case of sarcoma of the orbit, with diagnostic puncture and microscopic study of the fluid.** Arch. Soc. oftal. hispano-am. 9:60-67, Jan., 1949.

The diagnosis of intraorbital sarcoma in an infant, 29 months old, was made from a cytologic study of material aspirated through a puncture of the tumor. After aspirating the fluid with a syringe, a diathermy current was passed through the needle for 15 seconds.

Ray K. Daily.

Pallestrini, Ernesto. **Blepharospasm and palpebral tic from sinusitis.** Riv. oto-neuro-oftal., 23:275-283, July-Aug., 1948.

A woman, 35 years of age, had unilateral fronto-maxillary sinusitis with homolateral blepharospasm. The spasm disappeared after the sinuses were clear. Three years later with recurrence of sinusitis there was bilateral blepharospasm together with spasm of the frontalis muscle and lacrimation under strong light. After radical surgical operation on the sinuses, the spasmodic condition disappeared permanently. The mucous membrane of the sinuses was found to be thickened with pseudomixomatous degeneration.   Melchiore Lombardo.

Waugh, D. B. **Ocular prosthesis, with special reference to the conjunctival sac.** M. J. Australia 1:311-313, March 5, 1949.

It is important that the conjunctival slack present in both fornices be preserved following enucleation in order to preserve the palpebral fold and the facial characteristics of the person involved. An acrylic splint made from the impression of the closed eye which is to be excised should be slipped under the lid following surgery in order to prevent the upper lid from being drawn inward.

I. E. Gaynon.

15

EYELIDS, LACRIMAL APPARATUS

Bassenge, W. **Irrigation of the tearsac with penicillin in dacryocystitis.** Klin. Monatsbl. f. Augenh. 113:363-366, 1948.

After a series of irrigations with penicillin solution (50 Oxford units per cc.) in 20 patients, an improvement in the bacterial flora of the sac was the rule and in some cases the bacterial findings became negative. Whenever there was a patent sack originally or after probing, penicillin seemed effective. Patients with closed tearducts cannot be cured by this treatment. However, preparatory penicillin irrigation has a favorable influence on subsequent surgery. Dacryorhinocystostomy is recommended. (References.)   Max Hirschfelder.

Berke, R. N. **Motais-Parinaud type of operation for ptosis.** Arch. Ophth. 41:324-333, March, 1949.

Utilization of the superior rectus muscle to correct ptosis in 35 cases of congenital ptosis gave an excellent result in 4 cases, a good result in 14, a fair result in 8, and no improvement in 9. In 16 of 22 cases in which the Motais-Shoemaker-Kirby technic was used, and in 10 of 13 cases in which the Parinaud-Young-Dickey procedure was employed, im-

provement followed. Utilization of the superior rectus to correct ptosis induced weakness of that muscle in 26 of 35 cases. Lagophthalmos in sleep was present in most of the cases of corrected ptosis, but no evidence of corneal ulceration occurred. This type of procedure should be used only for ptosis with complete paralysis of the levator palpebrae and integrity of the superior rectus muscle function.

Ralph W. Danielson.

Chabat, H. **Operation for trachomatous trichiasis by the conjunctival route.** Arch. d'opht. 9:48-51, 1949.

Chabat favors the conjunctival route for the correction of trichiasis because 1, it does not mutilate the tarsus, 2, it leaves no externally visible cicatrix, and 3, it requires no assistant, thanks to the use of a simple lid everter with two hooks for the attachment of sutures. A conjunctival incision is made 0.5 cm. from the free border of the lid, extending through the tarsus only, and dividing the tarsus into two portions. The marginal portion of the tarsus is dissected free from the overlying muscle and skin up to the bulbs of the cilia, while the remaining portion is also dissected free, well into the angles but not into the tendon of the levator. Four mattress sutures are then placed in such a way as to bring the cut border of the tarsus into the sulcus formed between the marginal tarsal leaf and the overlying skin, the sutures presenting at the lid margin. This everts the cilia, producing an ectropion which lasts for several weeks. The author comments on the relative freedom from recurrences.

Phillips Thygeson.

Ferraris de Gaspare, P. **Congenital fistulas of the lacrimal sac.** Boll. d'ocul. 27:739-745, Nov., 1948.

Two patients with congenital fistulas of the lacrimal sac were observed. Histologic examination of one showed a fistula lined by epithelial cells similar to those of the lacrimal ducts. (References.)

K. W. Ascher.

Lagrot, Félix. **Dermo-epidermic free grafts of the lids.** Ann. d'ocul. 182:32-51, Jan., 1949.

The indications for this type of graft include cicatricial retractions, entropionlagophthalmus, primary gangrene, injuries of the lids, and lid conditions secondary to facial or orbital disease. The author prefers general anesthesia. After a horizontal lid incision with dissection, four sutures are placed into the upper and lower margins, and held with artery forceps. A compress of vaseline gauze is used to form a temporary mold to cover the lid wound. A graft is taken from the inner side of the upper arm and placed on the mold. The upper and lower lid sutures are used to close the wound. In 17 operations there was no failure. Chas. A. Bahn.

Marcks, K. M. **Repair of defects produced by excision of tumors in the eye region.** Plast. and Reconstruct. Surg. 4: 178-187, March, 1949.

The complete removal of the tumor is preferred to the biopsy of a small amount of tissue. Primary repair should be instituted in all surgical excisions. Six varied cases are presented by means of brief histories, description of surgical procedure, and 26 photographs but no drawings. Secondary repair is performed after it is certain there will be no recurrence or extension of the initial lesion.

Alston Callahan.

Moulié, H. B., and Baron, H. G. **Dacryocystorhinostomy in the young.** Arch. de oft. de Buenos Aires 23:298-301, Oct., 1948.

Sac extirpation should not be performed in the young because a life time of annoyance follows. Dacryocystorhinos-

tomy may be done in the young in chronic dacryocystitis or narrowing of the terminal portion of the nasolacrymal canal, and is almost always successful.

Edward Saskin.

Nordenson, J. W. **Jean-Louis Petit and the mechanism of lacrimal drainage.** Arch. d'opht. 9:5-8, 1949.

Nordenson reviews the studies of the celebrated French surgeon, Jean-Louis Petit, which were made in 1734 and published under the title of "Memoire on Lacrimal Fistula." Petit attributed the flow of tears into the nose to a siphon action of the lacrimal passages, and to action of the lids in closing the conjunctival sac and pressing fluid into the canaliculi. These theories need reëxamination in view of the data obtained from dacryocystorhinostomy. Neither complete incision of the canaliculus nor removal of the lacrimal sac interferes with lacrimal drainage. Petit's lid closure theory would explain the tear flow in such cases. After a review of the literature and a consideration of his own observations, Nordenson concludes that Petit's siphonal theory can only be accepted in rare cases in which the transport of tears occurs in spite of paralysis of the facial nerve, but the theory of lid closure has been unjustifiably disputed. If it is correct, dacryocystorhinostomy is indicated when the canaliculi have been slit.

Phillips Thygeson.

Pereyra, C. C. A., and Riva, A. **Conjunctivitis and palpebral itching.** Arch. de oft. de Buenos Aires 23:259-271, Oct., 1948.

Palpebral itching is a definite entity, and may exist alone as a result of mechanical, chemical, or medicinal irritation, chronic conjunctivitis, epiphora, refractive errors, allergy, or from neuro- or psychogenic factors. If the complaint be associated with a systemic condition such as arthritis, diabetes, or endocrine dys-

crasia, the latter should be given treatment as the possible initiating agency in addition to the therapy for the relief of the itching. The authors sometimes use the antihistaminic drugs.

Edward Saskin.

Shuttleworth, F. N. **An advocacy of external dacryo-cystorhinostomy.** Brit. J. Ophth. 33:183-187, March, 1949.

British ophthalmologists have not generally adopted the Toti operation and the author presents the results in 60 cases with a recommendation that the operation be more generally done.

Morris Kaplan.

16

TUMORS

Arjona, J. **Sturge-Weber syndrome with ocular melanosis.** Arch. Soc. oftal. hispano-am. 8:1207-1218, Dec., 1948.

A boy, 13 years old, had epilepsy, numerous angiomas, buphthalmos in the left eye, chronic glaucoma in the right and blue scleras. The tension in both eyes was normal, although the anatomic changes indicated that it must have been high at some time. He had a small sella turcica, and calcification about the occipital lobes. Gradual improvement in the epileptic seizures is ascribed to a diminution in the meningeal angiomas. Involution of the angiomas of the choroid probably accounts for the normal tension. The blue scleras caused by melanosis are attributed to an abnormal activity of melanoblasts because of excessive choroidal vascularization. The literature on the pathogenesis of Sturge-Weber disease is reviewed, and it is suggested that melanosis of the eyeball may be a fourth symptom in the syndrome of angiomas, ocular and cerebral disturbances. (5 figures.)

Ray K. Daily.

Bloch, F. J. **Retinal tumor associated with neurofibromatosis (von Reckling-**

hausen's disease). Arch. Ophth. 40:433-437, Oct., 1948.

A classification of the ocular complications of neurofibromatosis is given. The author reports a retinal tumor in a 60-year-old man with neurofibromas of the trunk and extremities. The tumor was ophthalmoscopically identical with tumors seen in tuberous sclerosis. In nine years of observation the fundus picture has not changed.   John C. Long.

Costi, C. Multiple teratoid dermoids. Arch. Soc. oftal. hispano-am. 9:28-33, Jan., 1949.

An unusual case of multiple teratoid dermoids in the lids and on both eyeballs of a child, 20 months old, is reported. The diagnosis was made by biopsy. (4 figures.)   Ray K. Daily.

Moehle, W. Myxosarcoma of the eyelid. Arch. Ophth. 41:317-323, March, 1949.

This myxosarcoma of the eyelid apparently resulted from trauma. There was no evidence of abnormality before the accident or in the next two weeks; then a lesion appeared on the upper lid and enlarged rapidly. The growth resembled a hematoma but changed within two months to a firm, unyielding mass. Partial resection of the tumor and radiation therapy were employed. The eye was removed two years after this operation. Biopsy specimens from the surrounding areas showed no residual tumor, and no evidence of metastasis has been found. The boy is in good health; he has developed normally and presents no defects other than the loss of one eye. At present, nearly seven years after the appearance of the initial lesion, there is no reason to suspect a recurrence of the malignant growth.   Ralph W. Danielson.

Nuti, F. An atypical case of Sturge-Weber's syndrome. Boll. d'ocul. 27:734-738, Nov., 1948.

A 20-day-old girl had a nevus flammeus, resembling a telangiectatic angioma, on the right cheek and eyelids, congestive glaucoma of the right eye and slight enlargement of the right cornea. Treatment with a 2-percent pilocarpine solution seemed satisfactory, but at the age of two years a typical excavation of the right disc was observed. The angioma gradually disappeared.   K. W. Ascher.

Paufique, Offret, G., and Vouters. Peripheral glioma of the orbit. A clinicopathologic study. Arch. d'opht. 9:9-26, 1949.

The authors deplore the confusion existing in the literature and in the current textbooks on orbital tumors, particularly the tumors of the optic nerve which are known as gliomas, neurinomas, or schwannomas. They point out the close relationship existing between the solitary nerve tumor and von Recklinghausen's disease. In the latter the diagnosis is facilitated by the associated lesions while in the isolated neurinoma diagnosis can only be made on the basis of microscopic examination. The relative frequency of isolated neurinoma of the optic nerve is stressed and its slow and usually benign evolution is described. Radiotherapy is of no value and the only treatment is surgical excision. This is always indicated because of the possibility of malignant changes and because of changes in the optic nerve resulting from pressure. The results of surgery are generally good; the exophthalmos disappears, usually leaving a slight degree of enophthalmos with slight limitation of motion. Visual acuity improves with disappearance of the papilledema.   Phillips Thygeson.

Saebø, Johan. Lipoma conjunctivae in three generations. Acta ophth. 26:447-450, 1948.

Lipoma of the conjunctiva at the outer angle of the right orbit is reported in

three generations. The inheritance is dominant and the tumor was larger in each succeeding generation. (2 figures, 1 table.) Ray K. Daily.

Suárez Villafranca, M. R. **Intraocular and orbital tumors.** Arch. Soc. oftal. hispano-am. 9:67-90, Jan., 1949.

The diagnosis of eight intraocular and six orbital tumors is discussed. The slow evolution of sarcoma of the choroid in contradistinction to the rapid growth of sarcoma of the ciliary body is noteworthy, and the fundus picture of exudative retinitis in the case of intraocular cysticercus is worth remembering. (16 figures.) Ray K. Daily.

17

INJURIES

Atkinson, W. S. **Delayed keratitis due to mustard gas (dichlorodiethyl sulfide burns).** Arch. Ophth. 40:291-301, Sept., 1948.

Late corneal lesions develop more frequently in cases with greater exposure to mustard gas and in those of greater susceptibility to it. The condition is aggravated if the eyes are bandaged during the acute stage that follows exposure to mustard gas. After recovery from acute symptoms, which in severe burns last from two to eight months, and sometimes longer, the patient is practically free from symptoms for eight years or more. Photophobia, lacrimation and failing vision mark the onset of the late corneal lesions. Superficial haze of the cornea just beneath the epithelium in the area of the palpebral fissure, lines or striae in the substantia propria and folds in Descemet's membrane may precede the formation of deposits of cholesterol and fat. These deposits increase in size, break through the epithelium and produce an exacerbation of the symptoms of irritation. Later, there is a heaping up of hard,

degenerative tissue on the cornea. The scarred cornea is so irregular that vision is improved only with contact lenses. There are also pale, triangular patches on either side of the cornea in the area of the palpebral fissures that resemble lesions produced by surface application of beta radiation. Intracorneal hemorrhages occur and seem to arise from the large varicose vessels, which extend up to the limbus. Recognition of the late effects of mustard gas is important, so that claims of veterans of World War I may be justly handled. Ralph W. Danielson.

Knudtzon, Karsten. **The prognosis of scotoma helieclipticum. Follow-up of 47 patients injured in July 1945.** Acta ophth. 26:469-494, 1948.

A review of the literature precedes the tabulated report of the ocular examination of 47 patients 18 months after injury by a solar eclipse. Forty had ocular damage. The damage produced by watching a solar eclipse without adequate protection is severe and permanent and justifies public warning before an eclipse. The usual inadequate sun glasses give a false sense of security. Knudtzon also warns against Bates' and Huxley's advice to accustom the eyes to direct sunlight. Ray K. Daily.

Lindblom, K. **Localization of foreign bodies in the eye by bone free radiography.** Acta ophth. 36:439-440, 1948.

Lindblom describes his mofidication of the Vogt method of bone-free radiography for localization of foreign bodies in the anterior ocular segment. (4 figures.) Ray K. Daily.

Minton, Joseph. **Occupational diseases of the lens and retina.** Brit. M. J. pp. 392-394, March 5, 1949.

Protective care of the workers must be taken, the author states, or soon there will be reports of severe anemias and

cataracts in industries in which workers are exposed to molten glass or metal, ultraviolet radiation, high-tension electric currents and Xrays.

<div align="center">Theodore M. Shapira.</div>

Saebø, Johan. **Automutilatia bulborum. A rare case of self-mutilation in an epileptic.** Acta ophth. 26:451-453, 1948.

An epileptic, 25 years old, destroyed both of his eyeballs, apparently painlessly, under the illusion that this action would lead to a cure of his epilepsy and subsequent restoration of vision. He sectioned the upper lids and conjunctiva with the nail of the index finger, and then introduced the finger behind the eyeballs, and emptied them of their contents.

<div align="center">Ray K. Daily.</div>

<div align="center">18</div>

SYSTEMIC DISEASE AND PARASITES

Bucek, Alois. **Stevens Johnson syndrome.** Lekarske Listy 4:203-204, May, 1949.

A case of Stevens-Johnson syndrome in a boy aged 2½ years is presented with two striking pictures.

<div align="center">F. H. Haessler.</div>

Cass, E. **Reiter's disease.** Arch. Soc. oftal. hispano-am. 9:176-179, Feb., 1949.

To the 200 cases of Reiter's disease reported in the literature the author adds one more case. The general examination was negative and therapy ineffective. The distinguishing feature was the rapid alleviation of some symptoms and the appearance of others, and the occurrence of interstitial keratitis, which is reported for the first time.   Ray K. Daily.

Croom, J. H., and Scott, G. I. **Retinal and vascular damage in long-standing diabetes.** Lancet 1:555-558, April 2, 1949.

The authors examined 60 patients who had diabetes from 15 to 26 years. Fifteen

patients were free of any degenerative disease, they had neither retinopathy nor vascular changes, although one of them had had diabetes over 26 years. Only 18 patients presented typical diabetic retinopathy and 9 of them had normal retinal arteries, whereas the others had only slight arteriosclerotic or hypertensive changes. Some factor other than arteriosclerosis must be responsible for the retinopathy. The Kimmelstiel-Wilson syndrome or intercapillary glomerulosclerosis characterized by hypertension with edema of nephrotic type, massive albuminuria and renal or cardiac decompensation was present in two patients only.

<div align="center">R. Grunfeld.</div>

Curtis, A. C., and Grekin, R. H. **Sarcoidosis: treatment with calciferol and dihydrotachysterol.** Tr. Am. Acad. Ophth. pp. 344-351, March-April, 1949.

Of 19 patients with sarcoidosis (4 had ocular lesions), 9 of whom were treated with calciferol and 5 with dihydrotachysterol, 3 were considered cured and 5 were improved. Both drugs increase the serum calcium and the excretion of serum phosphorus. Toxic reactions are not infrequent and occur less often if the calcium and nonprotein nitrogen is increased. It is not yet known which drug is more desirable. Both seem to produce approximately the same results. The toxic symptoms apparently occurred more slowly in patients treated with dihydrotachysterol. The optimal dose of calciferol is between 150,000 and 300,000 units daily; 3.75 mg. dihydrotachysterol is usually administered daily for three days and then reduced to 1.5 mg. The epithelioid cell reaction in sarcoidosis is apparently due to a phospholipid abnormality and the beneficial effect of calciferol and dihydrotachysterol is associated with the increased secretion of phosphorous. The authors believe that this treatment is not the ultimate one, but consider it more effective

than other treatments now in use.

Chas. A. Bahn.

Giardini, A. **Effect of methylthiouracil on the manifestations of Basedow's disease.** Boll. d'ocul. 27:706-721, Nov., 1948.

Seventeen Basedow patients were treated with methylthiouracil and the gravity of their signs and symptoms was listed in tables which contained the exophthalmometer measurments, estimations of the lid edema, 12 eye signs of Graves, Stellwag, Dalrymple, Gräfe, et altera, pupillary changes, and the basal metabolism figures. About half of the patients showed a slight reduction of their exophthalmos. Patients with reduced dark adaptation did not respond to methylthiouracil unless high additional doses of vitamin A were administered. (2 tables, references.)   K. W. Ascher.

Iribarren, R. **A case of subconjunctival filaria Loa loa.** Arch. de oft. de Buenos Aires 23:302-308, Oct., 1948.

This nematode and accompanying symptoms are described at length. A case is described in which a cyst containing the filaria was removed from a conjunctival sac and other microfilaria were demonstrable in the blood-stream. (4 figures, references).   Edward Saskin.

Scheie, H. G. **Ocular changes associated with scrub typhus.** Arch. Ophth. 40:245-267, Sept., 1948.

The eyes of 451 patients with scrub typhus were studied weekly for evidence of disease. Conjunctival injection was present in 38 percent, and subconjunctival hemorrhages in 6.4 percent. Ecchymosis, eschar of the eyelid, fixation nystagmus were seen occasionally. There was engorgement of retinal veins in 67 percent, retinal edema in 36; retinal hemorrhages and retinal exudate, uveitis and vitreous opacities in a few patients. Pathologic studies of eyes obtained at autopsy revealed that a subacute diffuse choroiditis was the basic lesion. The fundus changes not seen in other febrile diseases in this area were frequently helpful in diagnosis. The lesions in the eye are a fair index of convalescence.

Ralph W. Danielson.

Woods, A. C. **Sarcoidosis: the systemic and ocular manifestations.** Tr. Am. Acad. Ophth. pp. 333-343, March-April, 1949.

After a historical review, a brief résumé of the extraocular symptoms is given. Among these are increased sedimentation rate, increased globulin fraction and anergy to as much as 10 mg. tuberculin. Negroes are more susceptible in the ratio of 6 to 1. The ocular lesions are chronic granulomatous processes with epithelioid cell nodules. Although the individual lesions may be benign, secondary glaucoma and ocular atrophy are not infrequent. The eyes were involved in 44 of 94 cases of sarcoidosis. The eyes are frequently involved early in the disease, which may be associated with uveo-parotid fever and Mikulicz syndrome. Some authors consider that 5 to 10 percent of uveitis is due to sarcoidosis. Almost all parts of the eye may be involved. Nodular uveal lesions with interlacing vascular patterns and large gray precipitates are frequent. Primary choroidal and retinal lesions are rare.   Chas. A. Bahn.

19

CONGENITAL DEFORMITIES, HEREDITY

Albertto, Benjamin. **Marfan's syndrome.** Arch. de oft. de Buenos Aires 23:240-252, Sept., 1948.

A case of Marfan's syndrome in a girl, 12 years of age, is presented in great detail.   A. G. Wilde.

Bernoulli, R. **The mechanism of persistence of the hyaloid artery.** Ophthalmologica 117:169-179, March, 1949.

A rare congenital anomaly in a seven-year-old boy is described. The right eye was highly myopic but seemed to have adequate vision. The left eye was slightly microphthalmic. A heavy vessel-bearing strand of gray tissue originated in the region of the disc, traversed the vitreous cavity forward, downward and laterad and was inserted on the posterior surface of the lens a little below the posterior pole. No blood vessels could be made out in the retina which appeared to occupy a normal position. The strand in the vitreous is interpreted as a persistent hyaloid artery with hypertrophic glial sheaths. This overdevelopment of the glial sheaths probably prevented the development of the retinal vessels.   Peter C. Kronfeld

Broendstrup, J. M. Posterior embryontoxon in three generations. Anomaly of development of the anterior chamber of the eye with annular opacity of the cornea and membrane before the chamber angle. Acta ophth. 26:495-507, 1948.

The literature is reviewed and a family with embryontoxon reported. The bilateral malformation consisted of a massive adhesion between the iris and cornea. Around the entire circumference there was a whitish gray homogeneous peripheral band-like thickening on the posterior surface of the cornea, 0.5 to 2 mm. wide with a sharp serrated pupillary edge, and a peripheral boundary that faded gradually into clear cornea. There was definite hypoplasia of the iris and its stroma seemed to fuse with the corneal band. At 35 years of age glaucoma was discovered in one eye. Seven cases of this anomaly occurred in three generations of the family. All affected members were fair, short, blue eyed, and had high cheek bones. The unaffected members were dark and tall. (5 figures.)   Ray K. Daily.

Esteban, A., and Wolf, J. A. Bilateral aniridia with ptosis and embryontoxon.

Arch. de oft. de Buenos Aires 23:141-148, July-Aug., 1948.

A twenty-eight-year old woman who had one son with aniridia and another with congenital heart defect had bilateral ptosis with enophthalmos, congenital bilateral aniridia and nystagmus. The marked photophobia was mitigated somewhat by her ptosis. She had no strabismus, and convergence was normal. The cornea showed a peripheral clouding 2 to 4 mm. wide in the superficial layers resembling an arcus senilis, but more irregular in outline. There was anterior and posterior cataract. The visual acuity was limited to counting fingers at two meters.
                                A. G. Wilde.

Hallermann, W. "Bird-face" due to deformation of the mandible and congenital cataract. Klin. Monatsbl. f. Augenh. 113: 315-318, 1948.

Two cases of congenital malformation of the mandible with considerable shortening of its body which leads to the appearance of "bird face" are reported. Both patients had had bilateral congenital cataracts in each eye. It is not known whether the two abnormalities are related. (4 figures.)   Max Hirschfelder.

Lowe, R. F. The eyes in mongolism. Brit. J. Ophth. 33:131-175, March, 1949.

Mongoloid facies and almond shaped palpebral apertures do not invariably occur in the syndrome mongolism. One of the most important signs is the general retardation of growth affecting all the tissues of the body even to the extent of retention of fetal characteristics throughout life. In 67 patients, of which 40 were over 25 years of age, the skulls and all the skull bones examined exhibited a marked retarding of growth. Four skulls even had persistent frontal sutures. The diameters of the orbits were small and the inclination of the axis was 75 degrees

instead of the normal 45. This brings about a palpebral aperture which is more oblique and shorter than the normal. Epicanthus is normal in babies and disappears in the first few years. In mongolism it remains a little longer and is almost always gone by the 12th year. The lids and lacrimal systems are usually normal. The iris presents two characteristic changes: a general poverty of stromal fibers and noticeable depigmentation. Speckling of the iris is common. Arcuate lens opacities, the most common, develop during fetal life owing to the presence of abnormal capsulo-pupillary vessels, sutural opacities occur in the anterior Y sutures of the fetal nucleus and flake opacities are found in the juvenile and adult nuclei. About one third of subjects had very high myopia. Nystagmus was found in nine and in only 2 was it of cerebral origin. It is not considered characteristic of mongolism. Strabismus occurs about 20 times as often as in the general population. (23 figures.)

Morris Kaplan.

Lutman, F. C., and Neel, J. V. **Inheritance of arachnodactyly, ectopia lentis and other congenital anomalies (Marfan's syndrome) in the E family.** Arch. Ophth. 41:276-305, March, 1949.

Marfan's disease is a syndrome which in its fullest expression is characterized by an elongate, slender body build, especially evident in the extremities, skeletal deformities (kyphosis, scoliosis, pigeon breast, pes planus, hammer toes), dolichocephalic skull, poorly developed and hypotonic musculature, laxity of the joints and ligaments, scanty subcutaneous fat, malformation of the ears, malformations of the lungs, congenital heart disease, and ocular anomalies, especially ectopia lentis. There is great variability in the degree to which these traits are manifest.

The clinical records of several hundred visits by members of the E family have been accumulating at the Strong Memorial and Rochester Municipal Hospitals since 1928. In 1941, an attempt was made to reëxamine all the members who had hospital records. In a kinship of 40 persons, 17 members probably had Marfan's syndrome (arachnodactyly, ectopic lentis, indications of cardiac abnormalities and other congenital defects). There was a great variability in the expression of the syndrome in the affected members of the kinship. In addition to classic cases, there existed in this one family members so mildly affected that the diagnosis would be unsuspected or in doubt were it not for their genetic background. Ocular anomalies observed in all persons studied were, in addition to ectopia lentis or coloboma of the lens, abnormal zonular fibers, an iris lacking in the usual surface trabeculae and crypts, deficiencies of uveal pigment, particularly at the periphery of the iris, and amblyopia. In several cases there were other ocular defects. The syndrome is inherited as though due to one or more dominant autosomal genes. Although a final decision is not possible, the bulk of the evidence suggests that the entire syndrome may be due to one gene only whose expression is greatly influenced by other genetic, and possibly by environmental, factors.

Ralph W. Danielson.

Straith, C. L., and Lewis, J. R. **Associated congenital defects of the ears, eyelids and malar bones (Treacher Collins syndrome).** Plast. and Reconstruct. Surg. 4: 204-213, March, 1949.

In addition to a review of the literature, which is scanty, four cases of Treacher Collins syndrome are reported. The characteristics are as follows: flattened malar eminence, deficient lower orbital margin, oblique palpebral fissures,

bilateral notches in the outer third of the lower eyelids, eyelashes absent on medial two-thirds of lower eyelids, receding chin, and high, narrow, prominent front teeth, bilaterally deformed external ears, with frequently associated abnormalities of the external auditory meatus and loss of hearing. Plans for the plastic repair of these defects are discussed. Alston Callahan.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Eames, T. H. **The effect of glasses for the correction of hypermetropia and myopia on the speed of visual perception of objects and words.** J. Educational Research 42:534-540, March, 1949.

In 100 children an increase in speed of work perception followed the use of glasses for correction of refractive errors. The correction of lower degrees of hypermetropia than of myopia tends to produce increment in a larger percentage of cases per dioptric level. F. H. Haessler.

Jokl, A. **Death from eye disease and occurrences of death in ophthalmological practice.** Ophthalmologica 117:129-146, March, 1949.

The author reviews the eye diseases which have caused the patient's death, either directly or through circumstances which were the direct sequel of the eye disease or intimately connected with it. The diseases are grouped under the following headings: hemorrhages from the conjunctiva in hemophilia and from vascular tumors and bacterial diseases that gained entrance to the body through the conjunctiva or the lids, perforating injuries, or orbital cellulitis. The severe systemic intoxication due to the local application of "lash lure" is mentioned. Well known examples of death after operations are the fatal outcome of dacryocystectomies in chronic suppurative dacryocystitis and of enucleations in panophthalmitis. The malignant primary tumors of the eye and its adnexa are discussed in detail. Fear of blindness or unrelieved neuralgic pain may drive a patient to suicide. The first pair of bifocals makes the patient more liable to meet with an accident. Peter C. Kronfeld.

Mercier, Armand. **Visual aptitudes in railroad and aviation employees.** Ann. d'ocul. 182:24-31, Jan., 1949.

The relative merits of the requirements are discussed. The author believes that railroad employees require better sight than aviators. Chas. A. Bahn.

Sachs, M. **Nearly one hundred years of the ophthalmoscope.** Arch. Ophth. 40: 268-272, Sept., 1948.

This paper gives interesting facts about von Helmholtz and describes incidents in the discovery of the ophthalmoscope. Ralph W. Danielson.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

DEATHS

Dr. Harry Monroe Hendershott, Portland, Oregon, died March 26, 1949, aged 69 years.

ANNOUNCEMENTS

EGYPTIAN MEDAL FOR SCIENTIFIC WORK

To encourage scientific ophthalmic work, the Ophthalmological Society of Egypt will award each year a gold medal for the most valuable contribution of the year.

The competition is open to all members of the society of less than 20 years' practice, whether living in Egypt or outside of the country. Candidates desiring to enter the prize competition should submit their theses, in three typed copies, not later than the first of December each year.

In making the award, the committee will consider: (1) The originality of the work in its conception and execution; (2) its application to the major problems of ophthalmology; and, (3) general presentation.

Further information may be obtained by addressing: Dar El Hekma, 42 Kasr El Ainy Street, Cairo, Egypt.

CALIFORNIA POSTGRADUATE COURSE

The University of California Medical School, San Francisco, is offering a postgraduate course in ophthalmology from September 12th through September 17th. The course is open only to graduates of medical schools approved by the Council on Medical Education and Hospitals of the A.M.A. The fee for the course is $60.00, payable at the time of enrollment.

Dr. Frederick C. Cordes, clinical professor of ophthalmology, University of California Medical School, is general chairman of the course. Officers of instruction will be: Dr. Samuel D. Aiken, Dr. Crowell Beard, Dr. Dudley P. Bell, Dr. George S. Campion, Dr. Joseph W. Crawford, Dr. C. Allen Dickey, Dr. Owen C. Dickson, Dr. David O. Harrington, Dr. Margaret Henry, Dr. Michael J. Hogan, Dr. Bertram V. A. Low-Beer, Dr. Robert N. Shaffer, Dr. Joseph G. Smith, and Dr. Phillips Thygeson.

Further information may be obtained by addressing: Dr. Stacy R. Mettier, head of postgraduate instruction, medical extension, University of California Medical Center, San Francisco 22, California.

Preceding the postgraduate course in ophthalmology will be a course in otorhinolaryngology, September 5th through 9th.

TORONTO OFFERS GRADUATE TRAINING

The University of Toronto, Faculty of Medicine, offers a postgraduate course in ophthalmology extending over three years. The graduate instruction in ophthalmology in the teaching hospitals in Toronto has been coördinated under the direction of the university. The first year on a fellowship, the value of which is approximately $1,400, the student spends in one of the basic sciences of ophthalmology, and the final two years are spent on the intern service of one or more of the university teaching hospitals. Approximately four hours of didactic teaching are arranged for the students by members of the staff each week from October to May. On Saturday morning, staff ward rounds are made at the Toronto General Hospital and are attended by the interns from the other teaching hospitals.

A sound knowledge of neurology and metabolic diseases is desirable. The following courses are given: geometric and physiological optics, physiology of the eye, principles and practice of biomicroscopy, perimetry, ocular therapeutics, medical ophthalmology, pathology of the eye, bacteriology and external diseases of the eye, embryology and developmental anomalies of the eye, ocular motor anomalies, anatomy of the orbit, skull, and brain, radiological ophthalmology, industrial ophthalmology, intraocular and plastic surgery, pathology of the visual pathways, refraction, neuro-ophthalmology, glaucoma. Senior interns are given instruction in the preparation and presentation of scientific papers.

The fee for instruction is $50.00 per year payable to the chief accountant, University of Toronto. An application for appointment may be made to the professor of ophthalmology, Faculty of Medicine, University of Toronto. Appointments are made in December to commence on the following July 1st.

ORTHOPTIC TRAINING COURSE

The Rochester (New York) Orthoptic Center is receiving applications for its next training course for orthoptic technicians. The course is accredited by the American Orthoptic Council. Information may be obtained from the Rochester Orthoptic Center, 208 North Goodman Street, Rochester 7, New York.

MISCELLANEOUS

LIONS CLUB SCHOLARSHIPS

On June 21st, the Lions Club of New York presented four $500 scholarships to graduate students of New York University College of Medicine who

are planning to become eye specialists. The presentation took place at the annual Ladies' Day luncheon at the Savoy Plaza.

Walter Hoving, president of the Hoving Corporation, in behalf of the Lions Club, handed a $2,000 check to Dr. Daniel B. Kirby, professor of ophthalmology, New York University College of Medicine. Dr. Kirby said the funds would enable four students to undertake research projects, adding that even such small sums of money might be instrumental in obtaining important results.

The four students who will receive the scholarships are Dr. Irwin Cohen, Dr. Thomas Heslin, Dr. James Mayer, and Dr. Arthur Smith.

Ernest R. Fryxell, chairman of the Lions Club Blind Aid and Eye Conservation Committee, announced that the organization would suggest to the 7,203 Lions Clubs throughout the country that they undertake similar scholarships for ophthalmologists.

Earlier recipients of the Lions Club of New York scholarships are: Dr. Edward P. Danforth, Dr. Charles Goldsmith, Dr. Jonathan L. Harris, and Dr. Hugh McGree for the year, 1946; Dr. Edward Buckley, Dr. George R. Kolodny, Dr. Nathaniel Robinson, and Dr. Horace Shreck, for 1947; Dr. Goodwin Breinin, Dr. Edwin Kent, Dr. Walter Mayer, and Dr. Charles Toomey, for 1948.

BETTER VISION INSTITUTE

New members present at the annual meeting of the Better Vision Institute, June 10th, at the Park Lane Hotel, New York, were John Wiseman of Wiseman Optical Company, London, England; Tom Hood and Fred Soden of Continental Optical Company; Dr. John J. Brown of Perth Amboy, New Jersey; and Ray Farnum of Bausch & Lomb Optical Company.

Elections were held of new directors to serve two-year terms, and new finance committee members to serve for one year.

CAROLINAS MEETING

On September 12th through 15th, at the Hotel Poinsett, Greenville, South Carolina, the North Carolina Eye, Ear, Nose, and Throat Society and the South Carolina Society of Ophthalmology and Otolaryngology will hold a joint meeting. The following program will be heard:

Dr. A. D. Ruedemann, professor of ophthalmology, Wayne University, Detroit, Michigan: "The differential diagnosis between unilateral and bilateral ocular protrusion"; "The end results with new radium-D applicator in comparison to radon"; "Ocular manifestations of allergy."

Dr. Peter C. Kronfeld, Department of Ophthalmology, Illinois Eye and Ear Infirmary, University of Illinois, Chicago: "Differential diagnosis of acute glaucomas"; "Prognosis of retinal detachment"; "Newer drugs in ophthalmology."

Dr. Rudolph Aebli, professor of ophthalmology, New York University, Bellevue Medical Center, Post-Graduate Medical School, New York: "The

relationship of muscle imbalances to the palpebral aperture and pseudoptosis"; "Principles of ocular muscle surgery"; "Congenital muscle anomalies."

Dr. Carl C. Johnson, associate, Department of Ophthalmology, Harvard University, Boston: "Surgical treatment of ptosis"; "The diagnosis and surgical treatment of glaucoma."

Dr. Preston C. Iverson, New York: "Neoplasms of the lip, nose, and eyelid and plastic repair of the lesions"; "Congenital deformities of the face."

Dr. Louis H. Clerf, Philadelphia: "Cough viewed from otolaryngologic standpoint"; "Paralysis of larynx: Surgical treatment"; "Malignant neoplasms of larynx."

Dr. Kenneth M. Day, Pittsburgh: "Clinical management of deafness"; "Meniere's disease."

Dr. Russell A. Sage, Indianapolis: "Diseases of the mouth and tongue."

Officers of the South Carolina Society of Ophthalmology and Otolaryngology are: President, Dr. Pierre G. Jenkins; vice-president, Dr. Murdock Walker; secretary-treasurer, Dr. Roderick Macdonald.

Officers of the North Carolina Eye, Ear, Nose, and Throat Society are: President, Dr. James Harrill; vice-president, Dr. G. M. Billings, secretary-treasurer, Dr. MacLean B. Leath.

WEST VIRGINIA OFFICERS

The officers of the West Virginia Academy of Ophthalmology and Otolaryngology are: President, Dr. Garnett P. Morison, Charles Town; 1st vice-president, Dr. Charles T. St. Clair, Jr., Bluefield; 2nd vice-president, Dr. Arthur C. Chandler, Charleston; treasurer, Dr. Frederick C. Reel, Charleston; secretary, Dr. Melvin W. McGehee, Huntington; directors, Dr. Eugene C. Hartman, Parkersburg, and Dr. Ivan Fawcett, Wheeling.

PERSONALS

To GIVE FOURTH PROCTOR LECTURE

On Friday evening, September 16th, Dr. Jonas S. Friedenwald, Baltimore, will deliver the fourth annual Francis I. Proctor Lecture on Ophthalmology at the University of California Medical School, San Francisco. The subject of Dr. Friedenwald's address will be "Further studies on diabetic retinopathy."

RESEARCH ON CORNEAL TRANSPLANTS

Dr. A. E. Maumenee, head of the Department of Ophthalmology, Stanford University School of Medicine, San Francisco, will do research work on corneal transplants under a contract with the National Advisory Council of the U. S. Public Health Service.

In announcing the receipt of the grant, Dean Loren R. Chandler of the medical school said that the funds include an allowance for a research fellow and that applications for the fellowship are requested by the medical school. The research grant is for one year but is subject to renewal.

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CONTENTS

THERAPEUTIC RESULTS IN ADVANCED CHRONIC SIMPLE GLAUCOMA WITH TELESCOPIC FIELDS*

SYLVAN BLOOMFIELD, M.D., AND LEO KELLERMAN, M.D.

New York

In the treatment of chronic simple glaucoma it is generally accepted that surgery is indicated when medical therapy proves unsatisfactory. Reese[1] and, more recently, Kronfeld and McGarry[2] have demonstrated statistically that such operations are most successful early in the course of the disease, and that the results of surgery on eyes with advanced glaucomatous damage are generally poor. This is in agreement with the opinion expressed by Gradle[3] and others, that operation on an eye with advanced glaucoma is extremely hazardous.

Another observation concerning eyes in an advanced stage of glaucoma is of interest. Reese, in a footnote appended to his paper,[1] noted that such eyes, when reduced to telescopic fields, often seemed to retain central vision for long periods although their ocular tension might be uncontrolled. Kronfeld and McGarry[2] have stated that "it seems highly probable, however, that the chances of survival of the center of the field are not much poorer under nonnormalization than under normalization of tension."

If it is true that glaucomatous eyes with markedly restricted central fields retain their residual function in spite of elevated tension, and that operations for reducing tension in such eyes are dangerous, it would seem that surgery in these cases may acually be contraindicated. Such a conclusion, however, is opposed to the widespread opinion that in any eye an abnormally high intraocular pressure that does not respond to medical therapy should be treated surgically. The purpose of this paper is to evaluate statistically the advisability of surgical intervention in eyes reduced to telescopic fields by advanced chronic simple glaucoma that is medically uncontrolled.

For this study, the course of a series of unoperated eyes with advanced chronic simple glaucoma was investigated. Only those eyes were considered that had central fields reduced in all isopters to 10 degrees or less from fixation at their widest meridian. These fields were all measured on the tangent screen at one meter, with standard-sized objects. A few eyes were included in this group in which, in addition, small temporal islands of field were present but completely separated from the central field by at least 10 degrees. In none of these eyes was vision reduced to less than 20/200. This limit was decided upon so that later decreases in vision might be readily detected. Finally, all of the eyes included in this study showed tensions of over 35 mm. Hg (Schiøtz), on three or more occasions, to indicate the inadequacy of medical treatment in each case. The problem such uncontrolled tension presented was met in certain of these cases by resort to surgery, and in other instances simply by continuation of miotic therapy. A comparison of the results of each of these methods of treatment is the basis of this study.

The records employed for this investigation were obtained from the ward services of

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two large metropolitan ophthalmic hospitals whose files for the past eight years were reviewed. All eyes that fulfilled the above criteria were considered for this study. However, since relatively few eyes fulfilled all these conditions and since the records of many otherwise eligible cases were not sufficiently complete for critical evaluation, only 41 eyes were found suitable for consideration.

Of these 41 eyes, 19 subsequently underwent surgery to relieve a recurrently high tension that did not respond to miotic therapy. The remaining 22 eyes were not operated upon, although the tension in each case was inadequately controlled medically according to the criteria outlined above. The range of ages of the patients in the operated group was from 30 to 77 years, and averaged 62 years. The ages of the patients in the unoperated series was from 38 to 79 years, and averaged 65 years.

The preoperative visual acuities in the operated eyes ranged from 20/30 to 20/200. Of the 19 eyes in this group, 11 had vision of better than 20/70, and 8 had visual acuities of 20/70 or less before operation. The range of visual acuity in the 22 eyes that were not operated upon was from 20/30 to 20/200. Of these, 11 had visual acuities of better than 20/70, and 11 had acuities of 20/70 or less, at the beginning of the period under consideration in this study.

The range of tension in the eyes in each series at the beginning of this period was also quite similar. Thus the conditions of the eyes in each of these two groups, before surgery was applied to one of them, were sufficiently alike to permit a valid comparison of the results of alternative methods of therapy.

In evaluating the results of surgery, only the response to the first operation was considered in those three cases where several procedures were performed. The follow-up period under consideration was terminated before the second operation on these eyes, to permit attention to be focused in this study

on the results of a single operation in these late glaucomatous eyes rather than on the cumulative traumatic effects of many surgical procedures. However, the occurrence of postoperative complications did not exclude any eye from consideration inasmuch as they were considered relevant to the problem of determining the hazards such surgery entails. The operations done comprised 5 Elliot trephining operations, 2 modified Lagrange operations, 1 basal iridectomy, 8 iridencleisis operations, 2 iridencleisis with sclerectomy procedures, and 1 cyclodiathermy operation.

In evaluating the results of the treatment of these eyes, it was felt that the primary consideration was the eventual effect on visual acuity. Since all the eyes under consideration had initial fields limited to 10 degrees or less from fixation, further field restrictions would frequently have been difficult to distinguish and certainly, from the patient's point of view, would be far less important than the actual vision retained. All visions were recorded with refractive correction where so improvable.

It was usually very difficult to establish accurately the exact cause for the reduction in visual acuity that occurred in many of these eyes. Therefore, no attempt was made in this investigation to determine to what degree visual loss was due to cataractous changes in the lens, progressive neuroretinal degeneration, or vascular pathologic conditions. It seemed valid to assume that in these two series of similar eyes the incidence of such senile and glaucomatous pathologic processes would be statistically equivalent except for the surgery performed on one group, which would affect ocular structures, and the subsequent course of the glaucoma, only in the operated series.

STUDY OF OPERATED EYES

Of the 19 eyes operated upon, 11 (58 percent) showed some loss in visual acuity at the first postoperative examination, and that loss ranged from one line on the standard Snellen chart to loss of light perception, in

one case. From the point of view of useful vision, it may be noted that, whereas none of these 19 eyes preoperatively had less than 20/200 vision, the first acuity recorded post-operatively had fallen below this level in 6 (32 percent) of all these eyes.

The follow-up period for these operated eyes varied from 2 months, in one case that was reduced to perception of hand move-

of that time. Thus, for the periods recorded, it is noteworthy that only 3 of these 19 eyes retained a visual acuity equal to that present preoperatively, and 16 (84 percent) of the total suffered some visual loss. In the latter group, 9 eyes or (47 percent) of the total number operated upon were reduced in visual acuity to less than 20/200 by the end of their follow-up period. Of these 9 eyes

Fig. 1 (Bloomfield and Kellerman). Summary of visual status of operated and unoperated eyes.

	OPERATED	UNOPERATED
TOTAL NUMBER OF EYES IN EACH GROUP	19	22
NUMBER OF EYES WITH INITIAL VISION OF BETTER THAN 20/70.	11	11
NUMBER OF EYES WITH INITIAL VISION OF LESS THAN 20/70.	8	11
AVERAGE FOLLOW-UP PERIOD.	28 mos.	24 mos.
NUMBER OF EYES WITH SOME LOSS OF VISION. AFTER FOLLOW-UP.	16	8
PERCENTAGE OF EYES WITH SUCH LOSS.	84%	36%
NUMBER OF EYES WITH VISION REDUCED TO LESS THAN 20/200 WITHIN FOLLOW-UP PERIOD	9	3
PERCENTAGE OF EYES WITH SUCH SEVERE VISUAL LOSS	47%	14%

ments in that period, to 6 years. The average follow-up interval for the group was 2 years and 4 months. During this postoperative period, 11 of these 19 eyes showed satisfactory control of tension, as indicated by a tension range consistently below 35 mm. Hg (Schiøtz). In the remaining 8 eyes (42 percent) the tension remained uncontrolled postoperatively, even with supplementary medical treatment.

Although the follow-up period recorded for this operated series is not long, several interesting facts are revealed by a study of the visual status of these eyes at the end

with markedly reduced vision, 6 were eyes in the group of 8 with tension uncontrolled postoperatively and the remaining 3 were among the 11 eyes whose tensions were apparently successfully controlled by operation. Thus, of the eyes whose tension was uncontrolled, 75 percent showed a loss of visual acuity to less than 20/200, and of the postoperatively controlled group, 27 percent showed such extreme loss in acuity.

The small number of cases operated upon does not permit many conclusions to be drawn from a more detailed analysis of these results. Although the two eyes with highest

preoperative tensions were respectively reduced in visual acuity from 20/30 and 20/40 to perception of hand movements and finger counting, such a possible relationship of high preoperative tension to poor postoperative result is not borne out in other cases. Similarly, there seemed to be no correlation of degree of loss of vision to the age of the patient. In general, the immediate postoperative loss of vision seems to have been less in those eyes which underwent iridencleisis, but too few operations of the different types were performed to permit comparison of the results of the various procedures done on these advanced cases of glaucoma.

To determine to what degree these surgical results were influenced by systemic diseases that might predispose to operative complications, the blood pressure and fasting blood sugar recorded in each case at the time of operation were noted. In none of the 17 patients that underwent surgery was vascular hypertension present. In 3 of the patients, a mild degree of diabetes mellitus was recorded.

Four eyes of these 3 diabetic patients were included in the operated group. Three of these eyes showed no immediate postoperative loss of vision, which, as demonstrated above, is a better immediate operative result than that which occurred in the group as a whole. During follow-up periods similar to those of other patients in this study, a drop in visual acuity to less than 20/200 occurred in 2 of these 4 eyes, or 50 percent. As was noted above, this severe degree of visual loss was recorded in 47 percent of the whole operated group. It would, therefore, seem that the presence of diabetes mellitus in 3 of the operated patients did not appreciably affect the statistical evaluation of surgical results in this series.

It also seemed desirable to estimate the possible influence on these results of the varying technical skills of different operators. All these cases were operated upon in 1 of 2 large metropolitan ophthalmic hos-

pitals. Nine of these 19 eyes were operated upon by experienced ophthalmologists who were on the attending staffs of these institutions. The other 10 eyes were operated upon by resident physicians supervised and assisted in each instance by a member of the attending staff. An immediate loss of some visual acuity was noted postoperatively in 4 of the eyes operated upon by the residents, and in 7 of the eyes operated upon by the members of the attending ophthalmological staffs. After the follow-up periods noted, a drop in visual acuity to less than 20/200 was noted in 4 of the eyes operated upon by the residents, and in 4 of the eyes operated upon by members of the attending staffs. It would, therefore, appear that in this series, the operative results obtained by the residents was no worse than that obtained by the attending ophthalmologists, and that consequently the technical experience of the operators did not significantly affect the statistical results in this operated group of eyes.

STUDY OF NONOPERATED EYES

Of the 41 eyes with telescopic fields due to advanced chronic simple glaucoma here studied, 22 eyes in 20 patients were not operated upon although their tensions were inadequately controlled by medical treatment, according to the standard previously noted. These cases were closely followed for periods ranging from 8 months to 5 years, and averaged a recorded course of slightly more than two years. This approximates the follow-up period recorded for the group of comparable eyes that were operated upon, as previously noted.

During these periods, in spite of apparently inadequate therapy limited to the local instillation of miotics, a reduction in vision of any degree was noted in only 8 (36 percent) of these eyes. This visual loss ranged from one line on the standard Snellen chart to loss of light perception, in one eye. In only 3 of these eyes, 14 percent of all the unoperated eyes, was the visual acuity reduced below 20/200. It may be recalled that in the

eyes that were operated upon, 84 percent showed some visual loss over a comparable follow-up interval and 47 percent of the whole operated group had visual acuities reduced below 20/200 during that time.

INITIAL AND RESULTING VISION

A correlation was sought between the initial visual acuity in each eye of the two series and the vision eventually present. Among the operated eyes, a reduction in vision of at least one line on the Snellen chart occurred with equal frequency in the group with preoperative vision of better than 20/70 and that with initial acuities of 20/70 or less. This was true both for the results found at the first postoperative examination of acuity and for those recorded after the stated follow-up periods. Of course, the occurrence of further visual loss resulted more frequently in disablingly low acuity in the group with initially poorer vision. Similarly, in the group of unoperated eyes, the incidence of further visual loss during the period of this study was not significantly different in those eyes with initial acuity of better than 20/70, than in those whose vision at the beginning of the period of observation was already reduced to 20/70 or less.

CONFIGURATION OF CENTRAL FIELD

The possibility was also suggested that the configuration of the small central field present in these eyes at the beginning of this study might influence the eventual visual result in both the surgically and medically treated groups. The fields of all the eyes under consideration, although limited to those not greater than 10 degrees from fixation in all meridians, could be divided roughly into those which were round and those which were kidney-shaped. The latter configuration occurred in those eyes in which the nasal field was disproportionately constricted to fall within three degrees or less of the fixation point.

Among the 19 operated eyes, 9 fields were found to have been kidney-shaped in this way, preoperatively. Five of these eyes had visual acuities of better than 20/70, and 4 had vision reduced to 20/70 or less at the beginning of this study. Analysis of the effect of surgery on these eyes disclosed no significant difference in the incidence of reduced vision from that which occurred in the entire surgically treated group, either immediately after operation, or after the follow-up period. A reduction in visual acuity to less than 20/200 occurred in 44 percent of these eyes with kidney-shaped central fields; a result strikingly similar to the 47-percent incidence of such loss in the entire surgical group.

Among the 22 medically treated eyes, 8 presented kidney-shaped central fields as previously defined. Three of these eyes had visual acuities of better than 20/70, and 5 had vision of 20/70 or less. Under medical treatment that proved inadequate to control the tension, only 3 of these 8 eyes showed a further reduction in acuity during the follow-up period studied, and in only one instance did a loss of vision to less than 20/200 occur. The visual results in these eyes with kidney-shaped fields were, therefore, very similar to those which occurred in the medically treated group as a whole.

COMMENT

Although the number of eyes studied in each group is too small for detailed quantitative comparison of results, the grossly poorer visual status of the group of eyes that underwent surgery is striking. The immediate deleterious effect of operation on these very late cases of chronic simple glaucoma with telescopic fields is indicated by the early loss of some degree of acuity in 58 percent of these eyes. Over a follow-up period averaging over two years, this percentage of eyes with some visual loss postoperatively rose to 84 percent, and of the total number of operated eyes, 47 percent, or almost half, had suffered an extreme loss of vision to less than 20/200.

Contrasting results were presented by the

comparable group of eyes in which therapy was limited to miotic drops that proved inadequate to keep the tension within normal range. Of these, over a similar interval of time, 36 percent suffered some reduction in visual acuity, and in only 14 percent of this entire unoperated group was the loss of vision so severe as to reduce acuity to less than 20/200.

The reason for the unfavorable visual results following surgery in these cases is not clear. Certainly the restoration of normal tension to a glaucomatous eye would seem to be desirable in any stage of the disease. Nevertheless, in this series of cases of advanced glaucoma with marked field restriction, even operations that succeeded in controlling tension eventually resulted in a reduction in vision to less than 20/200 in 27 percent of the cases. In the 42 percent of cases in which operation failed to control tension, the incidence of such disabling loss in vision was 75 percent. In comparable eyes in which the tension was permitted to remain abnormally high by limiting therapy to local medication, such extreme loss was recorded in only 14 percent.

This suggests the possibility that, in advanced cases of chronic simple glaucoma, a functional equilibrium is attained that permits the retention of central vision in spite of abnormally high tensions over relatively long periods. Surgery apparently entails the hazard of disturbing this balance so that further loss of visual function is more likely to occur after operation even if the intraocular pressure is subsequently adequately controlled. When operation does not succeed in reducing ocular tension to normal range, as is common in these late cases, the disturbed functional balance plus continued tension elevation results in an extremely high incidence of severe visual loss.

Whatever the underlying cause may be, the facts here presented suggest that eyes with telescopic fields due to advanced glaucomatous damage tend to retain a useful degree of central vision for relatively long periods with simple medical treatment although tension may not be controlled. In such eyes, surgery employed to reduce the tension involves a significantly greater risk of incurring visual disability than does the continuation of apparently inadequate tension control through miotic therapy alone.

CONCLUSION

A study was made of the treatment of 41 eyes with uncontrolled chronic simple glaucoma sufficiently advanced to produce a constriction of central fields to 10 degrees from fixation.

In 19 of these eyes, surgery was performed to reduce the tension, with subsequent loss of some visual acuity in 84 percent of these cases, and a reduction in acuity to less than 20/200 in 47 percent, over a follow-up period averaging a little over two years.

In the remaining 22 eyes, the tension remained above normal range but no surgery was performed. In this group, over a comparable period, some visual loss occurred in 36 percent, and an extreme reduction in acuity to less than 20/200 in 14 percent.

These facts suggest that in eyes with advanced chronic simple glaucoma of this degree, central vision may be retained for long periods in spite of inadequately controlled tension, and that in such cases operation to reduce the tension is contraindicated.

1010 Fifth Avenue (28).
1095 Park Avenue (28).

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CATARACT AND TETANY PRODUCED BY PARATHYROID DEFICIENCY DURING PREGNANCY, LACTATION, AND MENSTRUATION*

DONALD J. LYLE, M.D.
Cincinnati, Ohio

INTRODUCTION

Parathyroid deficiency may be classified according to its etiology into that produced by

1. Operative damage.

2. Intrinsic impairment from disease, or degeneration, or lack of development of the glands.

3. Extrinsic factors demanding immoderate function of the normal glands such as (a) Low calcium intake; (b) Depletion from conditions destroying calcium or demanding it in excess.

4. Not determined, unknown or idiopathic.

Last year was presented a case history and discussion of cataract and papilledema in parathyroid deficiency resulting from operative damage. This year I should like to present a case history of idiopathic parathyroid deficiency and discuss the effect upon it of pregnancy, lactation, and menstruation.

CASE REPORT

A white woman, aged 28 years, presented herself for examination because of failing vision in both eyes. Discrete opacities of various densities were found beneath the posterior capsule of both lenses, with a few raylike riders arching through the periphery to the anterior subcapsular area. This type of bilateral cataract in a young adult was immediately suggestive of endocrine disturbance.

The history prior to the beginning of diminished vision was irrelevant. There were no illnesses of severe nature, no operations, and the family history was entirely without

pertinent disclosure. The loss of sight began gradually during the first pregnancy and increased with lactation and a subsequent pregnancy. Finally, with menstruation, the vision became more disturbed.

Positive Chvostek's and Trousseau's signs and a low serum calcium of 7 mg. per 100 cc. of blood established the diagnosis of idiopathic parathyroid deficiency. The patient was sent for further laboratory tests and X-ray studies and was given a note to her physician stating the diagnosis and suggested treatment. She was asked to furnish a brief account regarding the onset and development of her symptoms. The following is from her letter:

"This eye condition started in the spring of 1943, shortly after I became pregnant. It was more noticeable when I tried to read. I nursed my first child for seven months and during that time noticed that the vision in my left eye was quite blurred. An eye doctor was consulted and he prescribed tinted lenses. To my recollection I noticed nothing until a month after I became pregnant with my second child, in December, 1945. The vision becoming worse, I consulted another doctor who told me I had an opacity in the back of my left lens, which might get better or worse. My sight became progressively worse with each month of pregnancy, although I could still read without much strain.

"As I look back on it now, with both pregnancies I was extremely nervous and despondent, with a constant twitching of the muscles of my hands and feet and one muscle in my stomach. I suffered with many leg cramps and rheumatism.

"I nursed my second child for four months until I noticed an increasing difficulty in reading. I then went to another doctor, who

told me I had cataracts in both eyes. I immediately stopped nursing (the last of November, 1946) and had a complete physical examination. A parathyroid deficiency was revealed and I was put on a low-phosphorus diet, calcium chloride, and vitamin D.

"My eye condition seemed to remain stationary until May, 1947, when in two weeks' time the eyes became much worse, particularly the better right one. I became sick at my stomach and saw heavy black spots and wave vibrations before my eyes.

"I now notice that during menstrual periods my vision is much worse, when I also am highly nervous and twitching · returns with a tingling sensation in my fingers and feet at night. The muscles of one eye also twitch. My sight definitely is weaker during the week of menstruation."

From this personal account there is very little doubt that this patient had an idiopathic hypoparathyroidism as manifested by the cataracts and tetanic muscular spasms.

As there was no history of any disturbance before her first pregnancy, we must conclude that the idiopathic deficiency which existed at a latent asymptomatic level was increased and aggravated by the pregnancies and periods of lactation and subsequently even by menstruation, to the manifest symptomatic level.

HISTORY AND ETIOLOGY

Relatively few cases of idiopathic hypoparathyroidism or spontaneous parathyroid insufficiency have been described. Two hundred and forty cases of tetany in pregnancy have been reported to 1942, and have been reviewed by Anderson and Musselman.[1] Possibly three additional cases have been reported since then. Of this series, beginning with the report of a case in 1830, 146 were classified as idiopathic, which included those produced by pregnancy and lactation. The report of the presence of cataracts was infrequent. There is no doubt that lenticular changes were present in more cases, and would have been revealed had they been looked for or had better equipment for examination been available. Of still less frequency was the report of the presence of optic neuritis. Postoperative conditions, thyroid deficiency, and dietary lack of calcium and vitamin D comprise the remaining classifications.

The cause of idiopathic hypoparathyroidism is not well understood. It may be the result of an arrest in the growth of the glands, their pathologic destruction, or their degeneration after they have normally developed. They should receive a different and definite classification with the advent of additional knowledge. This loss, from whatever cause, implies, of course, the inability to produce the activating substance, the parathormone, whose chief action appears to be the maintenance of normal blood-serum levels of calcium and phosphorus. Other factors influencing the blood calcium level are the intake of calcium and phosphorus, the presence of vitamin D, the alkalinity or acidity of the ingested food, and the body tissues, and the pH of the blood.

The presence of parathormone increases the calcium level of the blood, as does a slightly acid state. The presence of phosphorus decreases the calcium level in direct ratio. The ingestion of calcium and phosphorus increases the amount of calcium and phosphorus available to the blood and tissues, the excess being excreted. Vitamin D is essential to normal absorption, utilization, and excretion of calcium, helping to maintain a constant normal blood level.

Ninety-nine percent of the calcium in the body is in the skeletal system, which, excepting the mature teeth, is labile and capable of being released back into the circulation. Calcium is found in all of the secretions and excretions of the body, especially in the feces. The regulation and maintenance of a relatively constant level of calcium in the blood depends upon the balance between the calcium intake, utilization, and excretion.

In the latent form of hypoparathyroidism with its accompanying reduced level of

serum calcium, equilibrium is maintained, with a narrow margin of safety, in an asymptomatic course. However, with the advent of pregnancy and lactation, the narrow margin of calcium reserve is reduced by depletion through fetal skeletal and lactogenic needs to the symptomatic level of manifest hypoparathyroidism. Because the previous serum calcium level is never reached after each pregnancy and lactation, subsequent menstruation may sufficiently deplete the reserve to bring about periodically the return of the symptoms.

During early pregnancy, the slight fetal demand for calcium results in no reduction in the maternal blood calcium level, unless there has been an inadequate intake in the diet or unless there is a deficiency in other factors conducive to maintaining a normal level such as is found in parathyroid deficiency. Normally, the necessary increase at this time is adequately provided by the stored calcium. During late pregnancy there occurs a reduction of maternal serum calcium, variously reported as from very little to 0.5 to 1 mg. percent below the previous level. This reduction is produced notwithstanding a hypertrophy of the parathyroid glands in a compensatory effort and the acquisition of a property in the blood of the pregnant woman, similar to that of parathormone, which increases the calcium serum level.

Whether this calcium reduction is still further produced by an altered parathyroid function or is the result of the influence of other endocrine glands which have been activated by the existing condition is at present conjectural. It has also been suggested that the placenta may produce a depressing agent which may influence the calcium level.

Thus, in pregnancy, lactation, and menstruation, it appears that, in addition to the somewhat variable calcium intake, not only the stored but the circulating calcium is called upon to meet the drain for fetal needs and for the production of milk and menstrual loss. When the level of serum calcium is lowered too far, symptoms of neuromuscular irritability and ectodermal trophic disturbance appear.

SYMPTOMS

The chief symptoms of hypoparathyroidism are included under the designation of tetany. The symptoms produced by tetany are common to all types alike. In order of their usual appearance and severity they are:

1. Tingling or paresthesia of the hands, feet, and face.
2. Carpópedal contraction.
3. Contraction of the abdominal muscles.
4. Laryngospasm.
5. Generalized convulsion.

The first three symptoms were found in the patient reported in this paper; the last two in the previously reported case.[11]

Vague or accompanying symptoms are:

1. Fatigue and musclar weakness.
2. Gastrointestinal irritability.
3. General nervous irritability.
4. Mental retardation.
5. Polyneuritis, which includes optic neuritis.

Most of the above symptoms are produced by irritation of the neuro-ectodermal system, chiefly as a result of the nervous excitability produced by a decrease in calcium acting upon the neuromuscular juncture as the contraction is arrested by the administration of curare.

Once more the question arises concerning the type and cause of change in the neural structures accompanying and producing visual loss in tetany. In a previous paper,[11] this condition was reported as possibly a papilledema and cerebral edema, although the marked and early loss of vision was more suggestive of optic neuritis. This condition again introduces itself, appearing during the menstruation in the patient whose case is presented in this paper. She complained of disturbed and diminished vision during her menstrual periods, which was in addition to the gradual loss of sight from her develop-

ing cataracts. Unfortunately, her lenticular opacities prevented a definite view of the papilla.

Papillitis and retrobulbar neuritis associated with pregnancy, lactation, and menstruation have been reported in the literature on rare occasions. The most recent reference found was by Lillie,[10] who described a "marked acute optic neuritis and swelling of the disc 2 to 3 diopters," with complete blindness, in a woman who nursed her third child for 2½ months. So far as can be determined, no laboratory tests were made in any of the reported cases, and no pathologic material was studied. No adequate discussion as to the probable primary cause was presented. It was stated that "the cause of such a neuritis is obscure." Some suggested[6] multiple sclerosis, metabolic, or toxic causes.

If one considers the general subject of polyneuritis, he finds that there is a remarkable similarity between the symptoms produced by this comprehensive nerve involvement and those found in tetany. In both polyneuritis and tetany the sensory, motor, and general symptoms, such as fatigue and mental deterioration, are alike. Restricting the polyneuritis to the cranial nerves, the so-called polyneuritis cranialis, the facial, oculomotor, and vagus are most frequently involved; the optic nerve rarely. These nerves are also involved in the same order in tetany. The literature gives a few sentences to relapsing recurring polyneuritis, and states that this classification includes the cases found in pregnancy and the puerperium. There is the suggestion that the repeated attacks during subsequent pregnancies are due to identical circumstances or minores resistentiae.[15]

Although I do not infer that all polyneuritis has a low blood calcium with tetany, it seems to me very likely that the optic neuritis found in these women during pregnancy, lactation, and menstruation is a type of aseptic polyneuritis which is induced by low calcium level. This polyneuritis, which also affects the central nervous system, may produce an interstitial edema and venous engorgement, with cellular infiltrates and exudates. It also may produce a wallerian degeneration of the axons with demyelinization and neuronal swelling, granulation, fragmentation, and necrosis. It is reasonable to assume that the edema or aseptic inflammation of the visual system occurring in tetany accompanying parathyroid deficiency is the result of the tissue changes produced by calcium deficiency with its concurrent metabolic disturbances and functional loss.

In addition to the neuro-ectodermal affections, changes also occur in the somatic ectodermal tissue, resulting in loss of hair, nails, dental arrest in childhood, and cataract formation.

Hypoparathyroid tetany may be differentiated from other causes by:

1. Reduced serum calcium below 8.5 mg. percent.

2. Normal or increased serum phosphorus above 4.5 mg. percent.

3. Decrease in urinary excretion of calcium and phosphorus.

4. Normal serum phosphatase.

5. Normal acid base equilibrium.

6. Absence of significant osseous changes as evidenced by X-ray findings.

7. Absence of renal insufficiency.*

TREATMENT

The necessity for various types of treat-

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* A low blood calcium with tetany is also found in rickets in the child and osteomalacia in the adult, and in renal insufficiency. Low blood calcium without tetany is found in:
1. Hypoproteinemia whenever there is enough free calcium to produce symptoms of calcium deficiency.
2. Hyperphosphatemia of nephritis and uremia where phosphorus ratio is lower than the calcium level.
Tetany occurring with hypoparathyroidism is found in:
1. Nutritional disturbances with lack of vitamin D and calcium.
2. Depletion from exhausting diseases, poisons, and toxins.
3. Need for greater calcium than can be provided: (a) hyperventilation; (b) alkalosis; (c) Possibly pregnancy and lactation.

ment may be determined by testing the urine or blood. The Sulkowitch urine test for calcium should be made at frequent intervals. If the test reveals a milky precipitate, there is an overabundance of calcium and hypercalcemia is present. If the test reveals clear solution, no calcium is being excreted in the urine and the blood calcium is probably 7 mg. percent or less, the patient being

cium lactate in water 3 times daily is recommended. Ten cc. of 30-percent solution of calcium chloride 3 times a day after meals will also increase the acidity of the blood, which in turn will raise the calcium level. The calcium and phosphorus intake must be increased 10 to 20 percent in pregnancy, and much more in lactation. This means an average daily intake of 1.5 gm. of calcium in
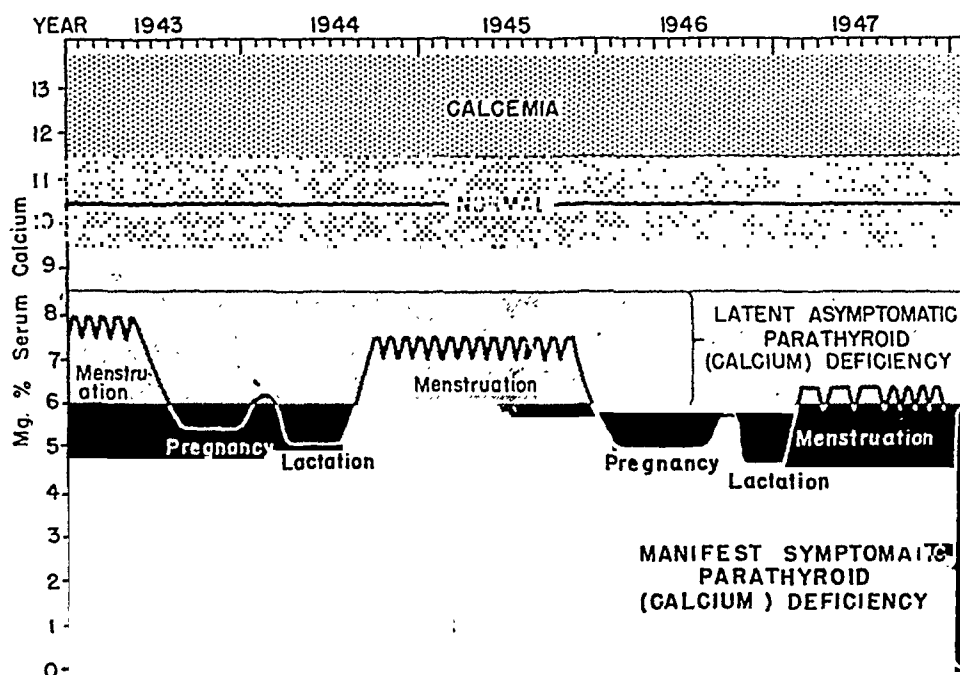
Fig. 1 (Lyle). A schematic arrangement charting the fluctuation of the serum calcium level in a patient with idiopathic parathyroid deficiency during pregnancy, lactation, and menstruation.

in a state of hypocalcemia. If the test shows a slight clouding, the serum calcium is probably present in normal amounts. If the Sulkowitch test reveals a hypocalcemia, 3 cc. of dihydrotachysterol should be given daily until there is a clouding, and then 1 cc. 3 to 5 times a week as a maintenance dosage. For further check, a blood calcium test should be made at monthly intervals.

The purpose of treatment is to elevate the blood serum calcium content and diminish the phosphorus. Prophylactic medication begun at the fifth month of pregnancy, terminated at labor and resumed at the end of the first month of lactation should be advised. One teaspoonful of calcium gluconate or cal-

pregnancy and more in lactation. It may also be needed after pregnancy, as it must be remembered that the blood serum thereafter is pegged at a lower level. In addition to the increased calcium, the phosphorus and phosphate intake should be restricted. Dihydrotachysterol and vitamin D should be given.

Dietary restrictions and needs should be considered. Dairy products, meats, legumes, potatoes and whole wheat cereals should be restricted or curtailed. One must remember that although milk contains an abundance of calcium, it also contains an abundance of phosphorus, which unites with the calcium to form an insoluble calcium phosphate which at least partially nullifies the benefit of the

calcium. Foods which may be approved are fruits, vegetables, fats, and carbohydrates.

If tetany appears, and with it the probability of cataract and optic-nerve involvement, active treatment is necessary to raise the blood calcium level immediately. In the acute state, inhalation of 5 to 10-percent carbon dioxide in air or oxygen will reduce the alkalinity of the blood and raise the calcium concentration. Ammonium chloride by mouth will have a similar effect. Sedatives to relieve the tetanic spasms of contraction may be necessary. Chloral hydrate, barbitals, or demerol may be of use for this purpose. Magnesium salts in various forms of administration may be employed to reduce the irritability and swelling. Calicum salts employed in a like manner may have an immediate effect of short duration. Ten to 20 cc. of 10-percent calcium gluconate may be administered intravenously and 25 to 30 gm. of calcium lactate may be given in warm water orally.

In the chronic state, the treatment, aside from dietary aids, is the administration of calcium in various forms, parathyroid hormone, vitamin D, and dihydrotachysterol.

SUMMARY

A case history of a patient having idiopathic parathyroid insufficiency was presented to introduce the subject (fig. 1). Her developing symptoms produced by cataract and tetany were described as she passed through pregnancy, lactation, and menstruation. A brief history of spontaneous or idiopathic hypoparathyroidism was presented. Possible causes of its production were mentioned. The sources, use and disposition of calcium to meet the body needs were described, and factors influencing its activity were enumerated. The changes produced by pregnancy, lactation, and menstruation were discussed, and the symptoms resulting from the additional presence of hypoparathyroid insufficiency were described and a differential diagnosis was outlined.

Treatment was recommended for prevention and for the latent and manifest stages of parathyroidism.

CONCLUSION

The increased demand for calcium during pregnancy, lactation, and menstruation may change an asymptomatic latent parathyroid deficiency into a symptomatic manifest hypoparathyroidism, with serious consequences to vision through ectodermal damage, both neural and somatic. These complications can be averted by routine examination during early pregnancy and lactation. Treatment, once the symptoms have appeared, may arrest but cannot entirely restore the visual loss.

601 Union Trust Building (2).

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ETIOLOGY OF TRACHOMA*

YUKIHIKO MITSUI,† M.D.
Kumamoto, Japan

This article is based on a series of investigations performed under the guidance of Prof. Shinobu Ishihara and Prof. Takeo Tamiya at Tokyo University. A total of 105 human inoculation experiments were performed, in cases hopelessly blind from other causes. The results have been published in a Japanese monograph.[21]

1. Adult inoculation with trachoma.[1-3] Material from cases of the late chronic stage of trachoma but with typical, confluent, turbid follicles was inoculated in 31 cases, with 26 positive results. The inoculum, obtained by scraping the follicles at the superior border of the tarsal conjunctiva with a knife, was rubbed into the conjunctival surface. The only aseptic precautions were an irrigation with sterile boric acid solution and the usual sterile procedures. In positive cases the incubation period was 3 to 9 days with an average of 5 to 6 days. The initial stage was always an acute conjunctivitis and, in all cases, follicles appeared within a few days. After several days, there was a full-blown acute follicular conjunctivitis. Acute inflammation reached its climax within a month, then began to subside, and within 1 to 3 months gradually went over to the chronic form. Prowazek-Halberstaedter inclusion bodies were found without exception.

In the majority of the cases, the signs of chronic follicular conjunctivitis were persistent. Examination even after 1 or 2 years revealed the typical signs. Perfect cure within several months was the exception. In 18 cases the disease went over to the second eye spontaneously. The symptoms and course were almost the same as those in the inoculated eye. Prowazek-Halberstaedter inclusion bodies were also found without

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* From the Kumamoto Medical College.
† Assistant professor of ophthalmology.

exception. Their numbers were in proportion to the severity of the clinical symptoms.

ETIOLOGIC NATURE OF PROWAZEK-HALBERSTAEDTER INCLUSION BODIES

A. DEMONSTRATING THE BODIES IN CHRONIC TRACHOMA

The first object was to establish a positive identification of the inclusion bodies, when present, in chronic cases, because it has been commonly believed that the Prowazek inclusion bodies cannot be readily demonstrated in the chronic stages of trachoma.

The following total of 823 cases were studied in order to clarify this point: (1) A preliminary study of 290 cases in the ophthalmology department of Tokyo University;[4] (2) A farmer's village, Naruse, Kanagawa Prefecture, 175 cases[6]; (3) A fisherman's village, Shinojima Island, Aichi Prefecture, 156 cases[7]; (4) A special series in the ophthalmology department of Tokyo University, 202 successive cases.[8]

Prowazek-Halberstaedter bodies were found in 537 (65 percent) of the 823 cases. These 823 cases consisted of both typical and suspected cases. Among 392 cases with typical clinical symptoms, 336 (85 percent) were positive for the inclusion bodies. The results are summarized in Table 1.

The percentage of positive findings, as well as the number of Prowazek-Halberstaedter bodies counted, paralleled the development of the follicles, that is, it followed the number, turbidity, and confluence of the follicles, and hence was more dependent on the presence of such follicles than it was on the early or late stages of infection.

This is in contrast with the conclusion, from unselected cases, that the finding of inclusion bodies decreases with increasing chronicity (table 1, column 1). If the advanced cases are selected according to typical

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follicle formation, and. the increasing pro-
portion of latent or doubtful cases are ex-
cluded, then there is only a small decrease of
percentage of cases positive for inclusion
bodies, as can be seen from the last three
columns of Table 1. Instead of 100-percent
findings of inclusion bodies, as occurred with
47 acute cases from the same districts, the
incidence of inclusion bodies in these
chronic cases with typical folliculitis was
of the order of 80 to 90 percent.

The question arises why even this small

the lesions by irrigation or other treatment.
The inclusion bodies were found in the
uppermost epithelial layers of those follicles
which had become turbid and confluent.
Scrapings were collected exclusively from
such regions, which occurred chiefly in the
conjunctiva of the upper fornix. Trans-
lucent, not confluent, follicles yielded few
inclusion bodies; papillas and cicatrix almost
none.

The conjunctival sac was anesthetized
by instillation, without irrigation, of 2-per-

TABLE 1

PERCENTAGE OF TYPICAL CASES OF TRACHOMA WITH PROWAZEK-HALBERSTAEDTER BODIES

Stage of Infection	Prowazek Bodies	Tokyo University, 1938		Prowazek Bodies Special Series		
		Percent Cases:		Naruse Village	Shinojima	Tokyo Univ. 1939
		Typical	Severe			
Acute	100	100	100	100	100	100
Chronic:						
Stage 1	59	73	25	81	76	82
Stage 2	54	60	4.4	87	83	87
Stage 3	37	50	0.8	74	100	96

Chronic Stage 1 is classified as an early stage without cicatrix.
Chronic Stage 2 is an advanced stage with superficial cicatrix but without complications due to cicatricial shrinkage.
Chronic Stage 3 is the late stage with thick, deep cicatrix and complications due to cicatricial shrinkage, such as trichiasis or entropion.
A typical case is a case with follicles which are turbid and confluent.
A severe case is a typical case in which the follicles are rich in number, markedly turbid and markedly confluent. It does not include the chronic cases wherein the appearance of severity is due to secondary changes dependent upon entropion, ectropion, blepharophimosis, or pannus formation.

decrease from 100 percent should occur. The
answer is simple. In the acute stage, the
follicular inflammation is not only typical
but also severe. Conversely, in chronic stages
the frequency of severe follicular inflamma-
tion decreases, as the conversion to milder
cases increases, even though the milder cases
may be still classified as typical (table 1,
column 2). It can be said that there is no
real trachoma without Prowazek-Halber-
staedter inclusion bodies.

The many reports asserting a marked les-
sening of positive findings in chronic stages
may be the result of technical differences
such as different procedures and classifi-
cations.

Technique. It was important not to disturb

cent cocaine. Turbid, confluent follicles were
scraped with a cover glass, taking care not to
rupture the follicles or cause hemorrhage.
The smear, spread as in the method of blood
smears, was then fixed with methyl alcohol
and stained. The most suitable staining was
obtained with 2 to 3 drops of Giemsa stain
(Grübler, prepared in carbon-dioxide free
distilled water; other brands were unsuit-
able) in 2 cc. of distilled water for 30 to 60
minutes at room temperature. More rapid
staining, adequate for diagnosis, can be ob-
tained by using 5 to 10 drops of stain in 2
cc. of the carbon-dioxide free distilled water.
The inclusion bodies are best located with a
magnification of 40 or 80 times, and then
studied under oil immersion.

B. Histologic investigation of inclusion bodies[5]

Tissue sections were positive for Prowazek-Halberstaedter bodies in 92 percent or 108 of 117 cases. The inclusion bodies were in the epithelial cells at the tops of the follicles. Inclusion bodies were never found in the subepithelial tissues; they were in epithelial cells only. It has been a question for some time, how they can occur only in this site if they are the infecting agent, and why they cannot be found in the follicles themselves, which are the site of the most significant changes in trachoma. Theoretically, it may be unnecessary to prove the existence of the virus in the follicle, since a toxic substance, elicited or elaborated by the virus, may cause the follicles.

Investigations were performed to determine whether the locus of the virus is identical with the histologic site of the inclusion bodies.

C. Absence of trachoma virus in subconjunctival tissues[9]

Ten cases of typical trachoma, trachoma with turbid and confluent follicles, in various stages, all Prowazek inclusion-body positive, were selected as donors. Subconjunctival tissue, usually from the tarsal tissue as indicated in Figure 1-a, was taken in order to avoid touching the conjunctival epithelium. The tissues were ground in Tyrode's solution so as to make an emulsion. Ten eyes of 6 patients were inoculated by dropping the emulsion into the conjunctivas and massaging. These recipients were blind from intraocular diseases, such as optic-nerve atrophy and absolute glaucoma, but were free of trachoma. The results were all negative.

Two control inoculations into 2 eyes were both positive; they reacted with a typical trachoma, and were positive for inclusion bodies. The inoculum for these controls was prepared in the same manner as above, except that the starting material was obtained as scrapings from the conjunctival epithelium

of the upper tarsus as in Figure 1-b from 2 of the same donors.

A second investigation was designed to determine if subconjunctival inoculation would result in trachoma.[10] The inoculum from conjunctival trachoma epithelium scrapings was prepared as before. It was in-
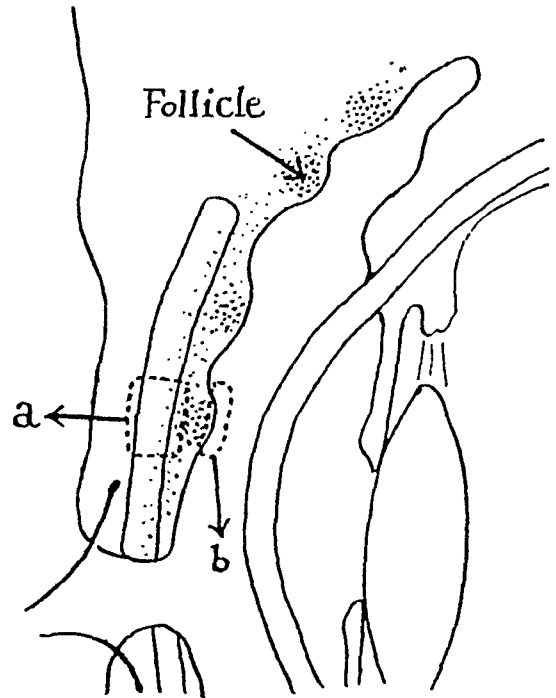
Fig. 1 (Mitsui). (a) Tarsal plate tissue of a typical trachomatous case was removed surgically from the cutaneous side, and inoculated with negative result. (b) Scrapings from the tarsal conjunctiva of the same case were inoculated with positive result.

jected, from the cutaneous side as in Figure 2-a, subconjunctivally into the region of the retrotarsal fold. Ten such inoculations were performed. They all remained negative for trachoma. A control instillation of the same inoculum into a conjunctival sac was positive, as in Figure 2-b. Absence of pathogenic bacterial contamination was demonstrated by culture and subsequent control inoculation of these cultures into human eyes.

From these results, it is concluded that (1) The trachoma virus exists only in the epithelial layer, not in the subconjunctival tissues; (2) the trachoma virus cannot cause trachoma when it is introduced into the subconjunctival tissues only, without touching the epithelium. It may be said that the tra-

choma virus and the Prowazek-Halber-staedter inclusion bodies are at the same locus, regardless of whether or not the inclusion bodies are the actual infectious agent.

D. PROVOCATIVE TESTS[11]

In the above investigations, it was easier to demonstrate the inclusion bodies in the
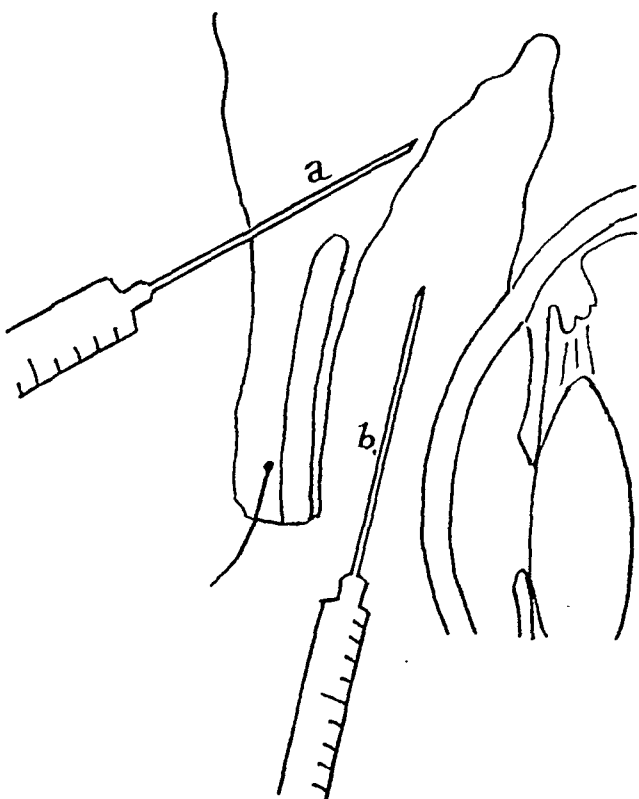
Fig. 2. (Mitsui) (a) Suspension of scrapings from typical trachoma cases was injected sub-conjunctivally from the cutaneous side. It could not start trachoma. (b) The same inoculum was dropped into the conjunctival sac. The trachoma started.

cases with the more severe folliculitis. Similarly the ease of demonstrating inclusion bodies lessens with the decrease of number, turbidity, and confluence of the follicles, during and after treatment.

To investigate the converse, whether the ease of demonstrating inclusion bodies increases, in the individual case, with exacerbation of the typical folliculitis, a method for provocation of the disease was utilized. The conjunctivas were scraped with the edge of a knife or rubbed with cotton. Then, without

irrigation, a bandage was placed over the eye. In 8 of 15 cases, the severity of the folliculitis was reached within 5 to 10 days and, at the same time, the number of inclusion bodies increased.

The inclusion bodies, on the whole, were smaller in the acute stages of the exacerbations, which also occurs in the acute stages of the spontaneous infection. But, when the typical follicular lesion in the provocative test increased gradually, the frequency of the larger cells, containing elementary bodies, increased also, just as in slowly progressing spontaneous trachoma.

E. PURE CULTURE OF PROWAZEK-HALBER-STAEDTER BODIES

The conjunctival sac was first thoroughly irrigated with sterile saline solution. A strip of conjunctival tissue with marked follicle formation was removed surgically and cut into 1 by 1 mm.-sized pieces in Tyrode's solution.

The sterile culture medium was made up of two stock portions: (a) Human blood plasma, 1 part, chicken blood plasma, 2 parts; and Tyrode's solution 10 to 30 parts. (b) Juice of chicken embryo. At the time of culturing, the stocks a and b were mixed in the ratio of 2:3 or of 3:5.

The epithelium grew by cell division. Inclusion bodies were found also in what appeared to be new cells.

In second generation subculturing, the above tissue cultures were ground to a suspension and diluted 10 times in Tyrode's solution. Tissue from normal conjunctivas was carried through this suspension and then cultured as above.

Smears of the cultures, at 2 to 5 days, were stained and examined. By comparison with the original tissue, the number of cells with inclusion bodies increased, as did also their size, with elementary bodies filling almost the entire cytoplasm. Of 2 cases with too few inclusion bodies to demonstrate initially, inclusion bodies could be demonstrated from the culture in 1 case. Cultivated

tissue introduced into the human eye in 4 cases, resulted in trachoma each time. Such inoculations from subcultures, however, were not successful. Hence, although these cultures suggest that the infectious agent has been cultured, they do not prove this conclusively.

RELATIONSHIP BETWEEN TRACHOMA AND INCLUSION BLENNORRHEA

Inclusion blennorrhea of the newborn was studied in 18 cases.[14, 15] This provided a basis for comparison.

Inoculations of suspensions from tracho-

The converse inoculation, from the conjunctivas of newborn children with inclusion blennorrhea into adult conjunctivas, was performed in 10 eyes[16] of 10 adults. The resulting disease in the adult was identical with inoculated trachoma of the adult,[1-3] but not with inclusion blennorrhea of the newborn.

To exclude possible individual variation, the 2 inoculations (trachoma inoculum and blennorrhea inoculum) into the 2 eyes of the same individual were performed in 7 cases. No essential difference between the two eyes was observed;[17] all exhibited the trachoma-
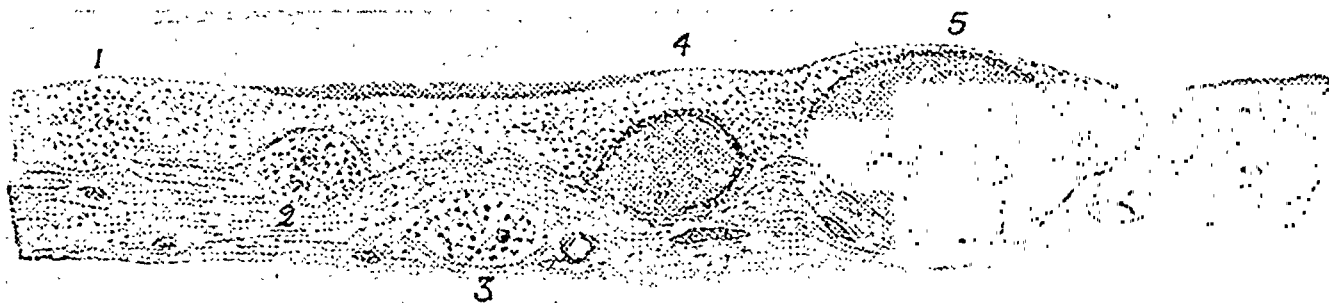
Fig. 3 (Mitsui). Trachoma follicles of the inclusion blennorrhea type.

matous scrapings were instilled into the conjunctival sacs of four eyes of four newborn children, blind from congenital anomalies such as microphthalmos and corneal degeneration but not having trachoma, at 5 to 29 days after birth. The response, a blennorrhea or pseudomembranous conjunctivitis, was followed clinically.

Follicles were not found until the babies became several months old, but these follicles were somewhat different from those of adults, just as those of spontaneous inclusion blennorrhea are different. They formed deep in the areolar connective tissue layer, as indicated in Figure 3, instead of the adenoid tissue, as in the adult trachoma (fig. 4). They had a "naked" appearance, that is, with little or no wall of lymphocytes (fig. 4).

Trachoma in the newborn is, therefore, quite different than that of the adult, but identical with the inclusion blennorrhea of the newborn, both clinically and microscopically.

tous type of infection.

Tissue sections of the cervical canals, but not of the vaginas, of mothers of babies with inclusion blennorrhea, had microscopic changes similar to those of conjunctival trachoma.[18] Prowazek-Halberstaedter inclusion bodies in the cervical scrapings were found in one case. Instillation of inoculums prepared from cervical canal scrapings, pre-
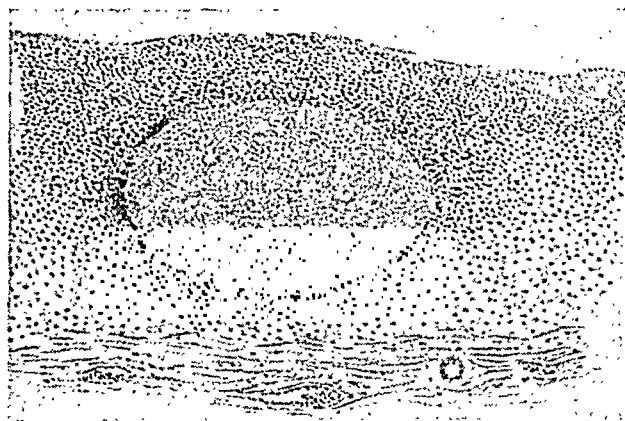
Fig. 4 (Mitsui). Trachoma follicles of the adenoid or adult type.

pared from 6 cases, into 6 adult eyes of 6 people resulted in typical trachoma.

The converse experiment,[19] inoculation of the female genital tract with trachomatous materials, produced the typical infection of the cervical canal as manifested by microscopic changes. In the cases of the 2 women so inoculated, continued presence of the infectious agent was demonstrated 14 days later, by a further inoculation into other adult eyes. Gynecologic examination 7 months after inoculation in 1 of the women demonstrated that there were clinical and microscopic findings of genital trachoma, including follicle formation, cellular infiltration, and numerous inclusion bodies, in tissue sections of cervical-canal epithelium.

No doubt can remain that trachoma and inclusion blennorrhea are results of the same infection. Inclusion blennorrhea is infant trachoma. Furthermore, trachoma is not exclusively an eye disease, but can alternate between the eye and the female genital tract. It may be assumed that the disease of the female genital tract is the usual source of infection during delivery, resulting in inclusion blennorrhea of the newborn.

TRACHOMA IN THE LACRIMAL APPARATUS[12]

It is well known that trachoma follicles are most readily found in the tarsal conjunctiva, or in the conjunctiva of the retrotarsal fold. These are loci of cylindrical epithelium, the epithelium of the fold being the more typically cylindrical. The cuboidally flattened epithelium of the bulbar conjunctiva or the squamous epithelium of the cornea are hardly affected by trachoma, except secondarily. Likewise, the genital tract trachoma showed that the cylindrical epithelium of the cervical canal could be easily infected, but the stratified squamous epithelium of the vagina could not.

The cylindrical epithelium of the lacrimal sac was also found to be affected by trachoma.

A suspension of trachoma material was injected with a lacrimal syringe into 6 lacrimal sacs through the inferior punctum. The sacs were removed 10 to 51 days after inoculation and were examined histologically. The changes were identical to those of trachoma of the conjunctiva. Inclusion bodies were demonstrated in 5 cases.

The lacrimal sacs were removed from 6 cases of early conjunctival trachoma; 1 of these had been experimentally inoculated, 1 was in the acute stage, and 4 were in an early chronic stage of infection. Histologic changes in the sacs were almost identical to those of the conjunctiva. Inclusion bodies were found in 5 of them. In 2 cases, the canaliculi were examined. Inflammatory changes consisting of round-cell infiltrations and follicle formations were slight, as compared with those of the sacs, yet inclusion bodies were present in the epithelium of each.

The lacrimal sac was examined in 1 case of conjunctival trachoma induced by inoculation from a case of inclusion blennorrhea. Changes were like those of spontaneous trachoma and many inclusion bodies were present.

Lacrimal sacs were also studied in 13 cases of chronic conjunctival trachoma. Follicle formation and cellular infiltration were slight as compared with the conjunctivas of the same cases; cicatricial changes were marked. In some cases, the resulting constriction had reduced the lumen of the sac greatly. Inclusion bodies were found in one case.

In nonspecific, chronic dacryocystitis, unaccompanied by trachoma, the inflammation was not specific and no inclusion bodies were found.

CLINICAL COURSE OF TRACHOMA

A. INITIAL ACUTE STAGE

Formerly, it was believed that trachoma starts insidiously, and so-called acute trachoma was thought to be only an exception. It was known that an inoculated trachoma started acutely, but this was considered to

be a special response to inoculation, such as might result from an infection with enormous numbers of virus at one time. For reasons to be summarized, it is concluded that without exception trachoma starts acutely and that the incubation period is 3 to 9 days, usually 5 to 6 days.

Inoculation trachoma, in 68 cases,[1, 9, 10, 13, 15-19] started acutely without exception. The incubation period was slightly shorter with larger doses of inoculum, and the folliculitis somewhat less acute.[17] Not only was the onset of the inoculated trachoma acute, but so also was that which went over spontaneously to the second eye, 21 cases.[1, 15, 16, 18] In none of these cases, whether by inoculatio nor by spontaneous spread to the second eye, did the trachoma start insidiously.

Acute trachoma is not a rare occurrence. In 6 months, 44 cases were seen in Tokyo University.[8] Meanwhile, 202 cases of chronic stages were observed. Of the 44 acute cases, the great majority had received prior treatment from their local ophthalmologists for what was evidently considered to be a simple follicular conjunctivitis rather than an acute trachoma.

Thirty-three patients,[8] with trachoma in the early chronic stage, gave a history of an acute conjunctivitis originating 1 or 2 years previously, starting in one eye and being followed 7 to 14 days later by a similar onset in the second eye. This long delay is consistent with the incubation period of trachoma, as contrasted with the rapid onset of a bacterial conjunctivitis, signs of which were lacking. The subjective symptoms had subsided slowly. Their local ophthalmologists had told them that they had an acute conjunctivitis; those who had been told that they had an acute trachoma were the exception.

Another reason for the persistent belief that an acute trachoma is the exceptional form of trachoma arises from the apparently benign nature of the disease. The cicatrix and pannus do not occur until several years later.

Still another reason that trachoma has

been easily overlooked in its acute stage, is evident from the statistical investigations in Naruse[6] and Shinojima,[7] where the initial affection of trachoma occurs in childhood, usually before 3 or 4 years of age. It is evident that, through the lack of an active complaint from the patients, any acute conjunctivitis in childhood may be considered and treated lightly. Hence the tendency to overlook trachoma of the acute stage. In regions of high trachomatous incidence, it may be presumed that acute trachoma should be a childhood disease.

This is supported by the relation of the percentage incidence of all stages of trachoma with respect to age, in the villages of Naruse and Shinojima. The incidence approached was 17 percent and 75 percent respectively. These levels were already approached at the school age and remained practically constant thereafter, although the trachoma progressed to more advanced stages of the disease in the advanced age groups.

B. INTERVAL FOR CHRONIC TRACHOMA

Analysis of cases of trachoma in Naruse and Shinojima indicated the following: Chronic trachoma occurring in young people is of the first-stage type, without cicatrix, in the majority of cases; in middle aged people, it is usually of the second-stage type, superficial cicatrix without complications; and the third stage, cicatricial retraction and complications, is almost exclusively observed among people over 40 or 50 years of age. This indicates that trachoma may persist for a long time, perhaps 10 or 20 years or more, after the acute stage and before formation of cicatrix; perhaps 40 to 50 years before cicatricial retraction and complications.

C. HEALING OF ACUTE TRACHOMA

It is known that numerous cases of early trachoma can be cured without leaving any trace. The earlier the improvement the more likely the cure. It is, therefore, a most important problem from the standpoint of pub-

lic health that trachoma be detected in the early stage. For this, examination for inclusion bodies is indispensable.

The procedure utilized and discussed herein for recognition of suspected, suspicious, typical, and atypical cases should become familiar to all ophthalmologists in routine examination of ocular infections.

Kumamoto Medical College.

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THE DUPUY-DUTEMPS DACRYOCYSTORHINOSTOMY*

ALTON V. HALLUM, M.D.
Atlanta, Georgia

Dacryocystorhinostomy has proved to be so highly successful in the hands of many surgeons that extirpation of an obstructed lacrimal sac has come to be supplanted by it, just as couching long ago was supplanted by cataract extraction. Another surgical analogy of extirpation versus dacryocystorhinostomy might be made of the orthopedic surgeon who would elect to amputate a patient's broken leg, rather than go to the trouble and time to help restore the function of the leg. The extirpation of obstructed lacrimal sacs is usually successful in relieving the pus and mucus, but the majority of the patients are doomed to a life of lacrimation and its annoying impairment of vision. A correctly performed dacryocystorhinostomy in selected cases can be expected to relieve completely pus, mucus, and tearing in at least 95 percent of the cases.

HISTORICAL REVIEW

The reader is referred to Chandler's[1] discussion on this subject in which he reports an exhaustive survey of the literature. According to Chandler, history shows that operations were performed by Celsus, to make a new passageway from the tear sac into the nose as long ago as the first century and by Galen in the second century. In modern times, in the early 18th century, Woolhouse and Platner performed operations to reestablish drainage of the lacrimal sac into the nose. The procedure was apparently forgotten or abandoned for approximately two centuries.

In 1904, Speciale-Cirincione[2] and Toti,[3] in Italy, revived the operation, each with a different technique. Speciale-Cirincione's

transplantation operation consisted of lifting the sac from its bed and pushing the lower end of the sac into the nose through a new bony opening. The transplantation operation is applicable only to those cases where the obstruction is limited to the lower end of the lacrimal sac and nasolacrimal duct.

Forsmark,[4] Stokes,[5] Gifford,[6] and others have reported highly successful series of operations using the transplantation method. Toti advocated removing the nasal wall of the lacrimal sac and a corresponding area of the underlying lacrimal and maxillary bone and muscosa, thereby reestablishing drainage from the lacrimal sac into the nasal cavity.

Many variations in the technique of Toti have been made by different surgeons. In 1912, Blascovicz[7] made the first significant change by cutting away all of the sac wall except a small portion immediately surrounding the opening of the canaliculi. In 1914, Kuhnt[8] was probably the first to approximate the mucous membranes by sutures. Ohm,[9] in 1920, advised making vertical incisions in the nasal mucosa and lacrimal sac wall and then suturing the respective posterior flaps and anterior flaps.

In 1921 Mosher[10] described a modification of Toti's technique. He advocated (1) exenterating the ethmoid cells in the vicinity of the lacrimal sac, (2) resecting the nasal mucosa from the bony window, (3) resecting the inner wall of the sac and duct down to the upper rim of the inferior turbinate, and (4) removing the anterior tip of the middle turbinate.

In an address in 1937, as guest of honor of the American Academy of Ophthalmology and Otolaryngology, Mosher[11] stated the operation should be successful in 90 percent of the cases if properly performed. He also said that in his opinion a high deviation of

the nasal septum should be previously straightened, to prevent blocking of the new opening. The technique as outlined by Mosher requires that the surgeon be an experienced rhinologist.

Also in 1920-1922, Dupuy-Dutemps and Bourguet[12] described a modification of Toti's technique, similar to Ohm's, which was much simpler than Mosher's, and required no intranasal surgery. They reported more than 1,000 operations in which 94 percent had been successful. During recent years, Chandler,[1] Rychener,[13] Yanes,[14] Hughes, Guy, and Bogart,[15] Hallum,[16] and others have reported series of operations using the technique popularly known as that of Dupuy-Dutemps. Each of the surgeons has reported successful results in nearly all of the cases, Chandler and Rychener in 100 percent of the cases. Chandler prefers to make T incisions instead of I incisions in the sac wall and nasal mucosa.

Traquair[17] reported 409 operations by the technique of Toti and a follow-up on 321 of the patients found that 80 percent of them had been relieved of watering. He altered the technique of Toti by suturing a flap of nasal mucosa to the anterior margin of the lateral sac wall after he had removed the inner wall of the sac. Thus his technique was very similar to that of Ohm and Dupuy-Dutemps.

Hogan[18] recently reported a series of 49 Toti-Mosher operations done at the University of California over a 20-year period, including the cases formerly reported by Martin and Cordes[19] and Martin.[20] These surgeons feel that the operation as done by them should be successful in 85 to 90 percent of the cases.

The postoperative care necessary to prevent granulation tissue from blocking the new passageway is a great task for the surgeon, and is one of the greatest shortcomings of this procedure. They perform postoperative irrigation of the lower punctum daily for the first week, then twice weekly for a month, and thereafter at monthly intervals.

ETIOLOGY OF OBSTRUCTION OF THE NASOLACRIMAL PASSAGEWAY

When this subject is discussed by rhinologists[21] some of them say that as high as 95 percent is of nasal origin. But when discussed from the standpoint of the ophthalmologist, it appears that the nose plays a relatively insignificant role in producing infection in the lacrimal sac. In Traquair's 409 cases he found only one with any obvious intranasal pathology. This patient had a few small polypi in the middle meatus, which were removed during the operation.

Most patients are unable to associate the onset of the epiphora and pus with any acute nose or lid infection. Trauma was the predisposing factor in 4 or 5 percent of most series, but in my series it was the cause in 17 percent. The most constant factor in most series is that the great majority of patients are women. The percentage of women was 80 in Traquair's series, 66 in Gifford's series, and 58 in my series. As Traquair points out, sex predilection alone rules out the possibility that the disease originates in the nose, since there is no nasal disease which is five times more common in females. According to Garfin,[21] Meller and Schaeffer believe that the anatomic difference of the nasal bones causes the lumen of the lacrimal canal to be narrower in women than in men. Traquair has noticed an hereditary factor in 11 percent of the latter part of his series.

It is of unusual interest here that congenital occlusion of the lacrimal ducts occurs about equally in the two sexes. It is also well known that congenital occlusion of the lower end of the canal is cured in the great majority of cases during the first year of life by massage only, and if this conservative treatment fails, one probing at the age of 6 to 12 months almost always gives complete relief without a tendency to become occluded again.

BACTERIOLOGIC PICTURE

Traquair did a bacteriologic examination of the conjunctival sac in 251 cases of oc-

clusion of the lacrimal sac of duct in which Toti's operation was subsequently performed, and repeated the examination in 95 of the cases after the operation. He did not state how long after the operation the second examination was made, nor whether he made more than one postoperative examination. Two hundred and twenty-five eyes examined before cataract extraction were used as controls. No growth was found in 12 percent of the cases of lacrimal obstruction, nor in 16 percent of the controls. Pneumococci or streptococci were found in 32 percent of the cases of lacrimal obstruction, and in 6 percent of the controls. Staphylococci were found in approximately the same percentage of cases in each group. The effect of dacryocystorhinostomy was to reduce the streptococci from 32 to 11 percent; whereas, the control group showed 6 percent. Several cases of cataract extraction were performed by Traquair after the Toti operation, and Arruga[22] reported more than 30 cataract extractions after the Dupuy-Dutemps dacryocystorhinostomy, without any infectious complication. According to Garfin,[21] Rollet and Bussey's series of obstruction of the lacrimal sac showed pneumococci in 60 percent, streptococci in 10 percent and no bacteria in 26 percent. They found mucoceles to be almost sterile.

INDICATIONS FOR DACRYOCYSTORHINOSTOMY

The operation is indicated in stricture of the nasolacrimal duct or any portion of the lacrimal sac, or in cases of absence of the lacrimal sac, provided the lower punctum and lower canaliculus are normal.

Dilation of the lacrimal obstruction should be attempted in every patient, regardless of how long-standing the condition. One patient suffering from an acquired unilateral obstruction of 20 years' duration was completely relieved of tearing and mucopurulent discharge by a single probing. The passage of a probe should be attempted in order to learn the level of the stricture. However, if

passing a No. 2 or 3 Bowman probe all the way into the nose does not relieve the obstruction after 2 or 3 weekly probings, it is useless to continue. In fact, repeated probings that progressively dilate the lower punctum are contraindicated, since they will cause tearing after a subsequent dacryocystorhinostomy. The lower canaliculus should never be slit, for the same reason. If an external fistula is present, it is disregarded in performing the operation, and it will close spontaneously, within a few days after reestablishing lacrimal drainage into the nose.

CONTRAINDICATIONS FOR DACRYOCYSTORHINOSTOMY

If either the lower punctum or lower canaliculus is not normal, watering will continue after the operation but the patient will be relieved of mucopurulent discharge. A normal upper punctum and upper canaliculus will usually not keep an eye free of tearing if the lower punctum and lower canaliculus are not functioning. The operation should not be done in tuberculous or malignant involvement of the sac, and should be postponed for at least a month after any acute inflammation of the sac or nose has subsided. Any obstruction in the nose should be remedied, and the patient allowed to recover from the procedure, before dacryocystorhinostomy. There is almost no age limit for the operation, if the patient is otherwise in good health. The youngest of my series was aged 4 years and the oldest, 73, and other surgeons have reported successfully performing the operation on even younger and older patients. The younger the patient the softer is the bone, and it is proportionately easier to make the bone window. The dimensions of the anatomic parts involved in the young are surprisingly close to the dimensions found in the adult.

Stallard[23] in 1940 reported on original operation that was successful in relieving epiphora in a patient who had both canaliculi cut in an accident. The upper end of the

sac was dissected from its bed, and transplanted through a stab wound into the lower cul-de-sac. After the upper end of the sac was sutured to the conjunctiva, anteriorly and posteriorly in the depth of the lower cul-de-sac, the dome of the sac was excised. This procedure might be found more effective than trying to reconstruct canaliculi and puncta.

TECHNIQUE OF THE OPERATION

ANESTHESIA

The usual preoperative sedatives should be given. The operation can be done under local or general anesthesia, depending entirely on the excitability of the patient. If general anesthesia is thought advisable, sodium pentothal intravenously has been found to be the most satisfactory, since it reduces to a minimum the necessity of the anesthetist working near the operative field. If ether anesthesia is preferred, after induction with gas or the ether cone, it should be vaporized by the ether machine through the side-lip mouth airway into the nasopharynx, thus eliminating the necessity of the ether cone.

If local anesthesia is desired, a long pledget of cotton saturated with one-percent pontocaine or nupercaine, or 4- to 10-percent cocaine, is placed high in the nasal fossa on the side to be operated. The face and operative area is cleansed in the manner that is usual for any ocular operation. It is best not to instill topical anesthesia into the eye, since the patient's normal blink reflex is desired to make him protect his cornea by keeping his lids shut.

Two-percent procaine hydrochloride, containing five drops of 1:1,000 epinephrine hydrochloride to the ounce, is injected into three areas, using a long, fine (27 gauge) needle. A small amount, about 0.5 cm., is injected along the site of the incision just beneath the skin; 2 cc. is injected just below the supraorbital notch, extending downward along the periosteum, infiltrating the region of the dome of the sac. This anesthetizes the supraorbital nerves supplying the upper

end of the sac. Another 2 cc. is injected in and over the infraorbital foramen, the last portion of which is directed upward and inward to infiltrate the region of the lower end of the sac. This anesthetizes the infraorbital nerve supplying the lower end of the sac. The surgeon stands at the side of the patient and the assistant stands at the top of the patient's head.

THE SKIN INCISION

The incision is made straight, as suggested by Mosher and reëmphasized by Hogan, because scar-tissue contraction accentuates the scar if the incision is curved. The incision is begun about 8 mm. nasally and level with, or 1 mm. below, the inner canthus (fig.1). If slight traction with the thumb is made on the soft tissue on the bridge of the nose to the side opposite the operation as the incision is being made, the angular vein and artery will not be cut as often. The initial incision is extended down through the periosteum in its entire length of about 2 cm. The incision extends downward and slightly outward, and should be made with one continuous stroke in order to obtain a straight skin incision. If a large vessel is cut, time will be saved if it is tied with catgut.

The Stevenson lacrimal sac retractor is inserted into the incision and spread tightly. This exposes the depth of the incision, and the pressure helps to control the bleeding. The internal palpebral ligament is not cut, unless the preoperative probing has shown the stricture to be high in the sac, that is, on the level with or just below the inner end of the lower canaliculus. The assistant's main duty is to keep the operative field free of blood by using the suction tip constantly. It is unnecessary to stop the oozing type of bleeding until the bony window has been completed. The best source of illumination is the large overhead portable spotlight with the light passing just above the surgeon's head.

A periosteal, or nasal mucous membrane, elevator is used to push the periosteum nasally and laterally. The first and only

real landmark is the anterior lacrimal crest which is uncovered as the periosteum is pushed laterally. The entire length of the crest is uncovered from the internal palpebral ligament above, downward to and including the lower extremity, where the crest turns laterally to form the anterior rim of the upper end of the nasolacrimal canal. The

The gouge is gently driven with the mallet so that a thin slice of bone is removed along the entire length of the anterior lacrimal crest up to the internal palpebral ligament. If the head block that is used in mastoid surgery has been previously placed under the patient's head, there will be less jarring produced by the mallet. Successive slices of
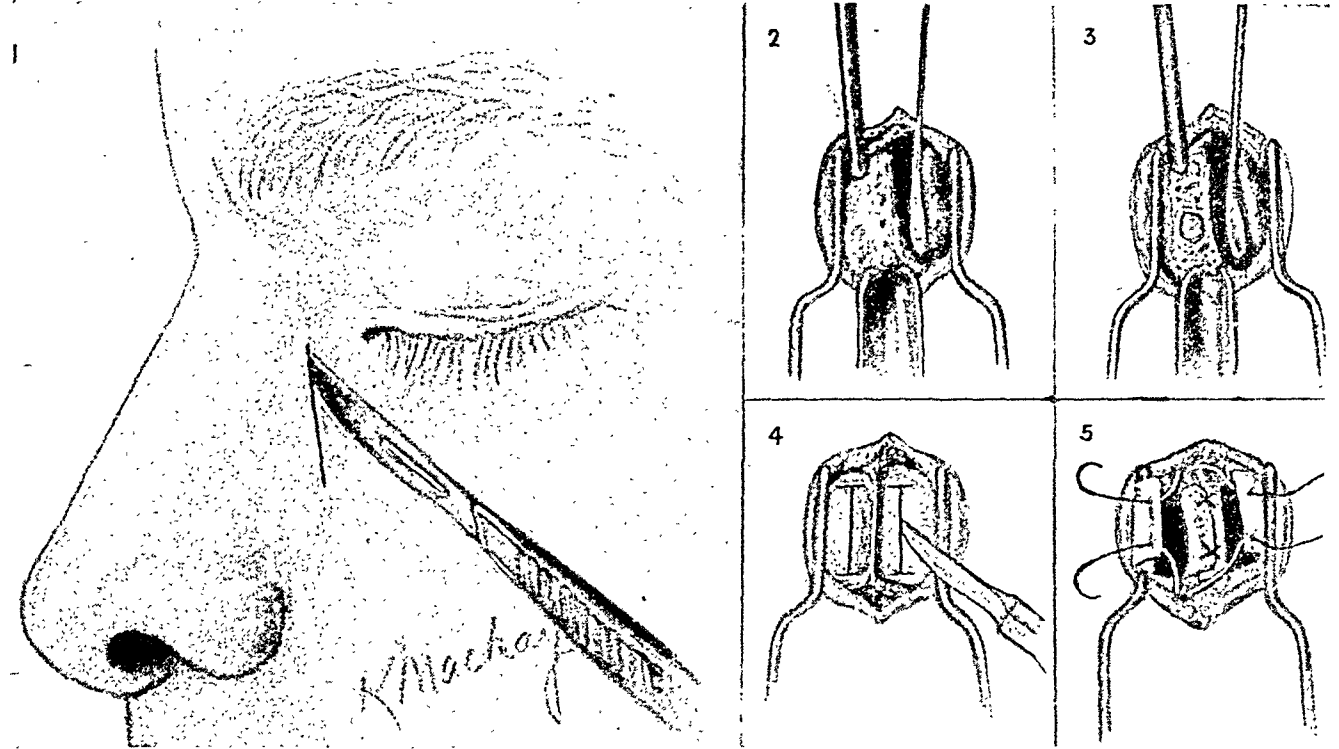
Figs. 1 to 5 (Hallum). (Fig. 1) The incision. (Fig. 2) Beginning the bony window, with the gouge astride the lower end of the anterior lacrimal crest. The assistant stands at the top of the patient's head, keeps the sac pushed laterally and uses the suction tip constantly. (Fig. 3) Several long, thin slices of bone have been removed and a small area of nasal mucous membrane has been exposed. (Fig. 4) Anterior and posterior flaps are made by making capital I incisions in the medial wall of the lacrimal sac and in the nasal membrane. (Fig. 5) The posterior flaps have been united. The sutures have been placed in the anterior flaps, and each suture includes some tissue on the anterior rim of the bony window, so that when the sutures are tied the flaps will be united and lifted out of the new passageway.

sac is easily separated from the floor of the fossa and pushed laterally to expose the posterior lacrimal crest.

PERFORATION OF THE BONE

For this procedure a mallet and bone gouge about 1 cm. wide (No. 8 or 10) is preferred. The gouge is set astride the lower end of the lacrimal crest where it turns laterally to form the anterior rim of the nasolacrimal canal (fig. 2). The assistant keeps the sac pushed laterally, using a nasal mucous membrane elevator as a retractor.

bone are removed in the same manner until in the bottom of the grove a small area of nasal mucosa is uncovered (fig. 3). This small bony opening is enlarged with a small bone curette, until the opening in the bone is large enough to admit the Kerrison forceps. Care must be taken not to perforate the nasal mucosa.

The opening in the bone is enlarged with the Kerrison forceps and sharp-pointed ronguer forceps. The window should be made low enough so that it extends down to the level of the upper end of the nasolacrimal

Fig. 6 (Hallum). The correct location of the bony window is outlined on the skull, astride the anterior lacrimal crest. The lower margin of the opening extends down to the upper end of the nasolacrimal canal.

vens' scissors are often useful in completing the upper and lower ends of the incision. A probe should be passed through the lower canaliculus into the sac and out through the incision in the sac wall to insure the fact that all layers of the sac wall are incised and that there are no other obstructions. The upper and lower ends of the incision are extended anteriorly and posteriorly from 1 to 3 mm., changing the vertical incision to the shape of a capital I, and forming a posterior and anterior flap.

Before making a similar incision in the nasal mucosa, all bleeding should be stopped. The retractor should be removed, the wound packed with cotton saturated with adrenalin, and pressure applied for 2 or 3 minutes.

After replacing the retractor, the site of the vertical incision in the nasal mucosa is then determined by grasping the posterior flap of the sac with forceps and drawing it medially toward the nasal mucosa. At the place where the flap touches the nasal mucosa, an incision is made parallel to the incision in the sac, extending to the upper and lower rims of the bony opening. The upper and lower ends of the incision are extended anteriorly and posteriorly, as was done to the incision in the sac, forming anterior and posterior flaps of nasal mucosa. It is unnecessary to make posterior flaps when the sac lies in contact with the nasal mucosa after the bone has been removed; indeed, in such cases it is occasionally unnecessary to make anterior flaps.

If the anterior end of the middle turbinate should be found to be more or less completely blocking the opening in the nasal mucosa, the visible portion of the turbinate should be excised through the incision with scissors or biting forceps. The small amount of bleeding that might follow can be controlled easily

canal (fig. 4). The bone forming the floor of the lacrimal fossa and enough of the bone medial to the anterior lacrimal crest is removed to make the horizontal diameter of the opening at least 10 mm. The opening is extended upward so that the vertical diameter is at least 12 mm. The opening in the bone must be made as low and as far forward as possible in order to avoid the ethmoid cells, and to place the opening anterior to the tip of the middle turbinate (fig. 5).

THE MUCOSAL INCISION

The nasal wall of the lacrimal sac is incised vertically from a point opposite the upper margin of the bony window to a point opposite the lower margin of the bony window (fig. 6). A No. 15 Bard-Parker knife blade serves best for this incision, but Ste-

by pressure applied to gauze inserted through the nares. The presence of polypi found in the same site should be treated in the same manner.

SUTURE OF THE MUCOUS MEMBRANES

The depth of the operative wound at this stage is usually as great as the length of the vertical skin incision and it is necessary to use extremely short needles in placing the sutures to unite the respective flaps, especially the posterior flaps. Probably the best needle available for this purpose is supplied by Davis & Geck, Inc., New York, and can be ordered by asking for Product C 269. Each of the ampules contains a 3-0 chromic catgut suture armed at each end with a one-half circle one-fourth inch atraumatic needle; each such double-armed suture is enough for one dacryocystorhinostomy.

The posterior flaps are first united by placing a suture at the upper and lower ends of the flaps; occasionally, only one suture is necessary (fig. 7). The anterior flaps are united in a similar manner by placing a suture at the upper and lower ends, except that each suture includes an additional bite of tissue close to the periosteum on the rim of the bony window superiorly and inferiorly, respectively. When these sutures are tied, after loosening or removing the retractor, they not only approximate the margins of the anterior flaps but lift them forward out of the bony window. Thus a new, open, epithelial-lined passageway extends from the lacrimal sac into the nose. The new passageway stays open because the epithelial lining prevents the formation of granulation tissue and adhesions.

CLOSURE OF THE SKIN AND DRESSING

Two or three subcutaneous sutures should be taken with the plain catgut, so that the skin can be approximated without traction on the skin sutures. The skin inci-

Fig. 7 (Hallum). The bony window, when correctly placed, opens into the nose just anterior to the tip of the middle turbinate.

sion can be closed equally well with interrupted or running silk, or with a subcuticular suture. Occasionally no skin suture is necessary. Five-percent sulfathiazole ophthalmic ointment is instilled inside the lids and along the skin incision. A thin layer of petrolatum is spread on the undersurface of the gauze eye patch which is applied over the closed lids. Additional gauze fluffs are added and moderate pressure is applied by placing several strips of one-inch wide adhesive diagonally from the forehead to the cheek.

POSTOPERATIVE CARE

At the completion of the operation the patient should lie face down for a few hours so that any bleeding into the nose will not be swallowed. It has not been necessary in a single instance to pack the nose to control postoperative hemorrhage. Usually only a few drops of blood trickle out the nose during the immediate postoperative period.

Bathroom privileges and regular diet are allowed 12 hours later, and the patient may leave the hospital at the end of 48 hours, after the dressing and skin sutures have been removed and a regular gauze eye patch applied.
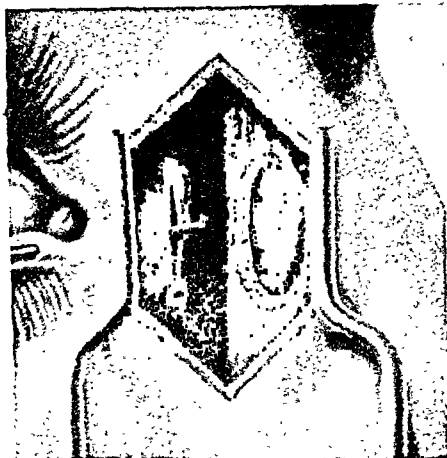
Fig. 8 (Hallum). (Arruga[22]). Canaliculirhinostomy. A vertical incision is made over the prominence of the end of the probe as it is held in the lower canaliculus. The margins of this incision serve as anterior and posterior flaps.

Physiologic solution of sodium chloride may or may not be irrigated through the lower canaliculus into the nose, using a syringe and needle, but apparently this is unnecessary. However, it makes both the patient and the surgeon happier to know that the new passageway into the nose is open. If fluid fails to pass from the lower canaliculus into the nose, the nose on the side of operation should be examined for obstruction produced by edema in the region of the bony window.

Edema of the nasal mucosa usually can be relieved easily by instilling some vasoconstrictor, either by drops or on a cotton pledget. Then if the fluid fails to pass from the lower canaliculus into the nose, a probe must be passed into the nose through the lower canaliculus and bony window, to break adhesions by gentle movements of the probe.

The patient is dismissed at this dressing if the skin incision is united and free from infection, and he is asked to remove the eye patch 48 hours later. He is warned against opening the incision by pulling on the skin in the region of the operation for a few days.

RECURRENCE

The patient is advised to return at the end of a week if epiphora persists, or at any subsequent time if epiphora returns, at which time the nasal mucosa must be shrunk with a vasoconstrictor and a probe passed to break adhesions. No cases of late obstruction of the new opening have been encountered, that is, several weeks or months later, but if such a complication should occur the procedure as described by Arruga[22] should be tried. He dilates the lower canaliculus until it admits a Weber knife, with which the membrane covering the bony window is incised across its complete diameter.

OPERATION IN CASES OF ABSENCE OF THE LACRIMAL SAC

When the lacrimal sac has been previously removed, or is completely occluded, reestablishment of lacrimal drainage into the nose can be obtained by slight variations of the above technique, if the lower punctum is normal and if the lower canaliculus is in good condition along its entire length. Arruga[22] first described this latter procedure and thinks that such an operation should be successful in two thirds to three fourths of the cases. Gifford reports two successful results in three cases, and Hogan one cure in three cases. Two of my series have been successful.

After the customary incision and exposure, the opening in the bone is made slightly larger so that longer flaps of nasal mucosa can be obtained. The medial end of the inferior canaliculus is identified by introducing a probe and maintaining pressure. A vertical incision is made in the tissue covering the prominence of the end of the probe, until the probe passes freely through the incision (fig. 8). The incision is deepened and lengthened until the anterior and posterior lips of the wound actually serve as fair anterior and posterior flaps. The remainder of the operation is the same as in the classic dacryocystorhinostomy.

In my two cases the only variation from Arruga's technique was threading a small silk suture through the lower canaliculus into the nose between the posterior and anterior flaps. This suture was placed after uniting the posterior flaps, but before uniting the anterior flaps. The end of the suture was brought out the nares and tied on the cheek to the other end of the suture. This suture was left in place for three weeks and the patient moved the entire circumference of the suture once daily by pulling the suture out of the nose for one-half inch or so. It was thought that this in-dwelling suture would prevent adhesions and encourage epithelization of the channel along the suture at the newly opened medial end of the lower canaliculus.

REPORT OF SIXTY CASES

Eight years ago it was decided to substitute dacryocystorhinostomy for extirpation of the lacrimal sac. Between January, 1940, and February, 1948, 60 dacryocystorhinostomies were performed, using the technique of Dupuy-Dutemps.

A follow-up has been obtained on 55 of these cases. Only one patient, the 21st operation in the series, reports no relief of pus or tearing, and refuses to return for examination. Her operation was uneventful four years ago at the age of 66 years, and my records show that at the first dressing normal saline solution was irrigated freely into the nose through the lower canaliculus. One other patient, the 13th operation in the series, who for four months had complained of epiphora only was not relieved. It was thought the stricture was in the naso-lacrimal duct, but it must have been a mistaken diagnosis, because at the recent follow-up examination six years after the operation, it was found that both upper and lower canaliculi were occluded to within 2 mm. of the puncti.

Six other patients were relieved of pus but were not completely relieved of tearing; in four of these patients the lower punctum was found at the follow-up examination to
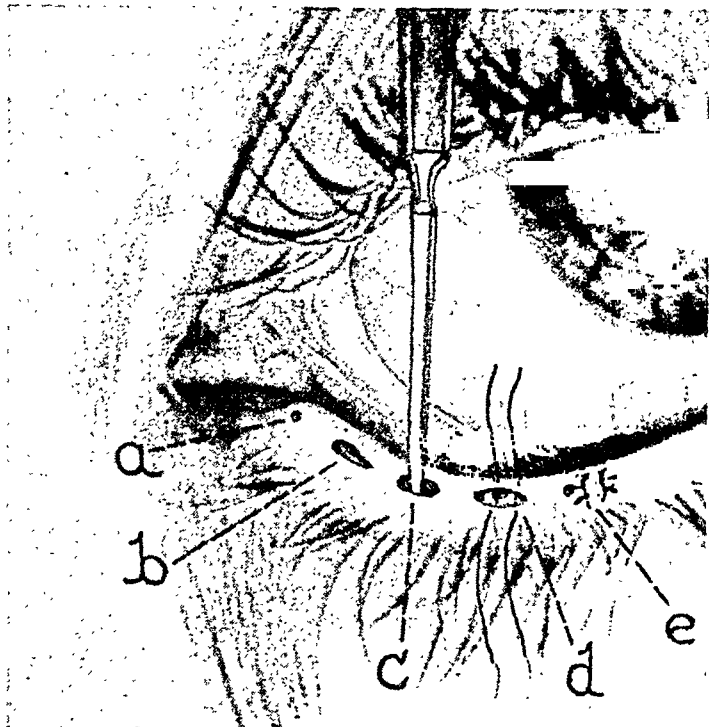
Fig. 9 (Hallum). Punctorrhaphy. (a) Normal punctum. (Added by artist): (b) Dilated punctum. (c) A cataract knife is used to denude the inner rim of the punctum, except its nasal portion. (d) Silk sutures have been placed across the margin of the lid, just deep enough to include the lips of the punctum. (e) After the sutures have been tied, the punctum is reduced to its normal size.

be dilated beyond normal size, one had had his lower canaliculus slit, and one had occlusion of the lower punctum. Punctorrhaphy (fig. 9) has been performed on two of the patients who had dilated lower puncta, and each has been completely relieved of tearing. In each of these cases the lower punctum was anesthetized by injecting a few minims of 1-percent procaine hydrochloride just anterior, and posterior, to the punctum. The tip of a cataract knife was used to produce denudation of the inner rim of the dilated punctum, except in the extreme nasal portion. A fine silk suture was placed across the lateral half of the punctum, from the anterior to the posterior lip, and left snugly tied for four days. In each of the two cases the decrease in tearing was immediate, that is, at the end of the operation.

Twelve of the patients were Negroes, seven of the patients had bilateral operations. Four of the patients who had bilateral operations were women, and three were men; all three of the men had bilateral con-

genital stenosis. There was only one patient who had unilateral congenital stenosis. The longest period of obstruction was 28 years —one of the men who had bilateral congenital stenosis. Thirty-five of the operations were done on the left side, and 25 on the right side.

Ten of the operations were done by the senior ophthalmic resident, under my direction, and all 10 operations were successful. Thirty-seven of the operations were performed under sodium pentothal intravenously and 23 under local anesthesia. Trauma was thought to be responsible for the obstruction in 10 of the patients; in one patient the obstruction developed after an antrum operation and the other nine followed blows on the nose, mostly in automobile accidents.

Two of the patients had external fistulas at the time of the operation, but they closed spontaneously after drainage into the nose was reëstablished. An abrasion of the cornea was produced in two patients; the abrasion healed in the normal time and without complications.

CONCLUSIONS

Dacryocystorhinostomy has given many

surgeons the highest percentage of successful results when done by the technique popularly known as that of Dupuy-Dutemps. Extirpation of the lacrimal sac leaves tearing in a high percentage of the cases, but dacryocystorhinostomy by the technique of Dupuy-Dutemps should relieve both tearing and mucopurulent discharge in at least 95 percent of the cases of obstruction of the lacrimal duct and sac, if the lower punctum and lower canaliculus are normal. Even if the lacrimal sac is absent or completely occluded, tearing should be relieved by this operation in the majority of the cases. The postoperative treatment is usually limited to the care of the skin incision.

Excessive dilation of the lower punctum should be avoided, as it will result in tearing in an otherwise successful dacryocystorhinostomy. For this reason, the lower canaliculis should never be slit, and one should never pass a probe larger than a Bowman No. 2 or 3 lacrimal probe. A dilated punctum when partially closed by punctorrhaphy can be expected to relieve the accompanying tearing.

478 Peachtree Street, N.E. (3)

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OCULAR ONCHOCERCIASIS*

M. Puig Solanes, M.D., Bertha Riveroll Noble, M.D., and A. Fonte, M.D.
Mexico City, Mexico

Translated by George P. Guibor, M.D.
Chicago, Illinois

More than 30 years ago, ocular onchocerciasis was reported by Rodolfo Robles[1] and its clinical characteristics were described by Pacheco Luna.[2] Clinical material was accumulated by Fonte from data obtained at Huixtla, Chis., Mexico, in 1943; from records compiled by Puig Solanes, Fonte, and Quiroz[3] in the same locality in 1945; and from studies of Bertha Riveroll Noble[4] in the endemic zones of Guatemala.

Nearly all of the 1,334 cases examined by these investigators presented the characteristic nodules of onchocerciasis and possessed positive cutaneous biopsies. In a few cases, the existence of nodules could not be demonstrated and the cutaneous biopsies were not always positive. These patients, however, did present ocular lesions in the form of superficial punctate keratitis and iridocyclitis.

Only three complete globes and a number of fragments of corneal and conjunctival tissue were obtained for study by Noble[4] and Vargas de la Cruz.[5] Enucleation is unnecessary in most cases of ocular onchocerciasis, but delay in treatment has caused almost complete destruction of the globe, in some instances, before enucleation could be performed.

Strong[6] reported the incidence of ocular involvement in 5 percent of the cases in the Guatemalan zone, while Calderón[7] found ocular symptoms in 100 percent of the cases in the same zone. The disparity in these percentages results from the variation in susceptibility among individuals and the additional fact that, in those districts in which there are facilities for periodic examination and treatment, fewer eye infections occur. In addition, examinations performed in many rural districts without the aid of the biomicroscope do not reveal the existence of early ocular lesions.

In Africa, Hissette[8] found ocular lesions of onchocerciasis in from 43 to 51 percent of those infected, in the villages of the Belgian Congo, and we found 66.3 percent among the 1,334 patients examined in other zones.

Statistical studies made by us disclose that ocular involvement in onchocerciasis is not varied or influenced by the age of the patient or by the duration of the disease. A significant difference in incidence of infection of the eyes was noted in relation to the number of the nodules present regardless of size, 77.2 percent in those with more than five nodules and 60 percent in those with less than five nodules.

Strong[9] reported that, on his African expedition, ocular complications were particularly frequent in patients with small but numerous nodules (25 to 100). In the study of the susceptibility of various races to the disease, it was indicated that the Caucasian race is less susceptible than the races native to the Americas and to Africa and that those of mixed genesis show a definite predisposition to infection. There were more men than women infected.

CLINICAL ASPECTS OF ONCHOCERCIASIS

ACUTE FORM

In the acute form of onchocerciasis, the skin and the eyes are severely affected. The hard, red swellings in the skin of the cheeks, eyelids, and about the ears (figs. 1 and 2) were diagnosed by Robles[1] "as erysipelas of the skin."

Ocular manifestations in the acute form are photophobia, blepharospasm, lacrima-

Fig. 1 (Solanes, Noble, and Fonte). Facial appearance in onchocerciasis.

tion, and injection of the anterior segment with edema between the superficial and deep tissues so great that on moving the globe, there is the appearance of a hyperplasia. The dermal irritation persists after the ocular symptoms have subsided but both reappear in the chronic form unless the skin is cleared of infestation.

THE CHRONIC FORM

The chronic form, the "true conjunctivitis of Calderon,"[7] existed in 22 percent of the cases of Puig Solanes, Fonte, and Quiroz. This form is characterized by vascularization and excessive pigmentation, resulting from small irregular granules in the epithelium. In the conjunctiva (fig. 3) are follicles resembling phlyctenules.

Corneal manifestations. Superficial punctate keratitis, the characteristic corneal lesion in onchocerciasis, appeared alone in 45 per-

cent of the cases of Puig Solanes, Fonte, and Quiroz[3] and was associated with iridocylitis in 20 percent of the cases.

Pacheco Luna[2] described these opacities as being a fraction of a millimeter in size and numbering from 1 to 12 in the same cornea, scattered, generally, but sometimes coalesced near the limbus. The biomicroscope shows them to be of powdery consistency in the vicinity of Bowman's membrane.

Interstitial keratitis, reported by Calderón,[7] is now believed to be only aberrant lesions of the superficial type. Vascular keratitis was noted by Hissette[8] as vascularization of the corneal limbus enmeshed in a weblike structure resembling a true pannus.

Chronic manifestations of the iris. Iritis, in association with lesions of the cornea, was demonstrated in 29 percent of the cases of Puig Solanes, Fonte, and Quiroz.[3] Puig Solanes[10] described fibrinous iritis with

Fig. 2 (Solanes, Noble, and Fonte). Cutaneous lesions of onchocerciasis.

and without displacement of the pupil. Calderón[7] spoke of acute and chronic forms, while Hissette[8] called it "diffuse atrophy of the iris."

Excessive pigmentation is present, in this manifestation, with microscopic obliteration of the folds of the iris. Exudation may occur near the pupil with synechias in the lower portion of the membrane (fig. 4). Gonioscopic studies of Puig Solanes[11] of 30 eyes of patients with onchocerciasis disclosed that the root of the iris is affected.

Choroidal manifestations. Choroidal involvement is noted most frequently in Africa. Hissette[8] described it as a diffuse

Fig. 4 (Solanes, Noble, and Fonte). The effect of iritis in onchocerciasis.

Fig. 3 (Solanes, Noble, and Fonte). Conjunctival alterations in onchocerciasis.

pigmented chorioretinitis with patches of atrophy.

SUBJECTIVE SYMPTOMS

Subnormal vision. Visual acuity is decreased in ocular onchocerciasis principally from opacities in the cornea. There is, in the acute type, recovery upon removal of the nodules.

Other subjective symptoms. These symptoms may exist with or without the presence of objective lesions. The principal discomforts noted are the so-called conjunctival triad—fever, pain, and the sensation of a foreign body in the eye.

This triad is frequently linked with dancing lights, photophobia, entoptic vision of

active microfilaria, poor visual acuity, and lacrimation.

DIAGNOSIS

Microscopic demonstration of the existence of microfilaria in the eye (fig. 5), positive cutaneous or conjunctival biopsies, and verification of the characteristic nodules constitute the general clinical diagnosis of onchocerciasis.

Parasites in the eye. Clark and Noble saw filariform bodies in the vitreous cham-
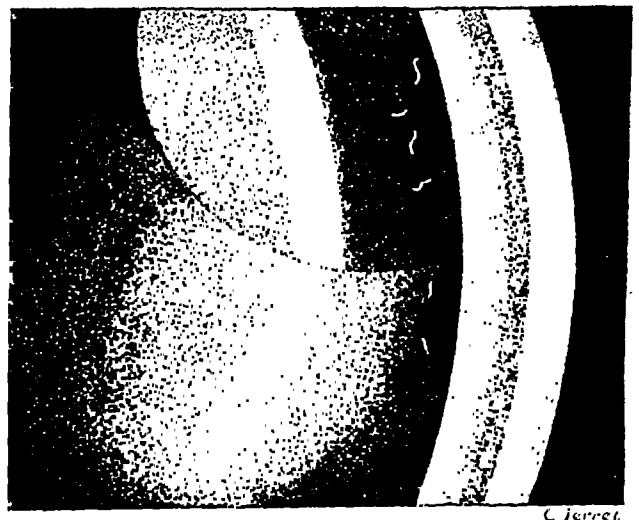
Fig. 5 (Solanes, Noble, and Fonte). Biomicroscopic representation of microfilaria in the anterior chamber.

ber but did not verify the type of filaria present. In 1945, Torres Estrada,[12] with the aid of intensive illumination and a lens of 20 to 25 diopters, demonstrated microfilaria as blackish filaments in the lower portion of the vitreous chamber.

Biomicroscopy of the eye. Torrella[13] first saw microfilaria in the anterior chamber of the eye by means of the biomicroscope in

sue. The number of microfilaria varies from day to day in the same individual. We found 16.3 per cent of our group with positive cutaneous biopsies and only 5 percent with positive conjunctival biopsies.

EXAMINATION OF NODULES IN THE SKIN

The nodules are of the greatest value in the diagnosis of onchocerciasis. They are
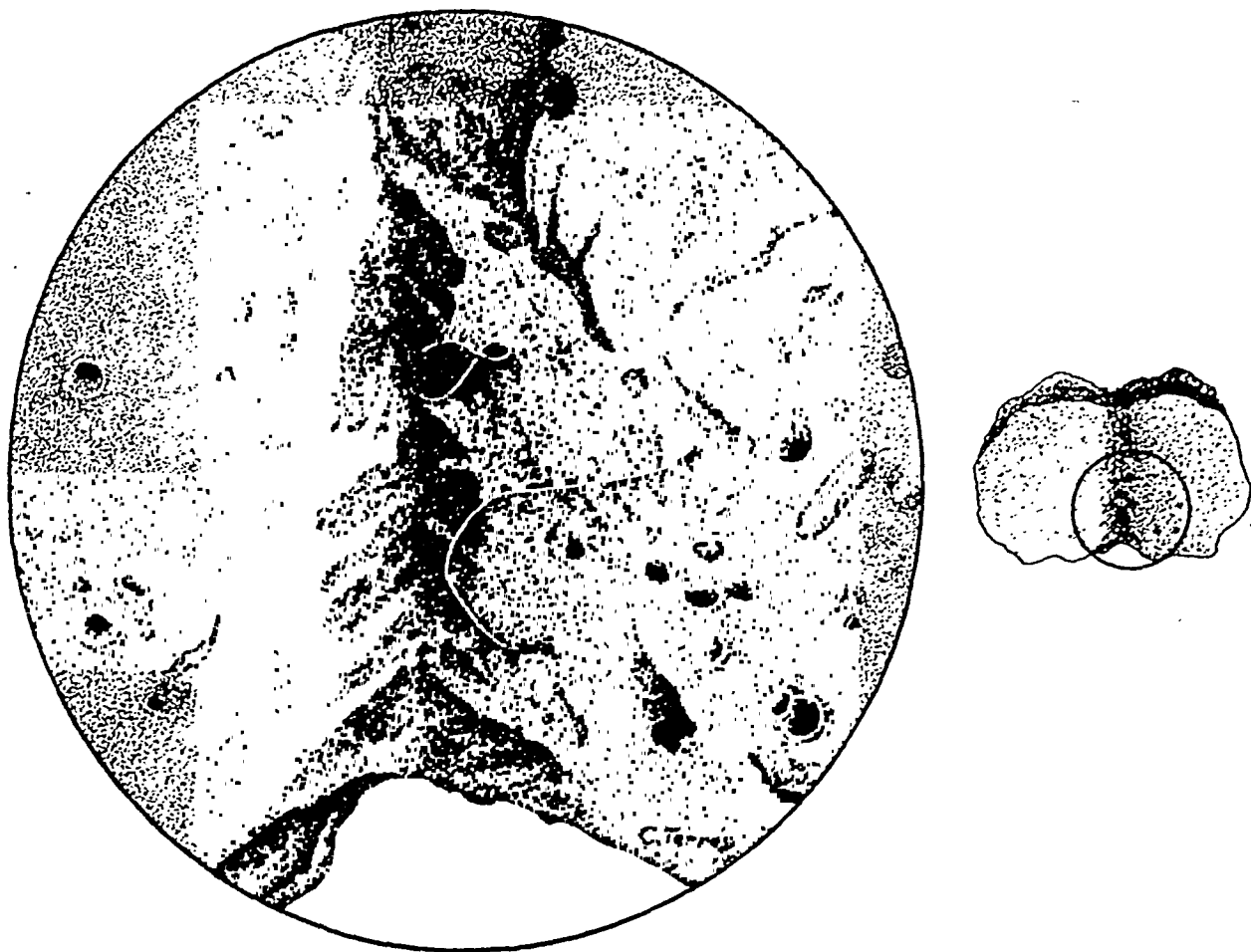
Fig. 6 (Solanes, Noble, and Fonte). A magnification of the adult parasites occupying the center of the mass of atrophied connective tissue in which the young are born.

1930. The parasites appeared to be refractive, thin, and to move about incessantly. The number varied from one to dozens and from day to day in the same patient. The parasites appeared to be phototropismic.

Biomicroscopy of the skin and the conjunctiva. Thin slices of the skin or of the conjunctival tissue are prepared for use with the biomicroscope in the usual manner with water or with whey. From 1 to 20 active microfilaria may be seen to 1 mm. of tis-

from 0.75 of a millimeter to 3 or 4 cm. in size. They are hard, not painful, and are adherent to the skin. They are found most frequently about the head, on the American continent, in numbers not over 7 or 8. In Africa, the trunk and the limbs may show as many as 25 to 100 nodules in a single patient. The nodules may exist also in the outer canal of the ear, in the lining of the cheek, and over the aponeurosis of a muscle (Nettel[14]). The nodules are filled with a

turbid liquid containing active microfilaria which swim about a core of adult parasites enmeshed in connective tissue in a state of atrophy (fig. 6).

HISTOLOGIC PATHOLOGY

Octerena,[15] Hissette,[8] Strong,[6] and the authors[3] studied the histologic pathology of ocular onchocerciasis. Their conclusions were similar in most instances. The following are our conclusions:

1. The corneal lesions are superficial and exhibit much vascularization and pigmentation.

2. The activity of the microfilaria observed in the histologic preparations is comparatively small in relation to the extent and the number of the corneal lesions encountered.

4. Atrophy of the stroma of the iris occurs frequently.

5. The attack on the posterior pigmented portion of the epithelium and the dilator muscle is sufficient to explain the paresis of the pupil.

6. The ophthalmoscopic appearance of the choroidal atrophy and of dispersion of the pigment in the choroid is similar to the atrophy seen in the iris.

7. The retinal alterations seem to be secondary to the choroidal alterations and to exist principally in the outer layers of the retina.

PATHOGENESIS

The pathogenesis of ocular onchocerciasis can be accounted for by the action of toxins generated by the filaria in the nodules (Robles[1] and Pacheco Luna[2]). It is possible that the periodic reproduction of the females may bear some relationship to the toxins produced (Calderón[7]).

The traumatic action of the microfilaria in situ in the ocular tissues may result in much disturbance, especially if the nodule is near the eye and contains female adults which produce larvae every two months (Nettel[14]). We are of the impression that there are fac-

tors other than these which are still undiscovered.

The morbidity in ocular onchocerciasis may accrue also from the products of the metabolism of the adult parasite or of its larvae (Martinez Baez[16]). However, Hissette[8] was the first to discover the tenuous refractive filaments in the corneal parenchyma of patients. These are the dead microfilaria. Torres Estrada[12] considered that the lesions of keratitis centered in the vicinity of these dead bodies.

There is also much controversy over the manner in which the parasite enters the globe. The logical manner is from the external toward the deeper portions of the eye but Hoffman and Vargas[17] and Nettel[14] hold the theory that they proceed from some hidden nodule to the inner portions of the eye. Nettel[14] presented cases of patients with microfilaria present in the ocular chambers but none in the eyelids or in the subconjunctival tissues.

PROGNOSIS

In general, the prognosis is not good. Microfilaria persist in the eyes months after the removal of the nodules from the skin. Considering the severity of many individual lesions, however, the visual acuity is good, especially in some of those cases in which there are many corneal opacities. In 45 of 61 cases there was visual acuity of 10/10 and in only 3, below 7/10.

Iritis in onchocerciasis, however, alters the vision considerably. The following percentages exclude incipient attacks of iritis, glaucoma, bulbar atrophy, and so forth, or of their sequelae. In iritis, there was visual acuity 10/10 in only two eyes of 22 examined, 1/10 in one of the eyes, 9 above 1/20 and 9 below 1/20. One eye was completely blind.

TREATMENT

The use of plasmoquina discussed by Torrella[13] has not proved permanently effective in the destruction of microfilaria.

Pacheco Luna has found surgical intervention disastrous in the treatment of affections of the iris.

The modern treatment of Bayer 205 (no reference given) would aid many if it were to . prove generally as effective as it has proved in Africa.

We are of the opinion, however, after 10 years of systematic effort on the part of the sanitary ministers of Mexico and of Guatemala, that it has been proved that periodic examinations and removal of the nodules of onchocerciasis lessens the number of acute attacks and decreases the number of microfilaria in circulation. This reduces the prob-. ability of ocular infection.

SUMMARY

A study of over 1,000 cases of onchocer-ciasis revealed an ocular infection in 60 to 77.2 percent of the cases. Caucasians were less susceptible, whereas those of mixed genesis were most susceptible.

Acute and chronic forms existed. In the former, the skin and the eyelids contained many papules.

In the chronic form, all tissues of the eye were infected, the cornea in 45 percent, iridocyclitis in 29 percent.

The diagnosis is made by: (1) The history of residency in the affected areas of Mexico, Guatemala, and Africa; (2) clinical signs and symptoms of nodules; (3) finding the microfilaria in the eye by slitlamp, and in the skin nodules by means of the microscope. The latter method is considered the most reliable.

Av. López Cotilla 811.

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OCULAR LYMPHOMAS*

PARKER HEATH, M.D.
Boston, Massachusetts

Ocular malignant lymphomas are uncommon. Hyperplasia of lymph and reticular tissue, however, is a common reaction to infection. Lymphoid elements are widely distributed under and in the conjunctiva of lids and globe, in the lacrimal gland, and in the lymph drainage system. The wide distribution and ready mobilization cause the borderlines of hyperplasia and malignant new growths to be far from sharply drawn. The lymph cells, however, even though they may undergo marked changes when they become neoplastic, still will tend to reproduce the cell of origin. This permits a classification based upon the principal cell types.

The purposes of this study of a significant series of ocular lymphomas are: to report the incidence, to classify the cases studied clinically and according to the principal cell types, and to report separately on both the incidence and the results of treatment of conjunctival lymphomas.

The material for this series was obtained from Massachusetts General Hospital, Collis P. Huntington Memorial Hospital, and the Massachusetts Eye and Ear Infirmary. Sixteen hundred records of patients with lymphomas of all varieties were consulted from the three institutions.

Ophthalmic literature, in contrast to that of general medicine, has scanty references to lymphomatous disease. Detailed reviews of the literature have been made by Shannon and McAndrews,[1] Leinfelder and O'Brien,[2] Ennema,[3] and McGavic.[4] Case reports on reticulum-cell sarcoma of the conjunctiva have been made by Siotto,[5] Black,[6] and Rados.[7] Verhoeff and Derby[8] report a case of plasmoma of the lacrimal sac and cite nine other cases reported. Because of the rarity of ocular lymphoma, most reports are made from small series. Ophthalmologists in general see but few of these patients. Laboratory reports are often confusing. The variety of early clinical signs and the irregular periods of remission of the disease combine to obscure further both reports and satisfactory classifications. One would expect this in a disease of unknown etiology and such wide variance in clinical manifestation. The reports in medical literature reflect this by showing variegated classifications, terminology, and conclusions. The matter of etiologic agent is not considered in this paper.

Clinically, the lymphomatous lesions are usually painless, moderately firm and vascular, and slow in growth. When presenting under a mucous membrane they appear grayish pink and yellowish pink to red and show coarse vessels superficially. Early stages may somewhat resemble a firmer kind of lipoma. They range in size from small, firm, discrete nodules in lid, globe, or orbit, to diffuse masses of tissue encircling the globe or involving the lids and found within both orbits. Biopsy removal and microscopic examination is of greatest value in diagnosis.

A clinical classification can be made based upon the appearance and the course of the growth as follows:

1. Benign hyperplastic node, located usually episcleral or subjunctival behind the lower or upper lid. It is a smooth-surfaced, fleshy nodule, yellowish pink in color without signs of inflammation. These often remain the same size for years, are sometimes congenital, but may develop malignant qualities, especially in the first and after the fifth decade of life.

2. Locally diffuse: (a) conjunctival or subconjunctival, grayish in color, somewhat

soft, gelatinous clusters of lymphoid tissue, with limited growth; very sensitive to X rays and not likely to recur; (b) this group is benign, at first lymph-cellular, later a fibrous, scirrhous, lymphoid hyperplasia involving lacrimal gland and lids, and the or-

may be found in skin, episclera, subconjunctiva, and orbit. As a rule these nodules become invasive relatively slowly. When the limbus is involved, there may develop a superficial pannus and red fleshy corneal overgrowth with rare superficial hemor-
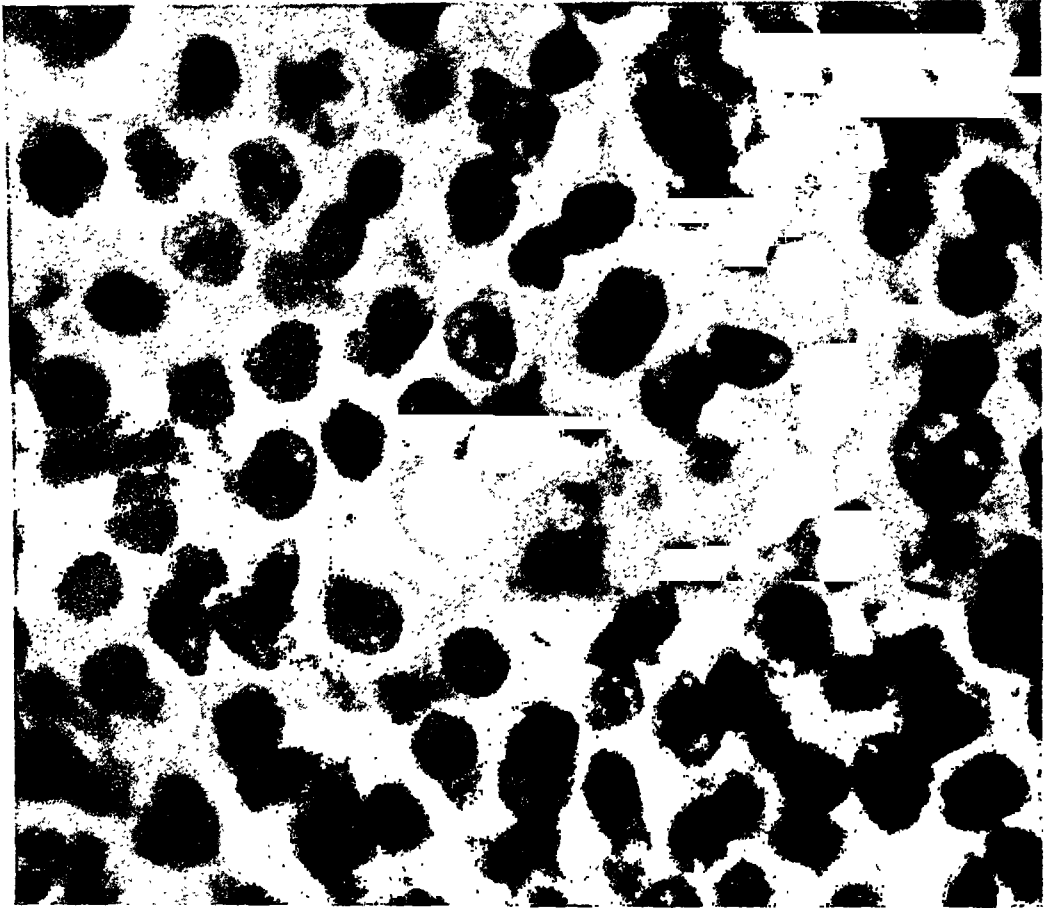
Fig. 1 (Heath). Lymphoblastoma (×1,200). Larger (9 to 20 micra) than mature cell; finely divided chromatin in single nucleus with well-defined borders. Narrow border of cytoplasm; no increase in reticulum.

bit in a self-limited extension; the "pure" form of Mikulicz's disease (Heath[9]).

3. *Associated ocular lymphoma*, eye involvement as part of general disease, leukemia or Hodgkin's and of the hematopoietic system including spleen, bone marrow, and lymph nodes, and liver. Small lymphomas

rhages. The insertions of the recti muscles or the plica and caruncle may be the sites of nodules. These nodules are composed of mature lymphocytes and of lymphoblasts showing a moderate reticulum and a stroma carrying blood vessels and capillaries.

4. *Invasively diffuse:* first seen as an ex-

Fig. 2 (Heath). Lymphocytoma (×1,200). (7 to 10 micra.) Dense mass of chromatin in nucleus; narrow cytoplasm. No increase in reticulum.

Fig. 3 (Heath). Reticulum cell (×1,200). (10 to 20 micra.) Abundant cytoplasm. Ovoid nucleus, chromatin fine in mature, coarse in immature. Prominent nucleolus, may be binuclear. Ameboid activity. Reticulum increased.
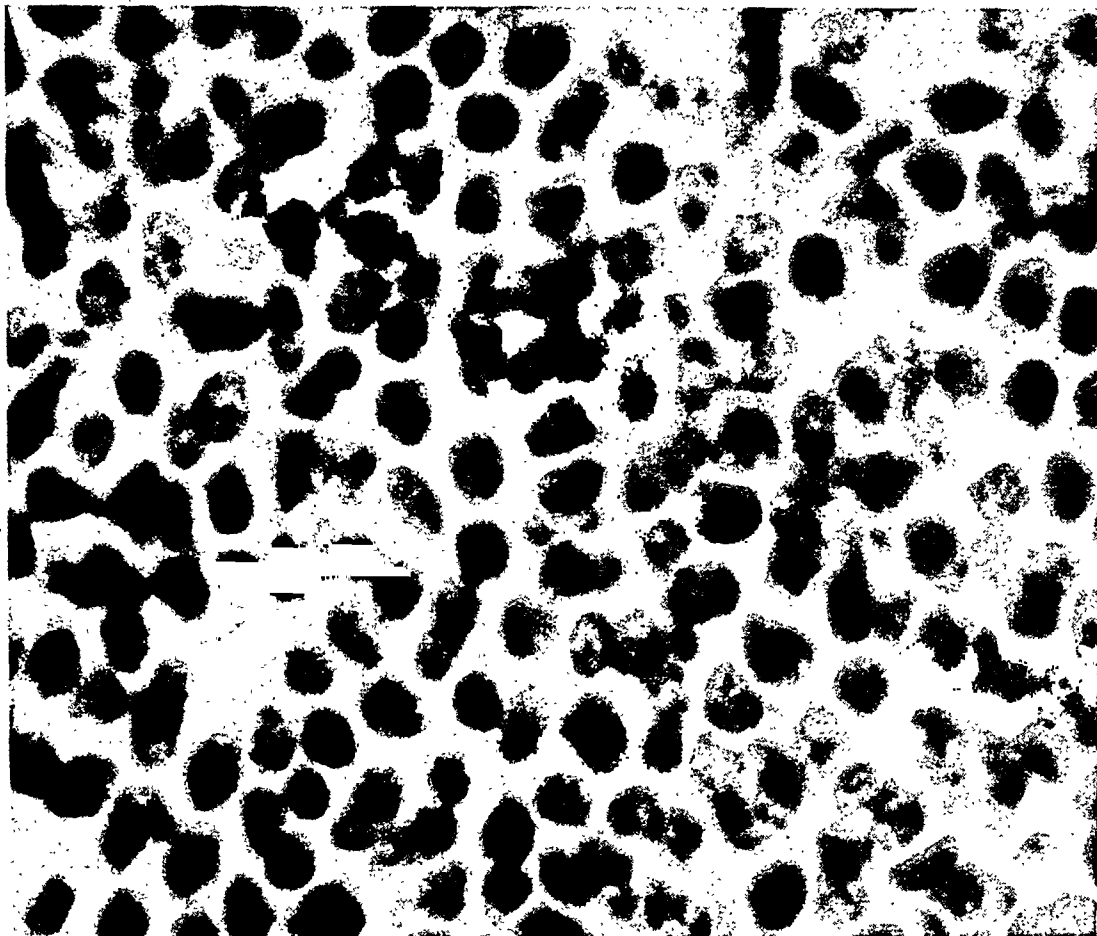
Fig. 2
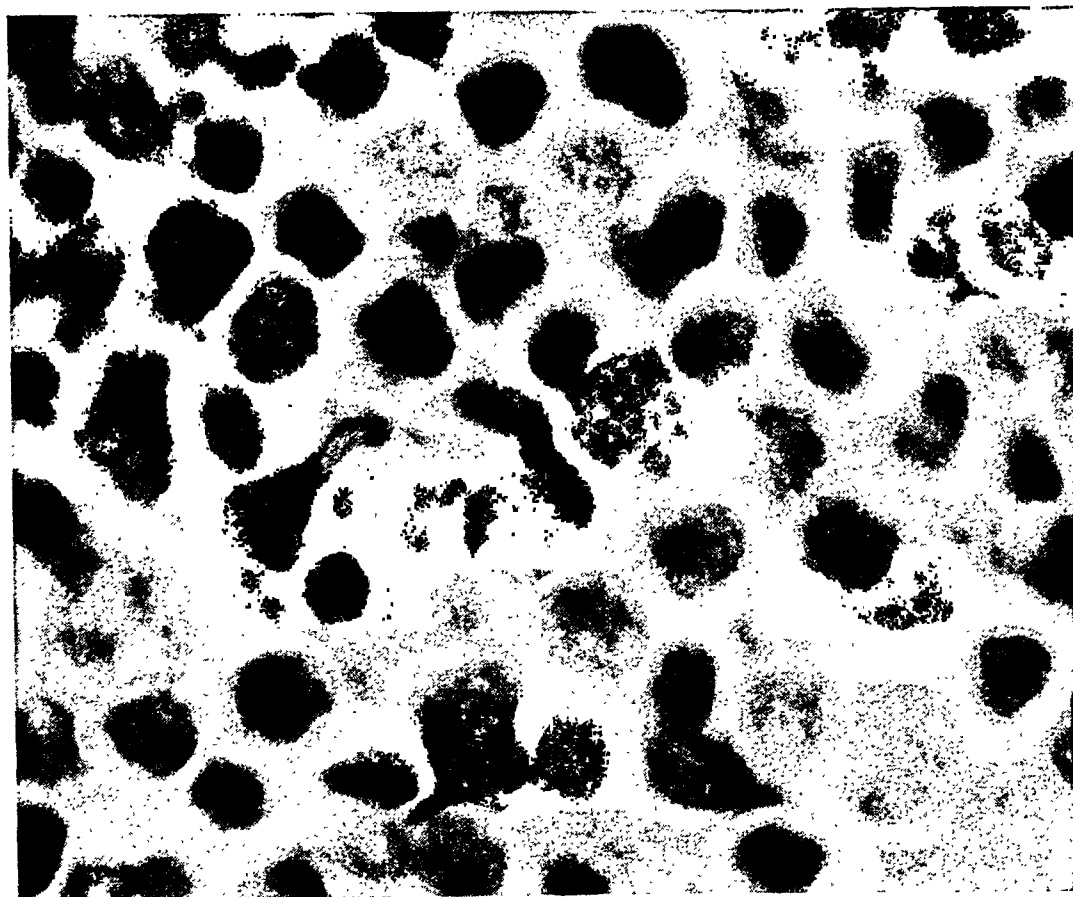
Fig. 3
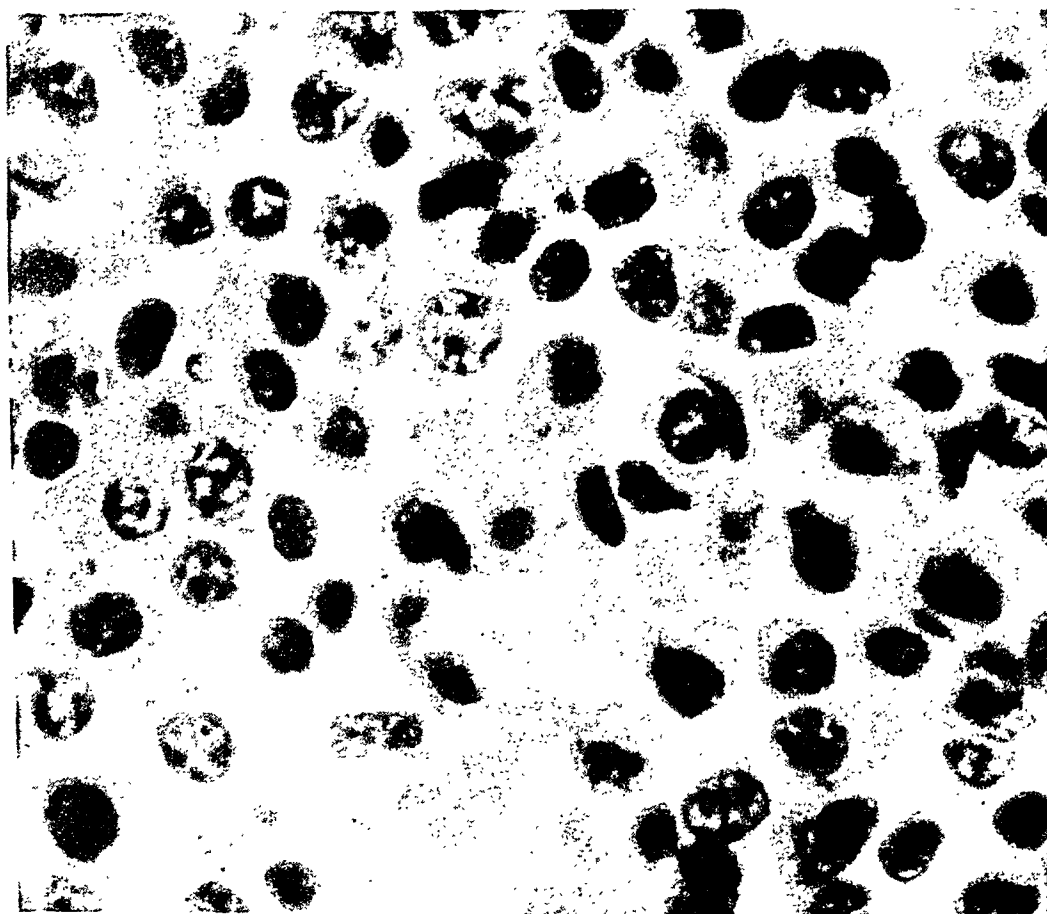
Fig. 4
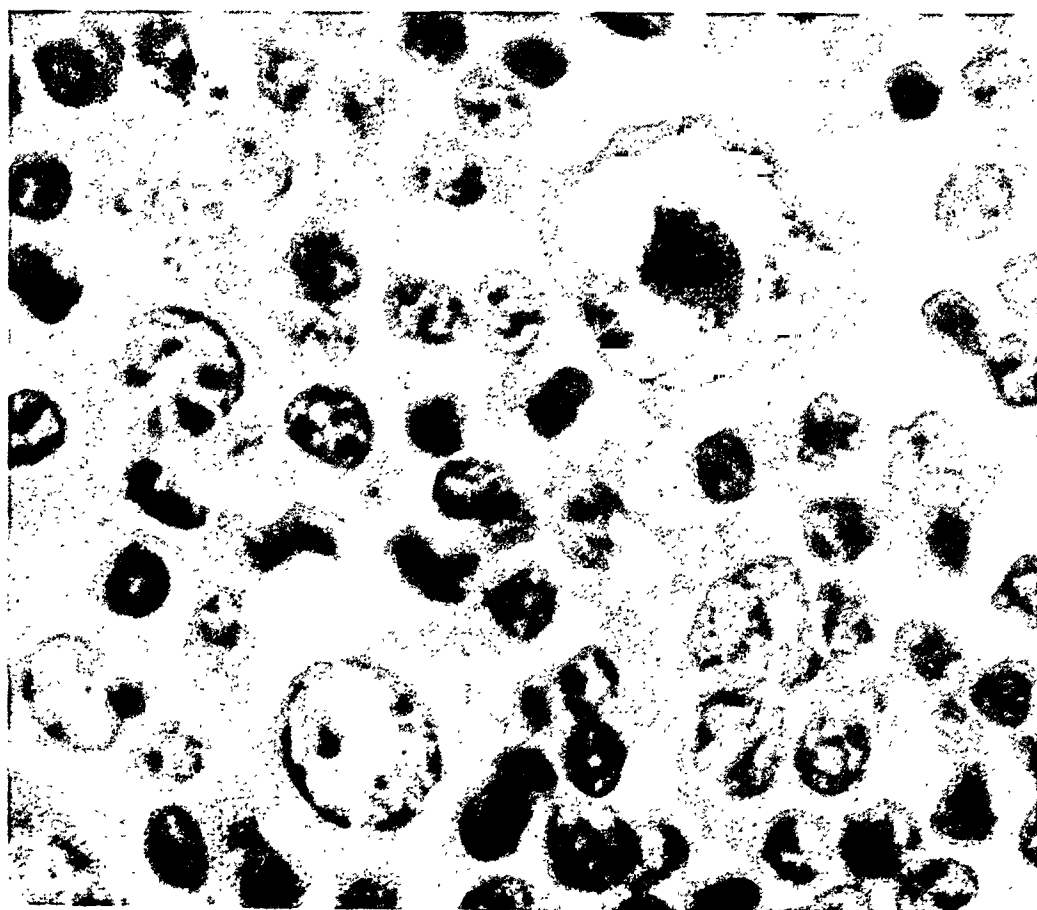
Fig. 5

panding, grayish pink, firm to hard, bulbar, subconjunctival, lid or orbit new growths, sarcomatous, and invasive by lymph channels; may be derived from group (1) or (2a) if the local process shows mature cells which have become more primitive and invasive. The conjunctival and subconjunctival red encircling swelling is firmly attached to the globe and has somewhat the

than chalazion. A biopsy, which should include part of the nodule, may show a reticulum-cell lymphoma.

This report uses the classification developed by Sparling, Adams, and Parker (Table 1).[10] It survives the test of usefulness in predicting the clinical course of the disease. The cells of the lymph structure

TABLE 1*

CELL TYPE

Lymphoblast { Lymphoblastoma / Lymphosarcoma, lymphoblastic type / Lymphatic leukemia

Lymphocyte { Lymphocytoma / Lymphosarcoma, lymphoblastic type / Lymphatic leukemia

Giant Follicle Lymphoma { Reticulum cell sarcoma / Hodgkin's granuloma or sarcoma / Lymphosarcoma / Lymphatic leukemia

Reticulum cell or Histiocyte { Reticulum cell sarcoma / Hodgkin's disease { Paragranuloma / Granuloma / Sarcoma } / Histiocytic leukemia

Plasma Cell { Plasmacytoma / Multiple myeloma / Plasma cell leukemia

* From Sparling, Adams, and Parker.[10]

tached to the globe and has somewhat the appearance of a brawny scleritis and some superficial capillary hemorrhages may be noted. When it occurs in the lid, an extensive firm edematous swelling is noted to be associated with a deep smaller nodule which is both opaque and shows frayed edges on transillumination. The process resembles at first inspection an acute chalazion with edema, but has less hyperemia; the vessels are fewer and coarser and small hemorrhages may be noted. The swollen lid is firmer and gives less pain to the patient on palpation

used in the classification are: lymphoblasts, mature lymphocytes, the reticulum cell, and the plasma cell.

When local lymph tissue extends and invades, it is called sarcomatous, and when found in the blood it is called lymphatic leukemia; the presence of Reed-Sternberg cells makes the diagnosis Hodgkin's disease. Table 2 gives cytologic detail. Four cell types are illustrated by photomicrographs selected from this series, a fifth to depict Hodgkin's disease.

Sixty-seven cases of ocular lymphoma

Fig. 4 (Heath). Plasmoma ($\times 1,200$). Plasmocytoma (2 to 12 micra). Polygonal or triangular outline. Nucleus round, eccentric. Chromatin masses in the periphery. Basophilic cytoplasm. No increase of reticulum.

Fig. 5 (Heath). Hodgkin's disease. Always shows Reed-Sternberg cells (10 to 40 micra). Pleomorphic nucleus, sometimes lobulated and multinuclear. Nucleoli common, large clumps of chromatin. The Reed-Sternberg cells are the large multinuclear cells.

TABLE 2

CYTOLOGIC DIFFERENTIATION

	Size	Nucleus	Cytoplasm	Reticulum	Mitosis	Necrosis	Local	Invasive
Lympho-blast	9 to 20 micra	Larger than mature cell. Border well defined; finely divided chromatin dispersed in nucleus. Single	Narrow; border may stain basically	Not increased	Rare	Rare	Lymphoblastoma	Lymphosarcoma of lymphoblastic type
Lympho-cyte	7 to 10 micra	Dense; massed chromatin	Slight; basic	Not increased	Rare	Rare	Lymphocytoma	If in blood, lymphatic leukemia. Lymphosarcoma of lymphocytic type
Giant follicle Lymphoma	Many separate or fused large follicles with active germ centers. Usually limited to lymph nodes and spleen	Germ centers contain young lymphocytes or reticulum cells					Border zone of mature lymphocytes	Half develop Hodgkin's or sarcoma
Reticulum cell	10 to 20 micra	Ovoid, one side often indented; fine chromatin if mature, coarse in young cells and with nucleolus prominent. Occasional binuclear	Abundant acid or basic. Some ameboid activity	Increased				Tend to invade veins, arteries
Hodgkin's Sarcoma form is mostly histio-cytes	18 to 30 micra	Variable cell mixture, lymphocytes, reticulum and plasma; some eosinophiles, polymorphonuclears Always Reed-Sternberg cells 10 to 40 micra. Pleomorphic nucleus, sometimes lobulated, multinuclear cells. Chromatin in large clumps and common nucleoli	Fine reticulated cytoplasm, acid or basic	Increased Common		Usual (except paragranuloma type)	Loss of nodal architecture (limited extent in paragranuloma)	Paragranuloma not invasive. Granuloma may change over to sarcoma
Plasma-cytoma	1 to 12 micra Polygonal or triangular outline	Round, eccentric, heavy chromatin masses at periphery	Basophilic	Not increased	Common	Rare	May remain local for many years	May involve bones and viscera

are reported in this series. Their site classification may be seen in Table 3. In the grand total of lymphoma patients the percentage of involvement of the eye is 4.0. These patients were referred by an active clinic especially interested in this disease. In a recent study of 288 patients at the Massachusetts General Hospital Lymphoma Clinic, 1.7 percent were classified as presenting lymphoma in the orbital adnexas.

Graph 1 shows the age and incidence of all lymphomas in this series and separately those of the conjunctiva, and thus permits a comparison.

TREATMENT

The treatments usually employed for the lymphomas are: surgical extirpation and roentgen ray, or both. Lymphoma tissue is by and large susceptible to small dosage of

TABLE 3
CLASSIFICATION OF CASES

Site	Number	Site %	Cell Types			
			Lymphocyte	Lympho-blast	Plasma	Reticulum Cell
Conjunctiva	30	44.7	20 Giant follicle 1	5	1	3
Lid	13	19.4	5	7		1
Lacrimal gland	2	2.9	1	1		
Sclera	1	1.4	1			
Globe	3	4.4	2		Lymphatic leukemia 1	
Orbit	14	20.8	8	5	1	
Combined site	4	5.9	3 Giant follicle 1			

In the McGavic[4] series of 21 cases, lymphoma accounted for 2.6 percent of the extrabulbar tumors, and Rones[11] found only 19 lymphomas in 11,500 ocular specimens of all kinds of diseases at the Army Medical Museum, and of these, three, or 0.025 percent involved the conjunctiva. At the Massachusetts Eye and Ear Infirmary Eye Pathology Laboratory, lymphomas of the conjunctiva represented 1.8 percent and lymphomas of the orbit 0.84 percent from approximately 1,671 tumors of all kinds and types, original in the ocular adnexa. These comparisons may be seen in Table 3.

In the conjunctival lymphomas, correlation of age, cytology and the aftermath of treatment may be seen in Table 4.

X rays. The usual technique of treatment in recent years (Massachusetts General Hospital) has been 200 kv., 20 cm. object-target distance, $\frac{1}{4}$ mm. copper filter, and daily doses of 200 to 300 r directed onto the conjunctiva for a total of 600 to 900 r. This has not resulted in any untoward effect upon the eye, immediate or remote. (One eye with an orbital lymphoma, not included in the present study, which received 1,200 r has developed an opacity of the lens five years after treatment.) The more scirrhous a lymphoid lesion, as in Mikulicz's disease, the less susceptibility is present. X ray sensitivity is variable enough to be used as a differentiating agent in diagnosis.

Excision is also recognized as good treat-

TABLE 4

LYMPHOMATOUS TUMORS OF CONJUNCTIVA—CORRELATION OF AGE, CYTOLOGY, AND AFTERMATH OF TREATMENT

Case	Sex	Age	Pathologic Diagnosis	Cell Type	Presenting Symptom	Duration on Admission	Local	Not Local	Treatment	Status	Duration Post Rx
E-47-158	F.	38	Lymphoma	Lymphocytoma	Conjunctival infiltration	2 months	x		Excision 800 r	Well; slight conjunctival injection	½ year
9-12,812 (MGH 44-7482)	F.	70	Lymphoma	Lymphocytoma	Conjunctival infiltration	?	x		Excision	Well	3½ years
8-12,452	F.	68	Lymphosarcoma	Lymphocytoma with a number of reticulum cells	Conjunctival infiltration	1 year	x		900 r	Well	5¼ years
9-12,929 (MGH 44-7482)	M.	60	Lymphoma	Lymphocytoma	Conjunctival infiltration	4 years	x		600 r	Well	3 years
9-13,034	M.	53	Lymphosarcoma	Lymphoblastoma	Conjunctival infiltration	1 year	x		1,000 r	Well	3 years
8-12,406	F.	58	Lymphosarcoma	Lymphocytoma	Conjunctival infiltration	3 months	x		1,000 r	Well; chronic blepharitis	5½ years
4-6,183	M.	78	Lymphosarcoma	Lymphocytic sarcoma	Tumor mass	1 month	x		Radium 58 mgh.	Dead without disease	2¼ years
E-47-29	M.	55	Lymphoma	Lymphocytoma and lymphoblastoma	Conjunctival infiltration; generalized	3 months		x	600 r	Alive with disease; spleen large	½ year
3-5,188	M.	8	Reticulum cell	Reticulum cell	Tumor mass; orbit involved	2 weeks		x	Exenteration 300 r Radium ++	Lost with disease	¾ year
4-8,209	F.	87	Lymphosarcoma	Lymphocytoma Many histiocytes	Tumor mass; cervical nodes	1 year		x	Exenteration	Dead with disease	1¼ years
MGH 47-9876	F.	82	Lymphoma	Reticulum cell	Tumor mass	3 months	x		X-ray	Well	¼ year
MGH 32-848	M.	71	Lymphosarcoma	Lymphocytoma	Tumor mass; generalized	4 years		x	Excision X-ray	Dead with disease	1¼ years
6-10-426	M.	76	Lymphosarcoma	Lymphocytoma	Conjunctival infiltration; generalized	3 months		x	600 r	Dead with disease	½ year

Case No.	Sex	Age	Diagnosis	Diagnosis	Clinical	Duration			Treatment	Status	Follow-up
3-2,686	M.	22	Plasmoma	Plasmoma	Tumor conjunctiva	?	x		Excision	Unknown	?
2-692	M.	16	Lymphoma	Lymphocytoma	Conjunctival infiltration	?	x		Excision	Unknown	?
8-12,024	F.	41	Lymph node	Lymphocytoma	Tumor mass	?	x		Excision	Unknown	?
7-10,601	M.	64	Lymphoma	Lymphocytoma	Thickening, conjunctiva	7 years	x		Excision X-ray	Well	1/4 year
5-8,482	F.	48	Lymphoma	Lymphocytoma	Tumor mass	2 months	x		Excision	Unknown	?
7-11,528	F.	?	Lymph follicle cysts	Lymphoblast	Cysts in conjunctiva	?	x		Excision	Well	7 years
7-11,120	M.	?	Lymphoma	Lymphocytoma	Conjunctival infiltration	?	x		Excision	Unknown	?
2-1,802	M.	?	Lymphoma	Lymphoblastoma	Unknown	?	x		Excision	Unknown	?
E-48-91	M.	28	Lymphoma	Reticulum cell	Conjunctival infiltration	?	x		Excision	Well	1/4 year
8-12,407	M.	67	Lymphosarcoma	Lymphocytoma	Irritation conjunctiva	Several months	x		Excision X-ray	Well	3 years
8-11,878	M.	34	Lymphoma	Lymphoblastoma	Conjunctival infiltration; nose involved	1 year	x	x	Excision X-ray Exenteration	Dead with disease	9 month
7-11,260	M.	7	? Boeck's sarcoid Lymphocytoma	Lymphocytoma with plasma cells	Conjunctival infiltration	?	x		Excision	Unknown	?
E-47-21	M.	42	Lymphoma	Giant follicle lymphoma	Drooping lid	3 months	x		Excision X-ray	Well	1 year
MGH 44-7310	M.	?	Lymphoma	Lymphocytoma	Conjunctival infiltration	2 years	x		Excision	Unknown	?
2-1,460	?	?	Lymphoma	Lymphoblastoma	Conjunctival infiltration	?	x		Excision	Unknown	?
3-4,729	?	?	Lymphoma	Lymphocytoma	Conjunctival infiltration	?	x		Excision	Unknown	?
4-5,453	F.	55	Lymphoma	Lymphocytoma	Conjunctival infiltration	?	x		Excision	Unknown	?

ment of conjunctival lymphomas. The lid and orbit growth may be treated both surgically and with X ray, dependent upon size and location. The aim may well be: (1) Complete surgical removal; (2) microscopic examination of the specimen; (3) further

Graph 1 (Heath). Age incidence of conjunctival lymphomas versus other ocular lymphomas.

treatment by surgery and X ray, or only by X ray as indicated by the nature of the site, size, and microscopic examination in the pathology laboratory.

The effects of various treatments in this series, other than the conjunctival, are difficult to classify accurately, because of the gaps in the follow-up history. We may say in general that those patients who have an involvement of the eye as a part of a generalized lymphoma have an average outside prognosis of two years. The local ocular treatment, however, has usually prevented recurrent involvement of the eye itself, even when extension has occurred elsewhere.

This is true even when the eye and adnexa were secondarily involved by extension. When the disease is localized, as in the conjunctival group, a remission may be sufficiently long to carry the patient through his usual age expectancy. In two cases in the conjunctival series the patient was untreated for four years. One is alive and one is dead. It just happens that in our series there have been no leukemic blood changes in the conjunctival lesions alone. This agrees with the reports of others (McGavic,[4] Rones,[11] Verhoeff,[12] and Bedell[13]).

SUMMARY AND CONCLUSIONS

The most common cytology in this series is the lymphocytoma. There are noted, however, other cell types, that is, lymphoblastoma, reticulum cell, and plasma cell. Prognosis is not materially altered by cell type. The lymphomas occur more often in the first decade and after the fifth. They respond to X-ray treatment in small doses and to excision when size permits. Long periods of remission may follow treatments. Lymphomas of the lid and orbit are like those elsewhere. If early, small, discrete, and primary, the immediate effects of removal and X-ray therapy are good, the remote poor.

The conjunctival part of this series offers similar findings to that group of lymphomas reported before by Schulz and Heath,[14] namely, that the primary lymphomas of the orbit and conjunctiva are rare and were responsible for less than one percent of a total group of 1,671 ocular tumors. The primary conjunctival lymphomas are relatively benign, if there has been no extension of the process at the time of treatment. A long interval may elapse before general involvement takes place. If the conjunctival lesion is extending and sarcomatous, the prognosis is—in time invariably fatal.

243 Charles Street (14).

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FUSIONAL VERGENCE*

EDWIN FORBES TAIT, M.D.
Norristown, Pennsylvania

It has long been recognized that ocular comfort and visual efficiency in individuals with binocular vision depend not only upon the neutralization of refractive errors, if present, but also upon the precision with which the visual axes of the two eyes can be directed toward the object of regard. While binocular fixation deficiencies are by no means as common as refractive errors, they are frequently the major cause of difficulty in a large proportion of the groups of individuals who are collectively considered as refraction problem cases.

Considerable attention has been given to the development of methods for measuring, designating, and classifying the end effects upon the extraocular muscles of the stimulus-response mechanisms concerned with binocular vision. The various forms of heterophoria and heterotropia have been familiar to every ophthalmologist since the time of Stevens[1] and Maddox. Relatively little work, however, has been done on the

identification and classification of the stimuli which, through the operation of reflex arcs, produce the binocular ocular rotations as responses to the various stimuli.

The present paper reports one of a series of studies on the stimulus-response mechanisms in these ocular vergences.

Although Donders,[2] in his epoch-making classic on refraction and accommodation of the eye, was the first to point out the necessity of coördinated accommodation and convergence in binocular vision, and Helmholtz,[3] a few years later, reaffirmed and amplified his viewpoint, it was not until Maddox,[4] presented the results of his studies of convergence that the importance of the afferent side of the stimulus-response process was recognized. Maddox, however, was unable to develop his concepts fully, as he lacked the essential understanding of the reciprocal innervation-inhibition of opposing muscle groups, which was supplied some years later in Sherrington's[5] work on the integrative action of the nervous system.[5]

In 1917, Sheard[6] amplified Maddox's ideas, and presented a report on a study of the three reflexes then considered to be re-

sponsible for binocular fixation. These were designated as tonic convergence, accommodative convergence, and reflex or fusional convergence. A few years later, a fourth stimulus for convergence was added, that of proximity, or the sense of nearness, and the convergence resulting from that stimulus has been designated as proximal convergence.

Ophthalmic literature is singularly barren in statistical studies showing the distribution and range of these functions. This is probably due to the general acceptance of some widely held but, unfortunately, inaccurate ideas as to the meaning of the results obtained by the binocular balance tests. In many quarters heterophoria is still considered to be an expression of the strength of opposing muscles, rather than the result of faulty reciprocal innervation to those muscles. Again, prism convergence or divergence tests are thought to indicate muscle strength and they are often considered to be faulty when the relationship between prism convergence and prism divergence is not three to one, respectively. Other workers are much distressed if an apparent excessive exophoria at near is found.

In 1942, the Dartmouth group[7] presented the results of a survey of the ocular functions of a large number of students in the course of a study of the influence of visual factors upon motivation. Included in this survey are the results of tests of prism convergence and divergence and reversion to fusion, and the values agree fairly well with those found in the present study. The conclusions as to the meaning and use of the data, however, vary widely from those presented herein.

The distribution of the results in the present study and an interpretation of the facts presented in other investigations of convergence indicate that the vergence functions are the result of reflex conditioning, such as is encountered in any learning process. The conclusions of Chavasse[8] support this concept.

The present report is concerned with the range of modifications in the position of the visual axes of the two eyes, relative to each other, occurring as the result of the efforts of the individual to retain, or to gain, single binocular vision. These efforts may be collectively known as fusional vergence, or, more precisely, as fusional convergence or fusional divergence, supra- or infravergence and cyclovergence.

While the data upon all of these fusional processes has been obtained in several thousand individual studies, from which the 500 considered in this report were drawn, because of limitation of time and space only the lateral vergences, relative to distance fixation, will be presented.

Investigative work in accommodation and convergence must be confined largely to statistical studies of fairly large selected groups, or to intensive studies of the accommodation and convergence reactions of single individuals. Both types of inquiry are necessary for the advancement of knowledge in this field, with perhaps the former being the more applicable to correlation with clinical observation and diagnosis. Animal experimentation can obviously contribute little, as clear single binocular vision, or its absence, can be determined only by subjective reports.

The fusional process, sometimes called the fusion faculty, or simply fusion, is a two fold entity. It is generally considered to be not only the anatomic and physiologic arrangement which permits the superimposition in the visual cortex of the sensory impulses arising in the two retinas, thus making possible single binocular vision and stereopsis, but also a stimulus-response mechanism whose duty it is to keep the object of regard on the proper corresponding retinal points or areas by means of reflex control of the extraocular muscles.

The first function of the fusional process, as outlined above, is concerned entirely with sensory perception and is that which should properly be designated as "fusion." All

cases reported in this study have good single binocular vision and stereopsis and thus have normal sensory fusion.

The second function of the fusional process, that in which there is a varying of the position of the visual axes of the eyes in order to retain or gain single binocular vision, should be considered as fusional vergence.

While these two functions are interrelated and interdependent, only the second will be considered in this paper.

Fusional vergence may be defined, therefore, as a modification produced by the fusional process in the distribution of tonic reciprocal innervation to the extraocular muscles, in order to preserve or to gain single binocular vision.

Fusional vergence, through the years, has been variously known as positive and negative fusional convergence, binocular adduction and abduction, prism convergence and divergence, ability to overcome prism, and prism vergence. Although the terms "adduction" and "abduction," originally introduced by von Graefe as a designation for the fusional convergence and divergence, are convenient, in recent years some writers have confused binocular and monocular duction terminology, so that it is probably desirable to use the more descriptive and accurate general designation of fusional vergence, which term can further be modified by describing the means, such as prism, or haploscope, used in the determination.

In all such studies, it should be kept in mind that the values obtained are relative to the means employed in the study and to the stimulus conditions. Thus a study of the fusional reflexes with prisms, and with stimulus objects of given intensity and at certain distances, would differ somewhat from fusional values obtained by the use of movable stereoscopic apparatus, such as a haploscope. In any type of investigative or clinical procedure, the normal distribution, with respect to the circumstances of the test, must first

be ascertained, after which departures from the usual value can be recognized and evaluated. In the present study, an effort is made to determine the normal distribution of values of the lateral vergence reflexes under certain rigidly controlled conditions.

The 500 cases reported in this paper were taken at random from a much larger group of individuals who have clear, comfortable, and efficient single binocular vision and who were wearing suitable glasses, if they were needed. The only limitation to selection was that, for convenience, only subjects with less than 2^Δ of esophoria or exophoria were included. When lateral heterophoria of greater amount is present, it becomes necessary to calculate the fusional vergence amplitude by including a correction for the esophoria or exophoria. Such cases, however, introduce an additional factor in comfortable vision, that of the constant presence of a considerable amount of fusional vergence effort necessary to maintain single binocular vision for distance, and these patients will be given separate consideration in a later paper.

In the series of procedures used in the present investigation, the object was a 6/30 letter, black on translucent base, and illuminated from behind with an illumination equal to 10 foot-candles at the plane of the letter. The prism values, base-in and base-out, were supplied by means of the Risley prisms in a standard phorometer. In the prism convergence break tests, prism power was increased before each eye simultaneously, making an effort to keep the increase equal in the two eyes, and with a speed of about 4^Δ per second. No attention was paid to the blurring of the stimulus object, but the prism dioptry value just before the patient reported that the object separated into two was recorded. At the speed of increase already noted, this procedure permitted an ample allowance for reaction time in practically all cases. Inasmuch as the accuracy in reading the Risley prisms is somewhat less than 1^Δ when both prisms are used, the

value obtained in the test was recorded in the distribution in the next lowest group. Thus, the two chief variables, the patient's reaction time and the experimental variations in reading the prism calibrations, were compensated for reasonably well.

The same procedure was carried through in the prism divergence test, except that the prisms were increased in the base-in direction.

After the prism convergence value was

TABLE 1

PRISM CONVERGENCE: DISTRIBUTION OF 500 CASES OF ADULTS OF PRESBYOPIC AGE

Prism Dioptries	Break	Reversion to Fusion
2–4	0	204
6–8	20	167
10–12	121	71
14–16	107	38
18–20	126	10
22–24	58	6
26–28	22	4
30–32	26	0
34–36	10	0
38–40	10	0

Values recorded in next lowest prism dioptry group.

obtained by the break-point test, the patient, of course, had diplopia and, in nearly all cases, seemed to fix with one eye, probably the dominant eye. In the remaining few, there was alternation of the eyes in macular fixation of the object. With the patient observing the diplopic images, the prism base-out power in the prism convergence test was gradually decreased at a somewhat slower rate than it had been increased, and the patient was encouraged to tell just as soon as he could see one object only. As soon as he reported that the two images had fused into one, the value was noted, and the value recorded in the next lower group, in order to allow for the errors already discussed.

The same procedure was carried through in the prism divergence reversion to fusion test. In each case, the results represent the average of at least three trials. It was rare,

however, for several trials to vary more than 2^Δ. In other words, the tests are satisfactorily repeatable.

Table 1 shows the distribution of these 500 cases on the prism convergence break and reversion to fusion tests. Table 2 presents the data obtained in the same group of cases in the prism divergence break and reversion to fusion tests. Figure 1 presents the percentage of subjects who failed to maintain fusion in each group during the prism convergence break tests. The reversion to fusion line in the prism convergence graph represents the percentage in each group who failed to obtain fusion as the prism power is reduced. Figure 2 presents the same data relative to the prism divergence break and reversion to fusion tests.

These data show that in a group of 500 subjects, as prism convergence is increased, more persons will fail to maintain fusion. At 26^Δ to 28^Δ only 10 percent can still maintain fusion. Of these few, some can overcome as much as 38^Δ to 40^Δ. The midpoint of the range is about 18^Δ to 20^Δ. In other words, about half the patients could overcome as much as 18^Δ to 20^Δ of prism conver-

TABLE 2

PRISM DIVERGENCE: DISTRIBUTION IN 500 CASES OF ADULTS OF PREPRESBYOPIC AGE

Prism Dioptries	Break	Reversion to Fusion
2–4	8	328
6–8	101	128
10–12	208	28
14–16	133	16
18–20	47	0
22–24	3	0

Values recorded in next lowest prism dioptry group.

gence and still maintain fusion.

With prism divergence, half of the subjects cannot maintain fusion with as much as 12^Δ to 14^Δ. Ten percent can go as far as 18^Δ to 20^Δ. Some can go as far as 22^Δ to 24^Δ.

After the break and consequent diplopia, the prism power is reduced until eventually
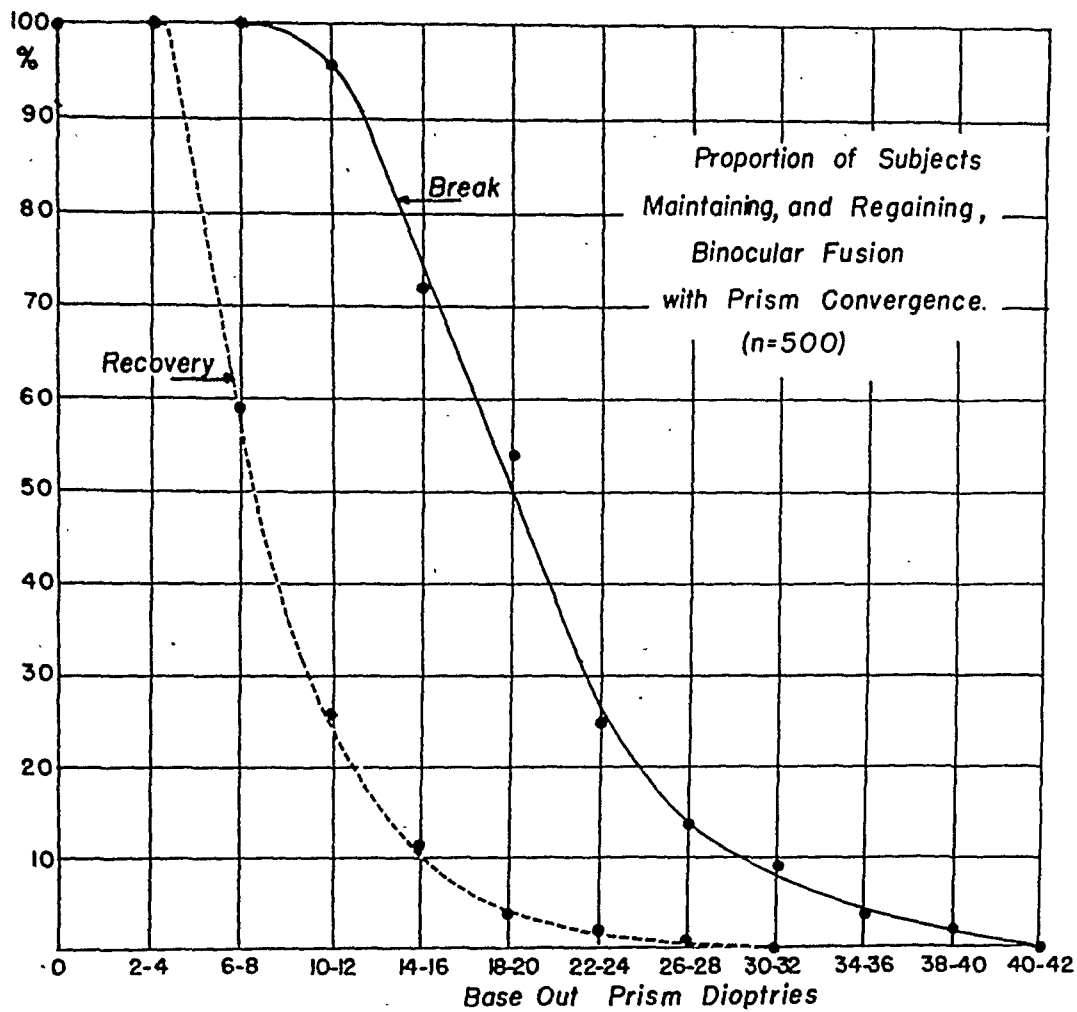
Fig. 1 (Tait). Prism convergence (500 subjects).
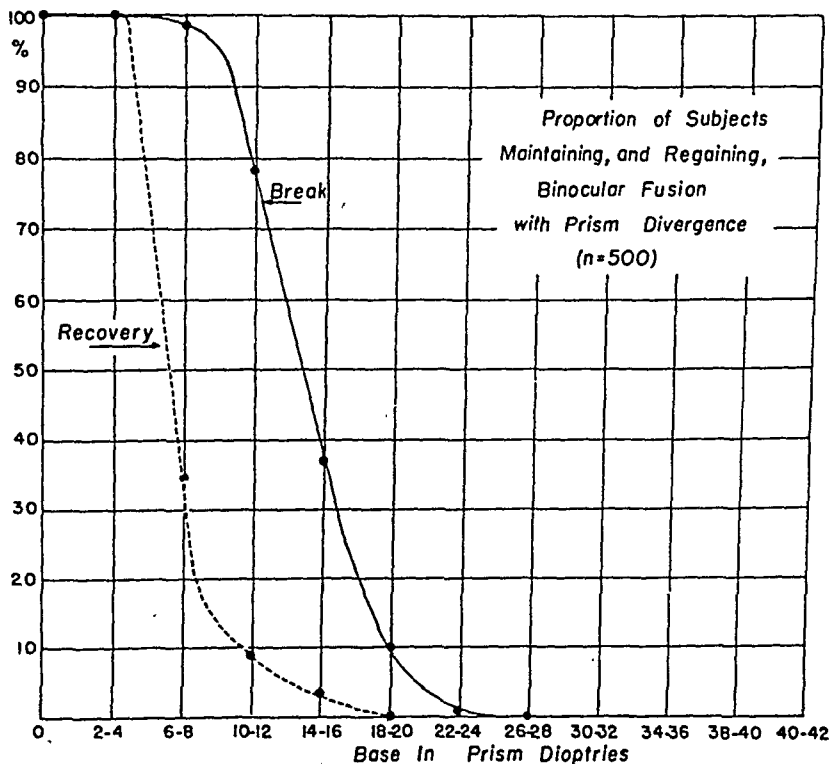
Fig. 2 (Tait). Prism divergence (500 subjects).

the fusion is regained. This occurred in all cases before the prism power was reduced to zero. Apparently the act of stimulating an area outside of the immediate perimacular area with an image similar to that stimulating the other macula (of the fixing eye) results in a change of fixation and rever-

THE EXTRA-MACULAR FUSION AREA OF THE RETINA

Binocular Images on the Maculae

After Prism Dissociation
(Base Out)

Extra-Macular Fusion Area
of Non-fixing Eye (Dotted Area)

Fig. 3 (Tait). Extramacular fusion area
of the retina.

sion to fusion. The probability of this reversion increases as the prism power approaches zero. With prism convergence, over 10 percent of the patients will regain fusion when 10^Δ to 12^Δ remain, and 100 percent have regained fusion at 2^Δ to 4^Δ.

With prism divergence, the extramacular fusion area is apparently smaller. Twenty percent have regained fusion at 6^Δ to 8^Δ, 50 percent require the prism to be reduced to, at most, 4^Δ to 6^Δ, and the remaining 30 percent require the prism to be reduced to 2^Δ to 4^Δ to regain binocular fusion.

From the standpoint of the stimulus-

response mechanism in fusional vergence, the data suggest that in the amplitude determinations, the response of the extraocular muscles is dependent primarily upon the stimulation of receptors which immediately encircle the macular area. If, for example, in distance fixation, one eye tends to deviate from the object of regard as the result of the presence of an underlying tonic convergence abnormality for that fixation, these perimacular receptors are stimulated by the image edging over from the macular area and, as a consequence of a probably quite complex associative linking, the tonus of the extraocular muscles is modified and the macula is again brought under the image.

When this process has been carried as far as possible, however, which, from the physiologic standpoint, probably represents the point at which no additional receptors are available, fusion is broken and the eye quickly moves back to somewhere near the primary position, and diplopia is produced. In this situation, the subject fixes the stimulus object with the macula of one eye and, in the other eye, the retinal image is in one of the peripheral fields.

As the prism power is gradually reduced, the image in the periphery approaches closer and closer to the macula in its eye until it finally reaches a point in the peripheral retina where the number of sensitized receptors is great enough, or where there is a synaptical connection effective enough, to actuate the fusional vergence reflex, with the result that the tonus of the extraocular muscles is immediately modified, the eye shifted for macular perception and single binocular vision regained. Thus it becomes possible to plot in a given individual the area on each retina within which images must fall, if there is to be single binocular vision. I have termed this area the "extramacular fusion area." It is shown graphically in Figure 3.

Disregarding the intermediate centers and tracts concerned in these reflexes, which can safely be done in an investigation with an objective such as the present study, we may

consider the perimacular and extramacular receptors and the ocular movements which result from their excitation, as the essential part of the stimulus-response mechanism which is charged with the maintenance of single binocular vision.

As far as the retinal receptors are concerned, it is uncertain whether those concerned in the fusional vergence reflex are rods or cones, or both, and for the present purpose it is immaterial, although the greater number in the perimacular area, as compared to the lesser number in the periphery, and the fact that the process is intimately connected with central vision, would suggest that the receptors are probably cones.

Although not presented in this study, the supra- and infravergence and reversions to fusion may also be obtained and the perimacular and extramacular fusion-area values determined in a vertical direction.

The practical clinical use of the procedures and data presented is beginning to be appreciated by those who are concerned with the abnormalities of binocular vision. The study of presumably normal individuals, at least those with apparent ocular efficiency and comfort, is necessary, in order to provide a precise knowledge of the range of normal variation. With a knowledge of the normal distribution and characteristics, the abnormal cases can then be studied, the faulty stimulus-response systems determined, and an intelligent attack planned to correct the difficulty.

The direct application of the stimulus-response mechanism, as discussed in this paper, to faulty binocular balance situations can be illustrated by the employment of the use-amplitude fraction. The fusional vergence function has, as its chief duty, the securing of single binocular vision and fusion in cases where the individual does not happen to be orthophoric for the fixation distance.

If he is other than orthophoric for this given fixation distance, the binocular images are held upon the two maculas only by the repeated and frequent stimulation of the perimacular fusional receptors, already discussed. If the need of such compensation is determined by a measurement of the heterophoria at the fixation point, the efficiency of the perimacular receptors in providing for its constant neutralization can be obtained by measuring the fusional vergence at that same point and in the proper direction.

For example, if the patient has 4^Δ of exophoria relative to his fixation at 6 meters, he has constant repeated stimulation of his temporal perimacular receptors on either or both maculas. If he has a sufficient number of receptors, and if they have well-completed synaptical reflex connections with the distribution of motor innervation to the extraocular muscles, the exophoria can be well compensated for and the individual will be comfortable.

If, on the other hand, the efficiency of the temporal perimacular receptors and their reflex pathways is not great enough, discomfort from the convergence effort will ensue. As yet unpublished studies in this connection suggest that the average individual may use from one quarter to one third of his total amplitude of prism vergence in the required direction without particular discomfort. If this amount is exceeded, there is a possibility, or a probability, of discomfort from the convergence situation.

In the case discussed above, let us assume that the prism convergence has been tested and found to be 2^Δ. In such a case, therefore, the fusional convergence required for the constant correction of the exophoria for distance would be 4^Δ, that is, the temporal perimacular receptors would have to be stimulated to that extent constantly. In addition to this, they can overcome 2^Δ prism base-out before diplopia occurs. Thus the amplitude of the positive fusional convergence would be the amount constantly used, 4^Δ, plus the 2^Δ of prism convergence, or a total of 6^Δ. Of this 6^Δ, 4^Δ would have to be used constantly, the use-amplitude fraction would

be 4/6, or considerably more than the one quarter to one third amount which could be used without distress.

The corrective process in such a case then would suggest one of two approaches: first, that an effort be made to lessen the exophoria for distance; or, second, to increase the amplitude of fusional convergence to the point where it could take care of the situation without stress. The third possibility, that of neutralizing the exophoria with a prism base-in, has not been considered, as experience through the years has shown that, in the long run, it would be apt to make the condition worse.

In such cases as that cited, attempts to modify the tonic convergence innervational distribution are generally unproductive, leaving, as the only other feasible alternative, a deliberate effort, by exercise of suitable type, to increase the amount of the positive fusional convergence amplitude.

All binocular balance deficiencies can be diagnosed in terms of the particular stimulus-response mechanisms which are at fault, and diagnosis in terms of these reflexes will permit an intelligent prescription of exercise or other corrective procedure designed to discourage or reinforce the appropriate reflexes.

Summary

The data on prism-convergence and prism-divergence trials in 500 adult clinical subjects has been presented.

These data have been interpreted in terms of the source of the stimuli for the motor responses noted. The function of the perimacular fusional receptors, those immediately surrounding each macula, and the extramacular fusional receptors, those further in the periphery, have been discussed. The data suggests that the function of the perimacular group is to retain fusion when once established, while the function of the extramacular group is to aid in establishing or gaining fusion.

The development of the use-amplitude fraction and its application in the diagnosis of binocular dysfunction is presented.

1324 West Main Street.

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SURGICAL REPAIR OF NEUROFIBROMATOSIS OF EYELID*

MAX M. KULVIN, M.D.

Hines, Illinois

In the *Virginia Medical Monthly* of November, 1941, and in the second edition of his textbook (1941) Spaeth writes, "Although much has been written about plexiform neuromata from a pathological and histological standpoint, the clinical correction of these cases has been neglected in the literature to an astonishing degree. This may be due to the various anatomical defects present, requiring quite a series of cases before any surgical procedures could be outlined."

After a short discussion of the characteristics of these tumors, Spaeth discusses the treatment he has evolved:

1. Roentgen therapy is of no value.

2. General anesthesia is necessary.

3. Dissection of the tissue, removal of all neoplasm, prevention of unnecessary scarring, and conservation of as much skin, tarsal plate, and hair line as possible is advised. Tissue extending into the orbit should be removed.

4. The skin, when removed, is replaced by a pedicle or sliding flap.

5. Cartilage grafts are frequently necessary as well.

6. Best results are obtained in those cases in which the various surgical procedures have been done with a fair interval of time intervening between each operation. From 2 to 4 years are usually necessary to obtain the best results.

When, in April, 1940, this type of case was seen for the first time at the Veterans Administration Hospital, Hines, Illinois, a search of the various available texts disclosed nothing but generalities in regard to

the treatment. I can, therefore, concur with the statement of Spaeth which appeared the following year. It became necessary to evolve, out of a combination of various operative procedures, something to fit this particular type of disability without attempting a complete removal of the lid. Inasmuch as there was hardly one centimeter of tissue which did not contain numerous tumors, it was not felt desirable to transplant such skin in the form of a flap, since we were not familiar with the reaction of such tissues.

General anesthesia was not considered necessary and was not used. Although our first case required no cartilage graft, the second one did, in a sliding-flap formation.

Each case required a number of operative procedures. The removal of various masses from the temporal region and eyeball necessitated a pause to allow for observation and reëvaluation of the result up to that time. The first case was almost completed in one step, but several small subsequent procedures were necessary before a satisfactory result was obtained.

Eight years later, the second case was carried out in more prudent fashion requiring about six procedures before completion.

ORIGIN AND PATHOLOGY

While it is not the purpose of this paper to discuss the origin and pathology of this disease, a short résumé of the essential features might be of interest. Von Recklinghausen's disease is considered to fall in the group of diseases resulting from developmental abnormalities of the ectoderm and mesoderm. It is a congenital condition, sometimes inherited and sometimes encountered as a familial disease. It is characterized by *tumors of the skin, cutaneous pigmentation,* multiple tumors arising from the sheaths of cranial, spinal, peripheral, and sympathetic nerves, abnormalities in bones, defective de-

velopment of the central nervous system, other developmental abnormalities, and buphthalmos.

Unger finds that this tumor may appear wherever there are nerves. In the skin, it may appear as tumors, or pigmentation in form of café-au-lait spots; in the iris, as brownish pigmented tumors; in the choroid, as a "string of pearls;" and as a plexiform neuroma in the region of the eyes, ears, forehead, and neck. The tumors occur along the vagus, acoustic, trigeminus, and sympathetic nerves.

Penfield and Young state that these tumors are invariably made up of tissue of tangled or reticular structure, described by Antoni as Type B, and sometimes contain areas of true perineural fibroblastoma, described by Antoni as Type A. The tangled areas are evidence of a connective-tissue reaction to that obscure abnormality characteristic of nerve fibers in this disease. They find three types of tissue involved—nerve trunk, meninges, and central-nervous system.

The tangled or reticular tissue constituting the background of all neurofibromas should be considered a connective-tissue and sheath-of-Schwann reaction about the fibers of the nerves. Antoni called this Type B—in which no palisading of nuclei or polarization of cells was present. Type A possesses both characteristics—there is an orderly appearance of long slender fibers with silver staining properties, a palisading of the nuclei produced by an orderly parallel arrangement of the cell nuclei, which are elongated with blunt ends. Some areas resemble the structure of the Wagner-Meissner tactile corpuscles.

The Type-B cells are haphazardly arranged and mucocystic degeneration may be present. The fibers are of the reticular type. Collagen bands are rare—Antoni believes that the Type-B cell represents a degenerative phenomenon, a jellification of Type A.

Throughout the three tissues in which neoplasm appears, there is definite evidence of a hyperplastic reaction of the cells peculiar to those tissues. This indicates, says Penfield, that in von Recklinghausen's disease an irritant or stimulating influence is exerted on various tissues causing hyperplasia. Superimposed on, or subsequent to this effect, is the appearance of neoplastic growth of these cells.

Recent work on the production of tumors by Oertel and Ricker suggests that previous to neoplastic growth of cells there is a stage in which, owing to some neurovascular stimulus, the cells that are destined to become neoplastic undergo a hyperplastic change. A chronic irritant is capable of initiating tumor growth. It may be that the congenital defect in the nervous system is capable of producing the necessary irritation of adjacent tissues, producing hyperplasia and later neoplastic growth.

In none of the tumors can the type cell be said to be embryologically undeveloped. The tumors produced preserve the peculiar characteristics of the connective tissue in question. This speaks in favor of the production of tumors by an irritative process rather than from some embryologic rest.

CASE REPORTS

CASE 1

The first patient, R. C. F., a man, aged 50 years, was admitted to Hines Hospital on April 1, 1940, and discharged on August 5, 1940.

Personal history. He had had the usual childhood diseases. He stated that he was born with a drooping eyelid and that he also had a growth behind the left eye which was discovered when he was eight years old. Nine operations for this growth were performed between 1902 and 1908. From the time he was 15 years old, his eyelid has drooped entirely over the eye and thickened blebs have been there ever since. At birth, he had some nipplelike cysts on various parts of the body and many brown spots all over the body. In 1920 he began to develop wartlike bumps of various sizes over his entire body. The biggest one was the size of a

walnut; the smallest, the size of a match head. The skin was dotted with smaller bumps, like prickly-pear spots. The large ones hurt if pressed, but not otherwise. Generally he felt well.

Physical examination revealed a fairly well-developed, well-nourished white ambulant man who did not appear acutely ill. His

Fig. 1 (Kulvin). *Case 1.* Tumors of the skin and café-au-lait pigmentation.

height was 5 feet 6½ inches; weight 133 pounds. His head was normal in size, but there were many nodules on scalp. A fairly large-sized nodule was present in the mucosa of the left cheek. There were countless nodules all over the body, ranging in size from a few millimeters to as large as a walnut (fig. 1). Hearing tests showed he could hear a conversational voice at 35 feet.

Neurologic examination revealed anesthesia and atrophy of the right leg.

Eye examination. The right eye was negative. The left lid was completely ptotic and was large, pendulous, and thickened,

especially at lid margin. A soft fatlike thickness in a roll-like formation extended from the lateral border of the lid over the zygomatic area. Distended vessels were noted in the skin of the upper lid (fig. 2).

With conspicuous effort, the lid could be elevated, revealing slight conjunctival injection. The fundus was normal. A large con-
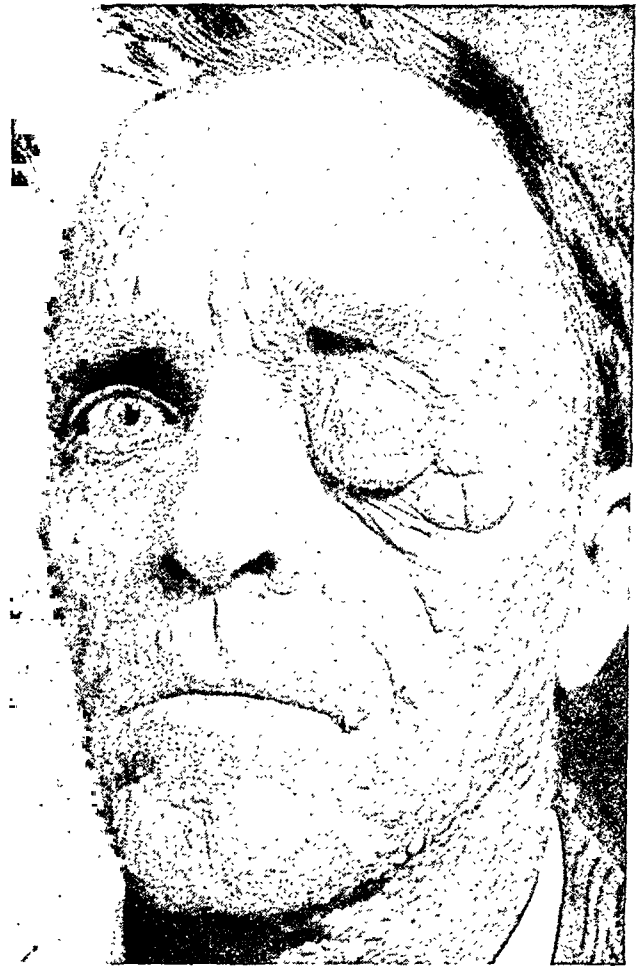
Fig. 2 (Kulvin). *Case 1.* Neurofibromatosis of the eyelid before plastic correction (May, 1940).

junctival mass was present on the sclera of left eyeball.

Vision was: R.E., 20/20; L.E., 20/100, correctible to 20/50. The pupils reacted to light and accommodation; the left pupil was smaller than the right.

Diagnosis. Generalized von Recklinghausen's disease, including left eyelid and eyeball. Plastic correction of left upper lid was recommended.

Operative procedure. The procedure carried out followed no recognized pattern, but

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Fig. 3-1 (Kulvin). *Essential steps in the surgical repair of the lid in Case 1 (figs. 3-1 to 3-6).* The large lipomatous mass in the zygomatic region was removed. The skin was undermined and drawn together and sutured.

was a combination of Hunt-Tansley method with some necessary modifications being added as we continued.
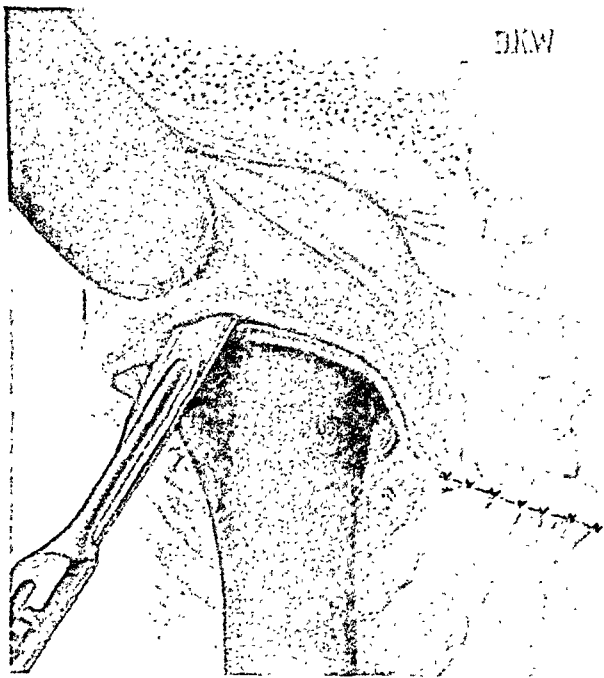
Fig. 3-2 (Kulvin). The upper lid was split, separating the tarsus and mucous membrane from the orbicularis and skin.

First, the large lipomatous mass in the zygomatic region was removed and the skin was undermined and drawn together and sutured (fig. 3-1).

The upper lid was split in the gray line (which was markedly thickened) across its entire length, separating the tarsus and mucous membrane from the orbicularis and skin (fig 3-2). The inner section of the lid was seen to be markedly enlarged and thickened. The thickened mass of tissue lying intermedially was removed as completely as possible. A wedge-shaped piece of tarsus and membrane was mapped out and removed (fig. 3-3) and the edges were approximated with silk beginning up near the fornix and going down to the lid margin (fig. 3-4). After the repair of the inner section, a large redundant skin surface was seen to be
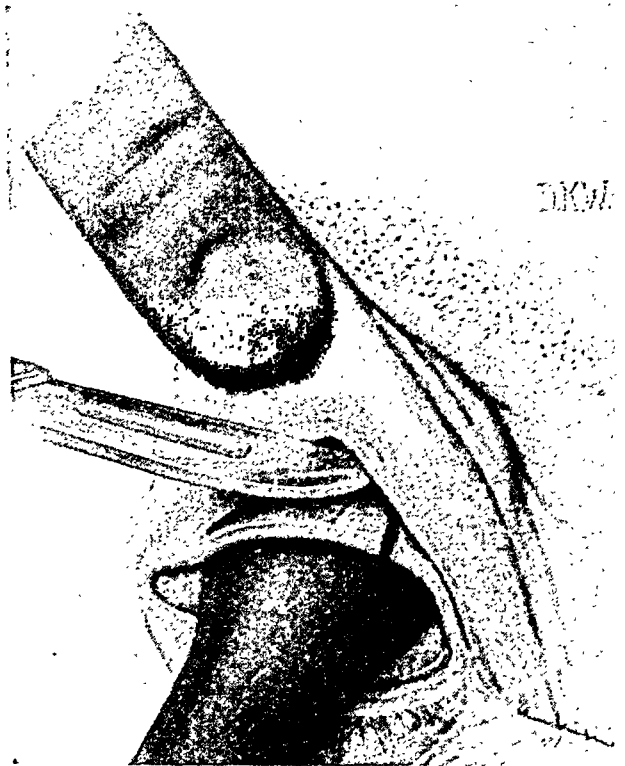
Fig. 3-3 (Kulvin). A wedge-shaped piece of tarsus and membrane was mapped out and removed.

present. A plastic correction of the outer lid surface was now carried out.

An incision was made 3 mm. above the lid margin, extending from each canthus to the midline and leaving a strip of tissue, 4 mm.

wide, between the incisions. The incisions were carried up to the orbital margin just below the hairline perpendicular to each other, and the incision lines were joined (fig. 3-5).

A curved incision joined the outer ex-
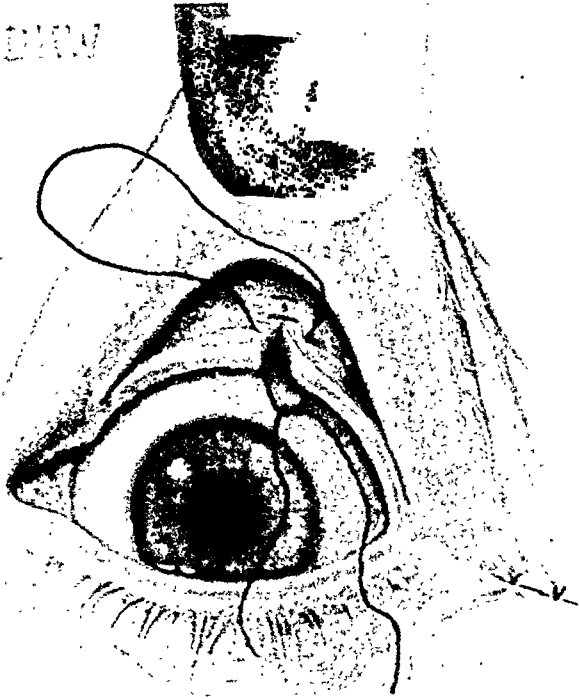
Fig. 3-4 (Kulvin). The edges were approximated with silk beginning up near the fornix and going down to the lid margin.

tremity of the incision at the lid margin with the perpendicular incision, making a triangular flap of skin which was removed. The ribbon of skin was dissected down to the lid margin. A double-armed silk suture was carried through the upper end of the ribbon strip. The cut edges were united with silk sutures. A stab incision was made 3 mm. above the eyebrow and tunnelled beneath the eyebrow down to the upper edge of the strip. The ribbon was drawn up by the sutures through the incision in the forehead, cut off flush with the skin, and fastened there by several silk sutures. The incision at the gray line was closed by interrupted silk sutures (fig. 3-6). Hot saline gauze dressings were applied because the skin appeared discolored—rubber drains were inserted for the purpose of continuous saline drip—oil
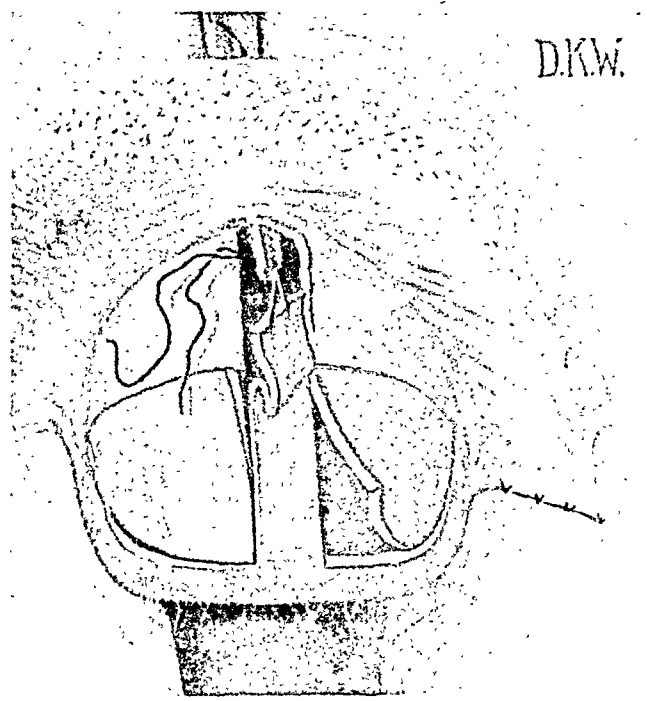
Fig. 3-5 (Kulvin). The incisions were carried up to the orbital margin just below the hairline, perpendicular to each other, and the incisions were joined.

silk covering was applied over this and the eye bandaged. Sloughing of the epithelium took place, with regeneration by granulation and scar formation. On August 5, 1940, the patient was discharged with the advice that further surgery was needed (fig. 4).

Pathologic report. The pathologic specimen was described by Dr. Robert Schreck,
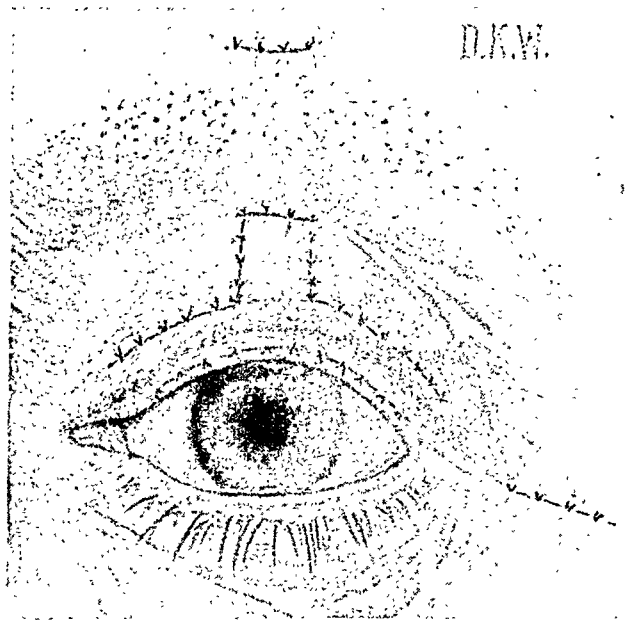
Fig. 3-6 (Kulvin). Placement of the sutures.

Fig. 4 (Kulvin). *Case 1*. Postoperative
appearance.

as consisting of normal epidermis, beneath
which were numerous, irregularly distribu-
ted, small fibroblasts with a small number of
intercellular collagenous fibers. The nuclei
of the fibroblasts were elongated, small, and
stained lightly. There was no inflammatory
exudate. The fibroblasts surrounded and in-
filtrated the normal glands of the corium and
subcutaneous tissue. The pathologic diagno-
sis was neurofibroma (figs. 5 and 6).

Second operation. The patient was re-
admitted on October 21, 1940, for removal
of a tumor mass involving the left sclera
and extending onto the cornea, well shown
in Figure 7.

On October 29, 1940, the operation was
intended to be an enucleation but, after in-
cising the conjunctiva and laying it back,
the mass was found to be easily shelled
away from its scleral bed and removed. No
infiltration of the sclera was found. The
blood supply to this mass from the inferior
pole of the eyeball was marked.

The specimen as described by Dr. Robert
Schreck consisted of a bundle of young
fibroblasts having small elongated lepto-
chromatic nuclei. A moderate amount of in-
terstitial collagen fibers was present. In a
few spaces there was a tendency to palisad-

Fig. 5 (Kulvin). Low-power view of section
showing irregularly distributed small fibroblasts,
small amount of intercellular collagen fibers, and
elongated nuclei.
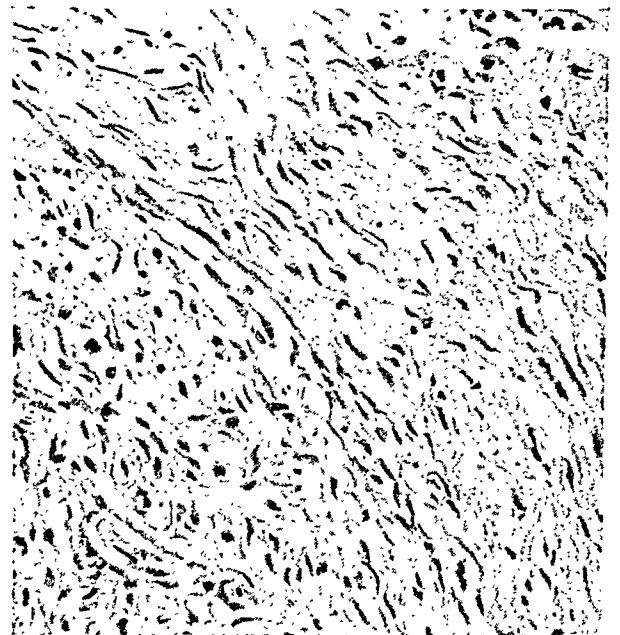
Fig. 6 (Kulvin). High-power view of section
showing lightly stained, elongated nuclei of fibro-
blasts.
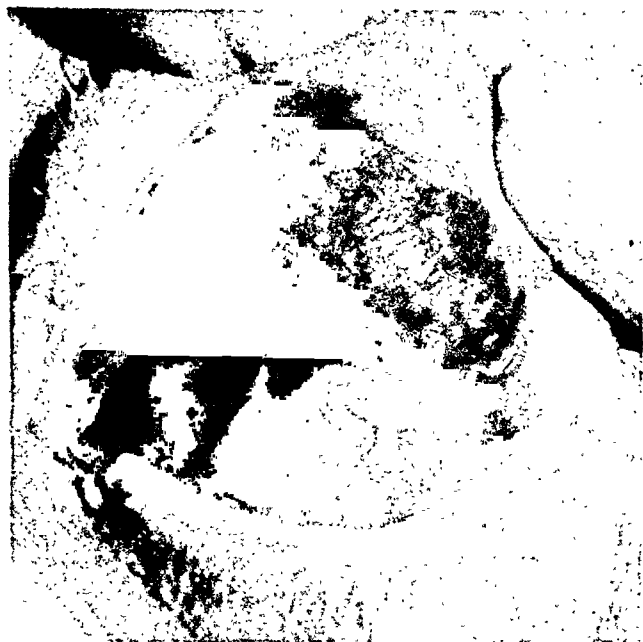
Fig. 7 (Kulvin). *Case 1.* Tumor of the eyeball (May, 1940).

Fig. 8 (Kulvin). Low-power view of section showing (x) palisading of nuclei and (y) moderate amount of interstitial collagen fibers.

ing of the nuclei. The capillaries were quite numerous and lined by young epithelial cells. The tissue was infiltrated with a moderate number of lymphocytes and plasma cells. The diagnosis was neurofibroma with chronic inflammation (figs. 8 and 9).

After a period of convalescence, the mass on the left buccal surface, which to all intents and purposes was also a neurofibroma, was removed (fig. 10).

Microscopic examination revealed a small papillary nodule, with many small and large acini, lined by flattened and cuboidal epithelial cells with uniform nuclei. The
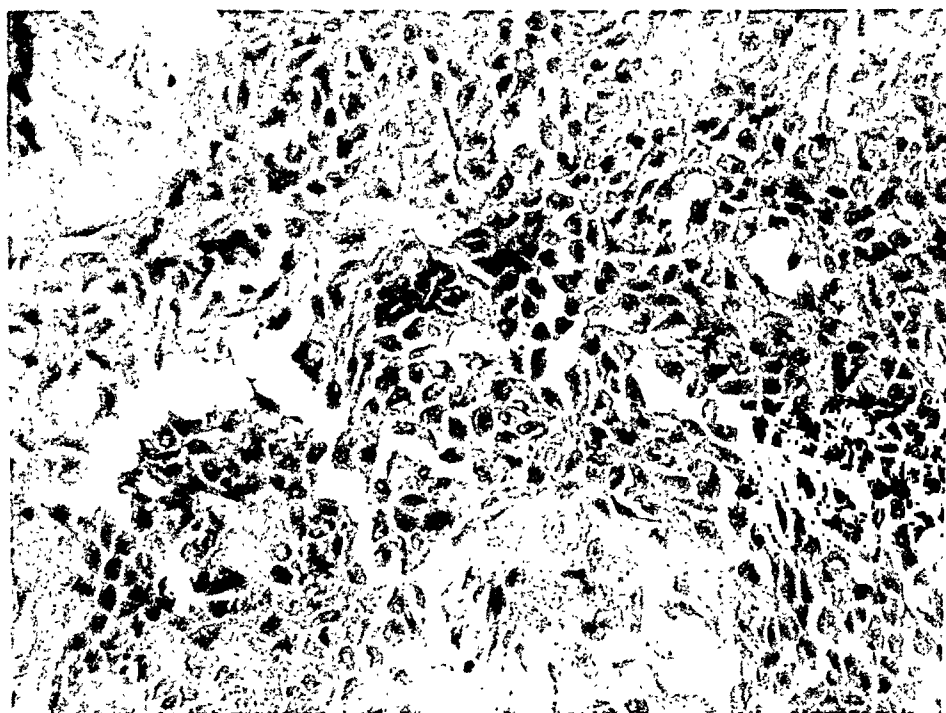
Fig. 9 (Kulvin). High-power view of section showing fibroblasts with palisading of nuclei.

Fig. 10 (Kulvin). Buccal mucosa tumor.
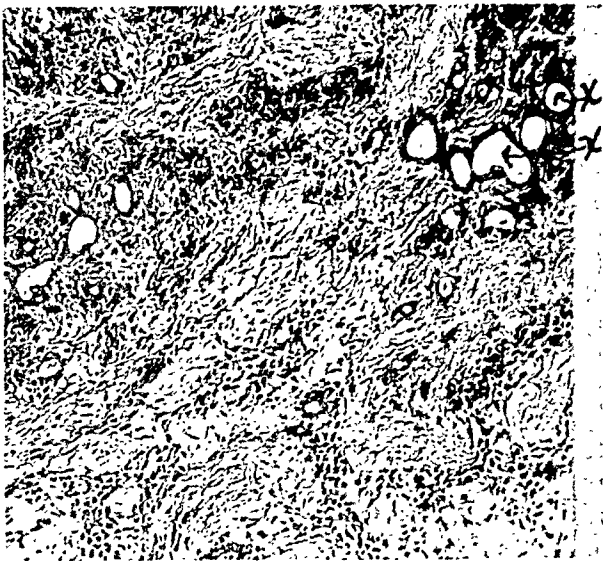
Fig. 11 (Kulvin). Low-power view of section showing (x) many large and small acini. The stroma consists of dense fibrous tissue and a small amount of myxomatous tissue.

Fig. 12 (Kulvin). High-power view of section showing (y) large mucous gland attached to nodule.
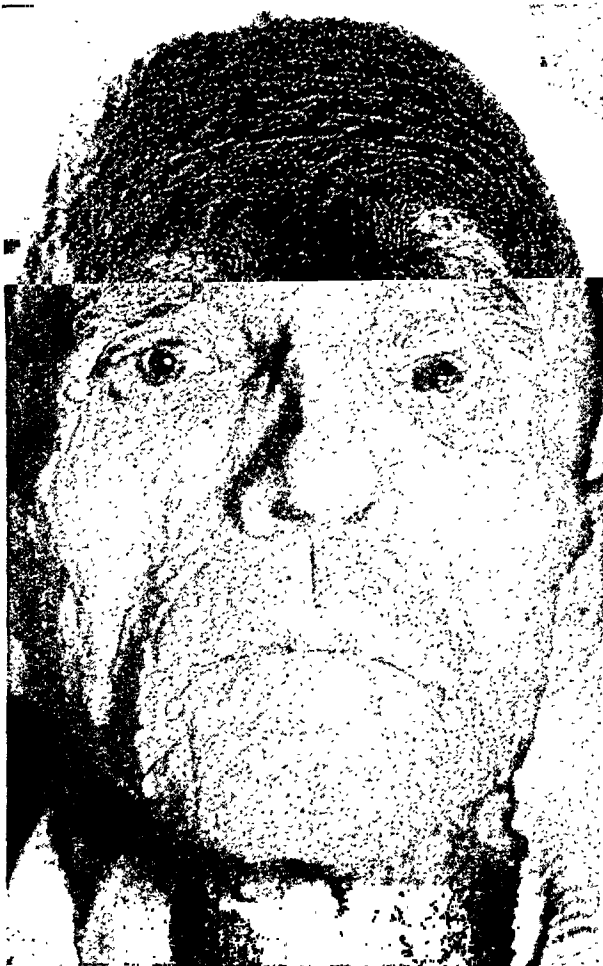
Fig. 13 (Kulvin). *Case 1.* Postoperative appearance on October 8, 1945.

stroma consisted of a moderate amount of dense fibrous tissue and a small amount of myxomatous tissue. The capsule of the nodule was thick. Attached to the nodule was a large mucous gland. The diagnosis was mixed tumor of the salivary gland (figs. 11 and 12). Of course this finding, when a neurofibroma was expected, was quite surprising.

A secondary plastic procedure was done. Some redundant tissue on the globe was removed, synechias were severed, and the ectropion which had developed was repaired. He was discharged on December 23, 1940.

Outcome. The patient was re-admitted on August 6, 1945, for a possible retroperitoneal tumor, possibly fibrosarcoma. On operation, a biopsy was taken which revealed fibrosarcoma. Nothing further was done. His lid showed no recurrence of the tumor and cosmetically was satisfactory (fig. 13).

Fig. 15 (Kulvin). *Case 2.* Neurofibromatosis of the left eye before correction (June 18, 1947).

CASE 2

The second case, seen June 9, 1947, presented a somewhat different problem. The patient, B. C. H., a man, aged 30 years, was admitted on that day to Hines Hospital complaining of drooping of the left eyelid for 22 years. He stated that the drooping lid became completely ptosed after a lid operation in 1937. He had had three operations on the upper lid of the left eye between 1937 and 1946 by a private physician. His past general history was negative except for hemorrhoidectomy in September, 1945.

Physical examination on admission showed numerous soft papular elevations of the skin over his abdomen, neck, and chest (fig. 14).

Eye examination. Vision was: R.E., 20/20; L.E., 20/200, correctible with pinhole to 20/40—2.

Right eye. The anterior segment, media, fundus, tactile tension, and ocular movements were normal.

Left eye. Anterior segment, media, and fundus were normal. The left upper lid was markedly thickened and indurated. The lid margin was three times its normal thickness. No tarsal plate could be felt. The lid was completely ptosed and could not be raised except slightly in the nasal angle by an exceptional effort of the frontalis muscle.

The conjunctival surface of the left upper lid had multiple scars adherent to the under-

Fig. 14 (Kulvin). *Case 2.* Tumors of the skin and café-au-lait pigmentation.

lying tissue. Fine bands of connective tissue ran between the bulbar and palpebral tissue in the upper and outer quadrant of the eyeball. There was a marked soft swelling over the loose skin of the left temple extending to the outer canthus of the left eye. The bone underneath the swelling seemed slightly irregular and the temporal fossa seemed deeper on the left side (fig. 15).

Laboratory. X-ray studies of the left orbit

Fig. 16 (Kulvin). *Case 2.* Postoperative appearance on July 17, 1947, after first surgical procedure and removal of plexiform neuroma from temporal region.

and left temporal fossa failed to reveal any evidence of significant bone abnormalities.

Urinalysis, complete blood count, complement-fixation and Wassermann tests, bleeding and coagulation time were all negative.

Course in hospital. A tumor mass of the left upper lid and left temporal region was removed June 28, 1947 (fig. 16). The pathologist, Dr. W. W. McNamara, described new growth made up of spindle cells, forming interlacing bundles and palisading, imitating nerve sheath. The growth was quite

cellular but with moderate amount of intercellular collagen in some areas. Cells grew diffusely resembling the so-called Antoni

Fig. 17 (Kulvin). Low-power view of section showing spindle-cell growth, interlacing bundles, and palisading. Diffuse cell growth resembles so-called Antoni-type tumor.
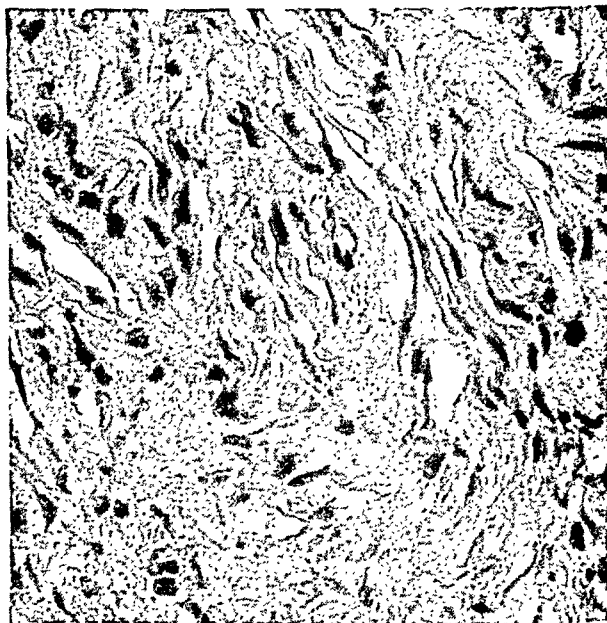
Fig. 18 (Kulvin). High-power view of same section shown in Figure 17.

type of neurogenic tumor. There was no capsule. The diagnosis was neurofibroma (figs. 17 and 18).

On July 23, 1947, a moderate-sized mass

was removed from the left upper lid. The sections showed spindle cells growing in whorls, fairly well vascularized. The diagnosis was neurofibroma (figs. 19 and 20).

These procedures were all preliminary to

Fig. 19 (Kulvin). Low-power section showing (x) spindle cells growing in whorls and (y) vascular section.
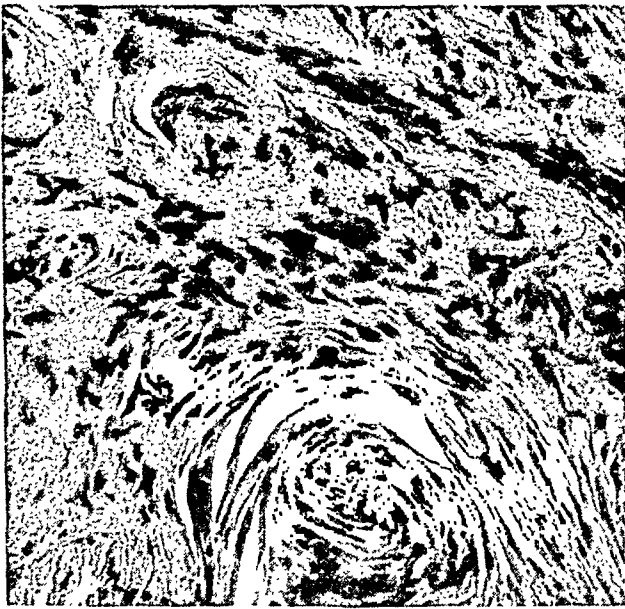
Fig. 20 (Kulvin). High-power view of same section shown in Figure 19.

the next step which consisted of the formation of a new tarsal plate for the upper lid. This was carried out by Dr. H. B. Field in a plastic reconstruction of the left upper lid.·

Operation. A lid spatula was introduced under the upper lid. An incision was made
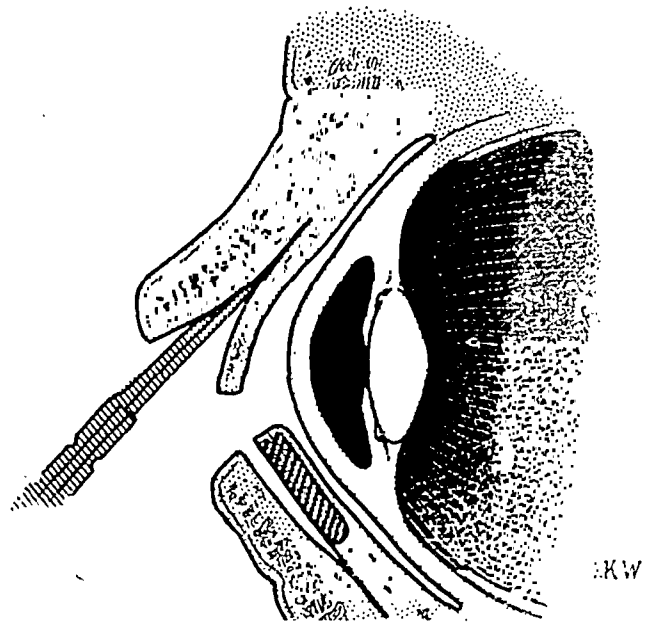
Fig. 21-1 (Kulvin). *Essential steps in the surgical repair of the upper lid in Case 2 (figs. 21-1 to 21-5).* An incision was made at the white line of the lid margin from the outer to the inner canthus.

at the lid margin, from the inner to the outer canthus, separating the conjunctiva from the remnants of tarsal plate and skin. The incision was extended, by blunt and sharp dissection and up into the region of the lid fold,
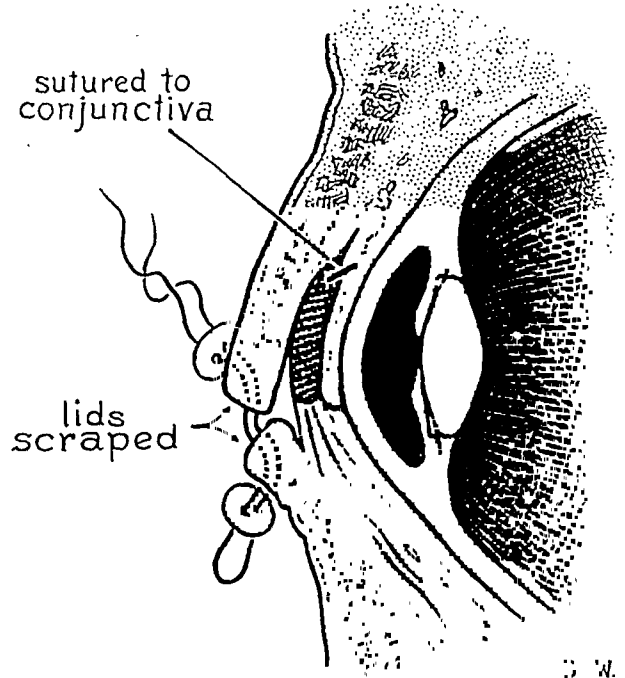
Fig. 21-2 (Kulvin). A sliding flap was slid into position across the palpebral fissure and anchored to the conjunctiva.
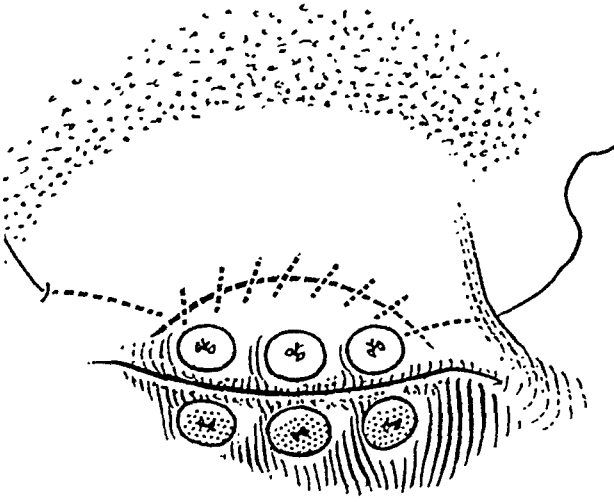
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tarsal plate
sutured to conjunctiva

Fig. 21-3 (Kulvin). Tarsal plate was sutured to
the conjunctiva.

D.K.Winter -48
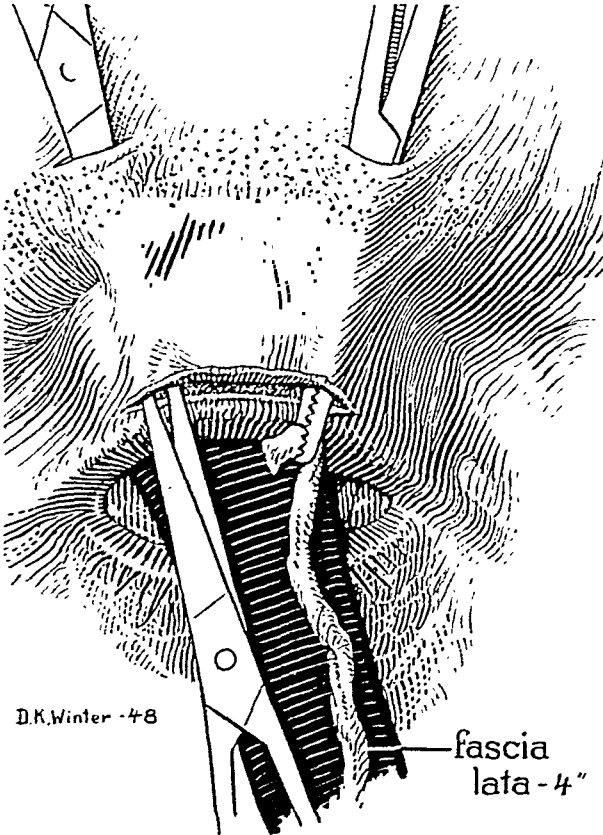
fascia
lata - 4"

Fig. 21-4 (Kulvin). Repair of ptosis was carried
out by the introduction of a fascia-lata sling.

incision was made at the white line of the lid
margin from the outer to the inner canthus
(fig. 21-1).

The conjunctiva and tarsal plate were
separated from the lid through this incision
but were left at their attachment inferiorly.

This comprised a sliding flap which was
slid into position across the palpebral fissure
and anchored to the conjunctiva of the su-
perior lid at its inferior portion (fig. 21-2).

A continuous No. 1, black silk suture was
introduced 1 cm. temporally to the lateral
canthus, and this was brought into the tarsal
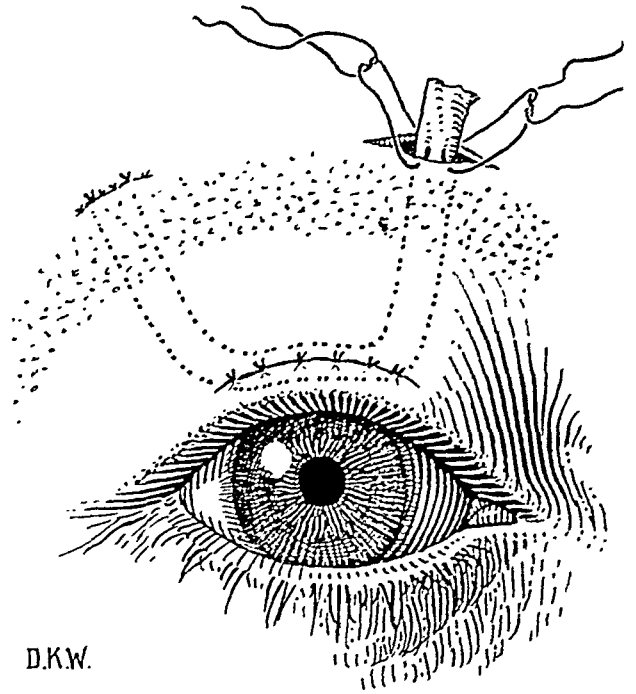
D.K.W.

Fig. 21-5 (Kulvin). Suturing after placement
of fascia-lata sling.

flap from the lower lid, comprising a run-
ning suture between the tarsal plate of the
lower lid and conjunctival flap of the upper
lid. This suture was carried the entire extent
of the flap and emerged 1 cm. nasally to the
nasal canthus and on the side of the nose.

The lid margins were then approximated
by means of three marginal notchings of the
skin proper and mattress sutures were placed
from the inferior lid to the superior lid,
tightly binding these exposed notchings to-
gether, so that complete union of the skin
part of the lids was established at these
three points. Drains were inserted at both

to the point which would be approximately
2 cm. from the lid margin. A similar maneu-
ver was accomplished in the lower lid, and an

lateral and internal canthi. A plastic silk dressing with pressure bandage was placed over this eye (fig. 21-3).

The pathologic examination showed the specimen to be similar to the neurofibromas previously described.

After two months' convalescence the tarsorrhaphy was opened, a slight repair of the lower lid was accomplished and the symblepharon present was released on November 19th.

The completion of the repair of the ptosis was carried out on November 26th with the introduction of a fascia-lata sling by Dr. H. B. Field.

Stage 1. A strip of fascia lata, 4 inches long, was excised from the left thigh.

Stage 2. An incision was made parallel to the upper lid margin of the left eye, 5 mm. from the lash line. A cataract knife was introduced and inserted up through the upper lid extending up to the upper edge of the brow. Two tunnels were prepared (fig. 21-4). The strips of fascia lata were inserted through the tunnels forming a suspension of the lid from the incision just above the lid margin. Both ends of the fascia lata were sutured to the periosteum in the brow region. The skin incisions were closed with black silk. A Buller shield with vaseline was used as an eye dressing (fig. 21-5).

Since some excess fibromatous tissue remained, this was removed January 12, 1948, and the defect was repaired by Dr. James E. Lebensohn. Some redundant bulbar conjunctiva and thickened mucosa were reduced with Ziegler cautery. A repeat cautery was required on February 1, 1948, for the persistent ectropion—this practically disappeared after the punctures. The palpebral
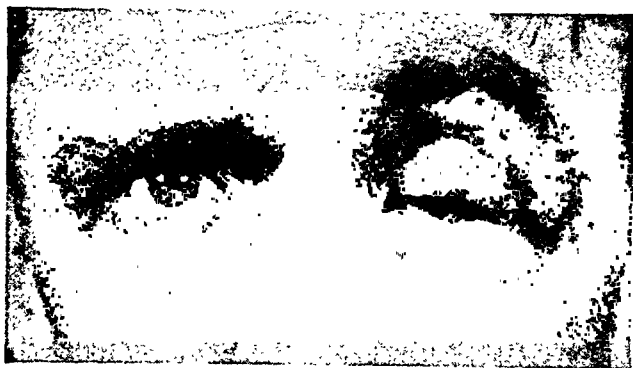
Fig. 22 (Kulvin). *Case 2.* Appearance of patient after completion of surgical procedures.

conjunctiva was greatly thickened and arranged in vertical folds. The lower lid showed a thickened conjunctiva arranged in papillary form (fig. 22).

Manifest refraction showed: R.E., 20/15; L.E., 20/50. There was an esophoria of three diopters for distance and near—and a right hyperphoria of two diopters.

CONCLUSIONS

In conclusion, we are aware that the eye results obtained were not artistically perfect. Unquestionably a cosmetic improvement was obtained, in comparison with the situation as it existed for so many years. In the second case, a readjustment of the fascial sling might be undertaken if no further contraction occurs. It must be remembered, however, that the many previous operative interferences certainly added to the difficulties to be overcome.

Veterans Administration Hospital.

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OPHTHALMIC MINIATURE

Here is the formula useful in both chalazion and styes. Take frankincense and myrrh, of each, one dram; gum labdanum, alum, Armenian saltpeter, of each one-fourth dram. Mix thoroughly with a sufficiency of lilies and old olive oil, and apply the mixture. If these remedies fail, the lid and tumor must be deeply incised with a round-headed lancet and the chalazion scraped out with a spoon at the end of the sound. When the operative wound is large and deep and the parts flaccid, the lips of the wound should be drawn together in the middle by a suture, after which dust on some yellow powder. When the tumor is on the inner surface of the lid, the latter should be everted and the tumor removed from its inner surface. Then order the eye to be irrigated with warm water.

Memorandum Book of a Tenth-Century Oculist
Translated by Casey A. Wood.

A SURVEY OF ANTERIOR SEGMENT PHOTOGRAPHY

EDWIN S. WRIGHT, M.D.

Los Angeles, California

At the present there are a number of methods in use for photographing the anterior segment of the eye. In the hands of its proponent each method is undoubtedly capable of producing good photographs. Many are called "simple methods" and some, perhaps, are. But, in general, the enthusiastic clinical photographer has a much greater technical knowledge of photography than the average ophthalmologist and not all methods advocated are equally easy to use. It would, therefore, seem advantageous to review the several methods in general use and to evaluate them with respect to simplicity, economy, general adaptability, and availability. In order adequately to explore the possibilities of the methods and to understand better the problems involved, an elementary knowledge of photographic optics, filters, film, and lighting is desirable. Optics should present no problem to the ophthalmologist, since the same formulas with which he is already familiar are used in spectacles and geometric optics. The other items will be of interest also, since a knowledge of them will improve his photographic technique in general, and materially increase his enjoyment of this fascinating hobby.

A. PHOTOGRAPHIC OPTICS

The basic relationship of object, lens, and image is expressed in the simple formula

$$\frac{1}{F} = \frac{1}{u} + \frac{1}{v}$$

where F equals the focal length of the lens, u equals the object to lens distance, and v equals the lens to film distance.

For practical purposes, u and v are measured at the lens diaphragm, for good lenses are not simple, thin lenses but are combinations of various lens elements often having considerable length to the assembly. Their equivalent plane is usually at the diaphragm.

EXAMPLE

With a certain lens, the distance from lens to film is 6 inches when focused on an object 12 feet away. What is the focal length of the lens?

12 feet = 144 inches

$$\frac{1}{F} = \frac{1}{144} + \frac{1}{6}$$

$$F = 5.76 \text{ inches}$$

The image size is expressed in the formula

$$R = \frac{\text{object size}}{\text{image size}} = \frac{u}{v}$$

where R is the reproduction ratio.

EXAMPLE

A camera is focused on an object 20 inches away. The lens extension is 5 inches. How much will the object be reduced on the film?

$$R = \frac{20}{5} = 4 \text{ times.}$$

If the object is 8 inches high, what will be the image size?

$$4 = \frac{8}{i}$$

Image size = 2 inches.

The power of a lens combination is expressed by

$$P = P_1 + P_2$$

where P_1 equals the power of the photographic lens and P_2 equals the power of the supplemental lens. The distance between the two may be disregarded due to the short distance between them and the relatively long focal lengths.

EXAMPLE

What is the power and focal length of a 50-mm. lens with a supplemental lens of 200-mm. focal length (plus 5 lens)?

$$P = \frac{1,000}{50} + \frac{1,000}{200} = + 25 \text{ lens,}$$

or

$$\frac{1,000}{25} = 40 \text{ mm.}$$

The ratio of the focal length to the diameter of a lens determines its "f" number.
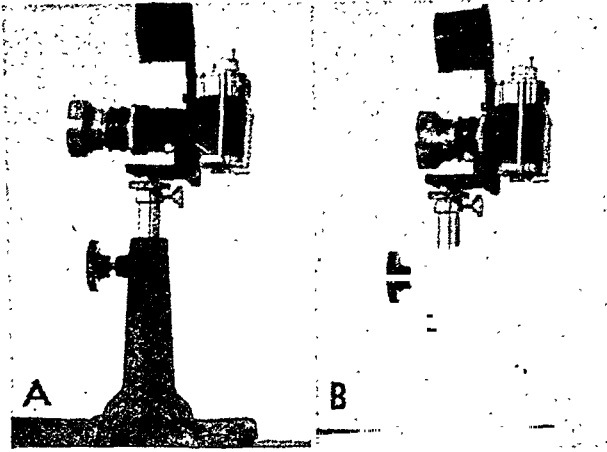
Figs. 1 A and B (Wright). Camera and copy attachment (A) with 35-mm. extension tube and (B) without extension tube.

The speed of a lens is inversely proportional to the square of the "f" number and the exposure required is directly proportional to the square of the "f" number. The amount of light received by the film is the product of the illumination and time of exposure; hence, if the lens speed is doubled, the exposure time is halved. Therefore, if the "f" stop is changed from f:4 to f:8, four times the exposure time must be used.

On the camera, each stop from higher to lower number doubles the amount of exposure of its predecessor. The actual amount of light passing through a lens is less than unity since each glass-air surface in the lens reflects back 5 percent of the light falling upon it. The number of glass-air surfaces in most lenses is 6 or 8, and exposure tables of lens manufacturers compensate for this. The "f" number marked is the proper one to use.

Stray light in lenses occurs from internal reflections at glass-air surfaces and may cause shadows to lighten the picture and cause poor contrast. Worse causes of poor contrast are fingerprints and dust on the lens. Coating of the lenses eliminates "ghosts," flare spots, and stray light. It increases the light transmission but its principal value lies in the fact that it improves contrast.
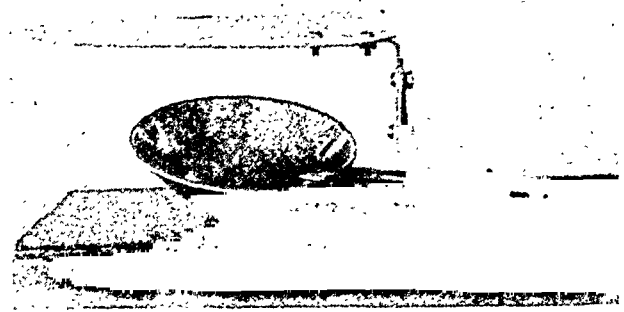
Fig. 1 C (Wright). Hand flashgun with bracket and two transparent X-ray films with tissue paper (diffuser) in between. This is to protect the patient if bulb shatters. Flashgun is shown resting on camera platform.

The speed of a lens varies with the bellows extension. Since the f number is accurate only when the lens is set for infinity, it is highly important to know the effective aperture when the lens is used for close up work. This is found by the formula

$$\text{Effective Aperture} = \frac{V}{F} \times f$$

where V = lens film distance
F = focal length of lens
f = marked lens aperture

EXAMPLE

A 4-inch lens is focused on an object 20 inches away. If the lens extension is 7 inches and the aperture is f8, what is the effective aperture?

$$EA = \frac{7}{4} \times 8 = f14$$

(To measure the lens extension, measure the amount it moves forward from the infinity mark and add it to the focal length.)
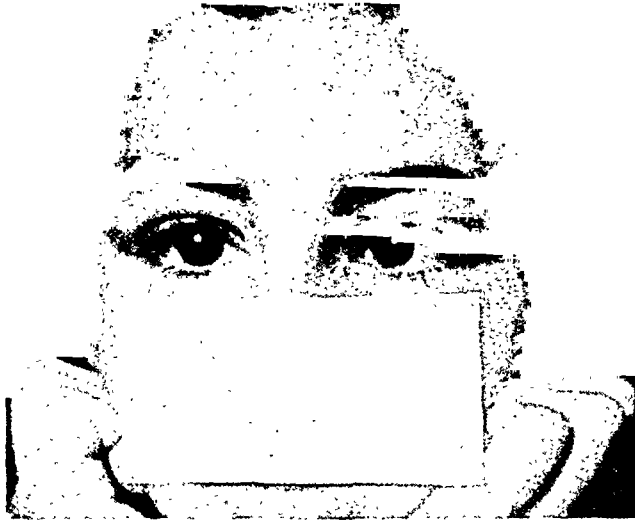
Fig. 2 A (Wright). Black and white copy of Kodachrome showing full face when using no extension tube.

Fig. 2 B (Wright). Black and white copy of Kodachrome showing use of 11-mm. extension tube.

If a supplemental lens is used to bring near objects into focus instead of a lens extension, then the "f" number does not change *provided the lens is set for infinity.* The exposure correction can be computed directly from the formula

$$E = E_1 \times \frac{v^2}{f^2}$$

where E = correct exposure
E_1 = indicated exposure (by meter, and so forth)
v = lens film distance
f = focal length of lens

To avoid computations, the *Effective Lens Aperture Kodaguide* may be purchased for 10 cents and automatically performs them.

Figs. 2 C and D (Wright). Black and white copy of Kodachrome photomicrograph, using same apparatus as in 2 A and B. (C) Anterior synechia. (D) Diabetic retinopathy.

Fig. 3 (Wright). Ziegler cautery for entropion (from a color transparency).

Supplemental lenses are weak meniscus lenses which are used to focus the object closer and enlarge the image. A plus supplemental lens shortens the focal length; whereas, a minus lens lengthens it, and, therefore, requires a longer bellows extension. Both enlarge the image.

A supplemental lens attached to a camera focused at infinity will focus the camera on a plane whose distance from the camera is equal to the focal length of the supplemental lens used.

EXAMPLE

A plus 5D. lens will focus an infinity-set camera at 8 inches. Spectacle (meniscus)

Fig. 4 (Wright). Vernal catarrh.

lenses obtained from the optician are quite satisfactory in lower powers. Camera lens corrections are not upset by the supplemental lens (except for negligible chromatic aberration) when the supplemental lens is used with the camera set for infinity. To find the magnification caused by the additional lens, the formula is

$$Ratio = \frac{V}{U}$$

where V equals camera lens-film distance and U equals supplementary lens-object distance

50-mm. lens
200-mm. supplemental lens

$$R = \frac{50}{200} \text{ or } \frac{1}{4} \text{ the size.}$$

The depth of field is that area on each side of the focused plane which will appear acceptably sharp in the picture. It varies according to the focal length, f-number of the lens, lens-subject distance, and acceptable degree of sharpness (circle of confusion). In general, the smaller the focal length and the f-number, the greater is the depth of field. A general rule is that a lens performs best at one half its maximum aperture (twice its f-number).

Correct viewing distance aids in perspective. The picture should be viewed from the center of perspective, which is the point originally occupied by the camera lens. Only so will the relative angular dimensions be correctly reproduced. A small transparency viewed through a magnifier having a focal length equal to the taking lens suddenly acquires an enormous improvement in naturalness. A picture taken with a 5-inch lens and enlarged three times should be viewed at 15 inches and thereby appears more realistic. Pictures projected on a screen should be viewed at the projector-screen distance times the ratio of camera lens-focal length to projector-focal length. Departure from this relation by more than twice markedly reduces the realistic reproduction.

B. Filters

Filters are transparent pieces of colored glass, or gelatin between glass, mounted so that they can be attached to the camera lens. In ophthalmic photography they are used, when necessary, to enhance certain color tones (warmth), or convert different light temperatures to the film requirements. They are not always necessary but are specified by the manufacturer of the film whose recommendations should be carefully followed.

is rarely indicated. Only color film can show the details of inflammation, pigmentation, and fine structure. For 35-mm. cameras, Eastman's Kodachrome Type A or Kodachrome, Daylight Type, and Ansco's Daylight or Tungsten film are available. For larger cameras, each company provides sheet film in both daylight and tungsten types. Such film is for positive transparencies. Kodachrome film, either daylight or tungsten type (K828), may be used with an
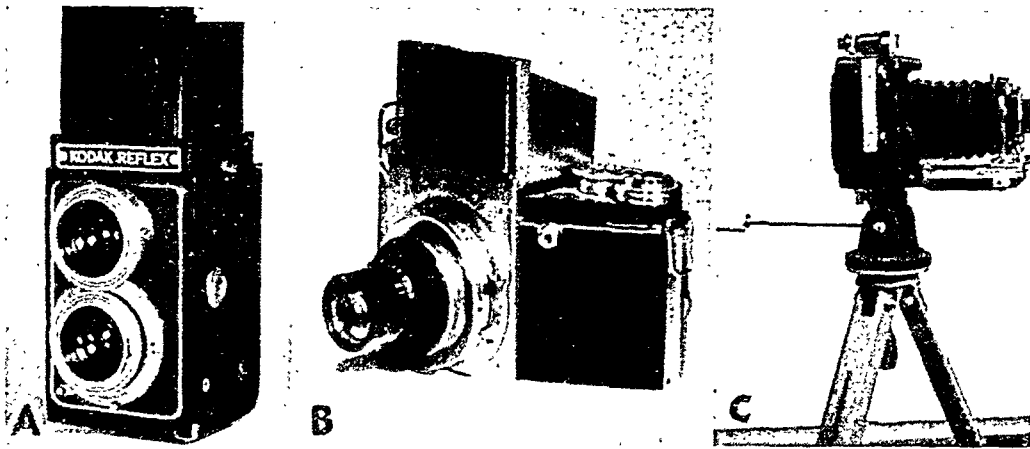
Fig. 5 (Wright). Suitable types of cameras. (A) Twin-lens reflex. (B) Single-lens reflex. (C) Double extension bellows.

In addition, Polaroid filters may be used to diminish corneal reflections. White light striking a glass surface at an angle of incidence of 57 degrees from the normal is perfectly polarized. This is one of the three ways in which natural light is polarized and the chief one with respect to the cornea. At angles other than 57 degrees the light is partially polarized. The Polaroid filter stops the polarized (glare) light and passes the unpolarized (diffuse) light when it is turned so that the polarizing element has its axis at right angles to the axis of the polarized light. This position is really determined by looking at the cornea through the filter and turning it until the glare disappears. Since the filter stops part of the light, the exposure must be greater (roughly, one full stop).

C. Film

The advantages of color photography are so great that the use of black and white film

adapter in larger cameras to obtain the economy of small-size film and positive transparency. In addition, roll film may be used although Kodacolor is a negative transparency. Preference for one or the other is an individual matter.

D. Lighting

There are several methods. One is the use of flood lights of the recommended color temperature for the film in use. This method can produce good pictures but has many disadvantages, namely, excessive heat, glare, and bulkiness. Moreover, a child will not readily tolerate the discomfort, and various switches are needed to focus in dim light and then turn on full brilliance for the picture.

A second method is the use of a projector lamp (that is, a T10) enclosed in a tube. This can be combined with a camera shutter to give just the right exposure time but is also bulky and requires an extra focusing
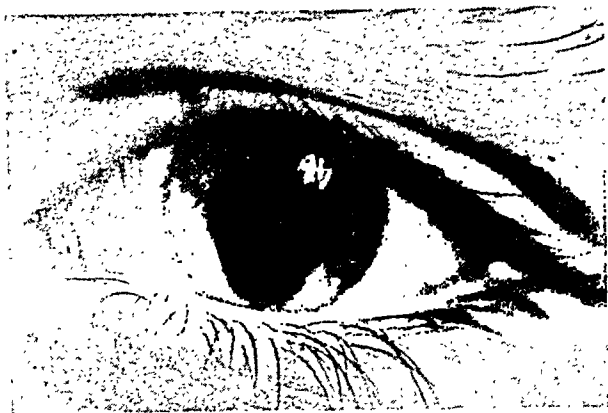
Fig. 6 (Wright). Congenital coloboma of iris (from a color transparency taken with a single-lens reflex camera).

light. It is not so suitable for full face. It may require a filter to convert to the correct color temperature.

A third method is the use of flash bulbs. This includes stroboscopic flash bulbs. This method entails some expense for each bulb but is virtually fool-proof. Provided the camera setting is proper, a good picture is obtained with every exposure. There are suitable bulbs for each film. The Speed Midget bulb with a time of exposure of 1/200 seconds gives adequate light, stops motion of the eye, and requires no filter with Kodachrome, tungsten type film. Used with an f:2.8 lens (50-mm. focal length) with a 35-mm. extension tube, an aperture of f:8 for brown eyes and f:11 for blue eyes has proved satisfactory when the lamp is held at 14 to 16 inches. One test roll will quickly establish the optimum for the combination used. With Ansco tungsten film, a filter is necessary to eliminate excessive blueness; with Kodachrome tungsten film, no filter is required. With daylight type film and blue bulbs, no filter is required.

E. The camera

The problem is the conversion of a lens system whose near point is 3 to 4 feet to a system that will focus at 6 to 8 inches. The most universally used cameras are those of the miniature type. They have short focal length, speedy, highly corrected lenses, are compact, and have a wide variety of auxil-

iary lenses and other equipment. In addition, their transparencies are readily projected and make excellent slides. They range in size from 35 mm. to 2¼ by 3¼-inch machines.

There are two general types. One employs an eye level or split-field rangefinder, that is, the Leica, Contax, Clarus, Argus, and so forth. To adapt these for eye photography a copy attachment is used, and focusing is done with the ground glass of the copy attachment after which the camera is slid into place and the picture made. The camera is focused with the lens wide open and the lens must be stopped-down prior to releasing the shutter. This method is slow and involves many steps but for the owner of this type of camera it is perfectly satisfactory in results.

The second type is a single lens reflex camera. Here, focusing is done through the taking lens, with the ground glass already in the camera. Either a supplementary lens or an extension tube is used for the close up, just as in the previous system, except that here focusing requires only one step. The lens must be stopped down after focusing prior to releasing the shutter. This method is considerably faster than the preceding one. Examples of such cameras are the Exacta, Graflex, Korelle, and Praktiflex. The Graflex has an automatic stop-down which enables wide open focusing and automatic stop-down on snapping the picture. It is the simplest of all.

A third method is the use of a twin-lens reflex camera such as Rolleiflex, Ciroflex, Kodak, and so forth. Here the focusing is done directly and no stop-down is required, as the taking lens is simply left at the proper setting (f-stop). This would be ideal except for the problem of parallax. The viewing lens is above the taking lens and for close-up work does not correct for the difference. There are attachments which overcome this; or, after focusing, the camera may be elevated the required distance. To adapt this fine camera for eye work, a +5D. meniscus lens is placed on the lower lens by use of an

adapter ring and a +5D. lens, with a 14-degree (24.5 diopter) prism ground in it, is placed base down in front of the viewing lens. These may be obtained from the optician. With the object at 8 inches, very slight focusing is required and the normal lens setting is used. An 828 film in a proper adapter makes this a precision instrument for fine miniature films. The transparency can be projected in a 35-mm. standard projector. For full-face shots the supplemental lenses are removed and the regular focus at 3½ feet is used.

The fourth method is the use of a camera with a double extension bellows. Focusing is done by viewing through the ground glass at the back of the camera, after which film plate is inserted, lens stopped-down, and picture made. This is a perfectly feasible method but quite slow and subject to blur if the camera is moved while inserting film plate.

With the fast exposure of a flash bulb, elaborate fixation of the patient's head is not necessary. The chin and head rest of the slit-lamp are sufficient, and there is room behind the slitlamp to mount a camera. It takes only a moment to position the patient, focus, and flash the picture. Synchronization is not necessary. Open flash (bulb) is preferable because the distance of the flash gun (held in the hand) can be varied at will. Gener-

Fig. 7 (Wright). Subconjunctival aqueous in an iridencleisis (from a color transparency).

ally, a distance of 14 inches and partly to the side is best. Lighting directly in front of the eye (at the camera) does not give as good texture definition as cross lighting from the side.

SUMMARY

An elementary review of photographic optics is presented. Lighting methods are enumerated, methods of photography of the anterior segment of the eye are detailed, and advantages and disadvantages are set forth. A method of converting any ordinary camera to anterior segment photography is described.

511 South Bonnie Brae Street (5).

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TALC GRANULOMAS OF THE EYE*

G. L. McCormick, M.D., W. L. Macaulay, M.D.,
and G. E. Miller, M.D.

Marshfield, Wisconsin

In 1912 Lambert[6] first demonstrated the ability of foreign-body substances to stimulate the production of giant cells in tissue cultures. Two decades later Antopol[1] called attention to the clinical and pathologic significance of Lycopodium powder granulomas in surgery and suggested that talcum powder was capable of producing the same reaction. Since then, a fair number of reports have appeared in the literature on granulomatous reactions resulting from the accidental introduction of Lycopodium spores or talcum powder into surgical wounds. As a rule, the gloved hand of the operator is the source of contamination. The abdominal cavity has entertained the greatest number of the reported talc granulomas, but this site is by no means exclusive. Other portions of the body where such lesions have been found include the scalp,[5] brain,[4] maxillary sinus,[4] neck,[1] breast,[1] pleura,[10] bladder neck,[1] epididymis,[1] cervix,[8] vagina,[9] rectum,[7] and other regions. To our knowledge a foreign body granuloma of the eye due to talcum powder has not previously been recognized and consequently is worthy of a report in the literature.

CASE REPORT

History. Mrs. C. J., a white woman, aged 32 years, was seen on September 23, 1947, complaining of rapidly growing tumor masses on the temporal and nasal portions of the right eye. She claimed the lesions were first noticed about two weeks before. Their exact duration was unknown, but the patient emphatically denied the possibility of their existence a month previously. In fact, aside from alarm occasioned by the rapid growth of the tumors, the patient was annoyed be-

cause each of her aquaintances, when met, was startled and inquisitive about her eye. There were no subjective symptoms. There was no history of recent injury.

A review of her past history revealed that on August 18, 1933, a right convergent strabismus, originating in early childhood, had been corrected by resection of the right external rectus muscle and partial tenotomy of the right internal rectus muscle. The post-operative course was apparently uneventful; and, to the patient's knowledge, wound healing was not abnormally prolonged. Other incidences in the past history included an appendectomy in 1932, a Neisserian vulvovaginitis and urethritis associated with a Bartholin gland abcess in 1934, and bronchopneumonia in 1941.

Examination of the right eye disclosed smooth, semitranslucent, grayish tumor masses temporally and nasally at the sites of previous muscle surgery (fig. 1). The mass on the temporal side was larger and measured 10 mm. by 4 mm. The other was only slightly smaller. There was slight injection of the adjacent sclera, and telangi-

Fig. 1 (McCormick, Macaulay, and Miller). Showing semitranslucent tumor mass on temporal portion of right eye at site of previous eye muscle surgery.

ectatic vessels coursed over the tumors. The differential diagnosis this time included keloid, sarcoidosis, and lymphoblastoma. The blood and urine were normal. The serologic test for syphilis was negative. There were no lesions of the skin. Roentgenograms of the chest as well as the small bones of the hands and feet revealed no evidence of sarcoidosis.

On September 24, 1947, a biopsy was performed. The pathologic findings were as follows.* "The sections consist of dense fibrous connective tissue in which are embedded nodules of epithelioid cells. A few poorly developed multinuclear giant cells are

Fig. 2 (McCormick, Macaulay, and Miller). Showing typical foreign-body reaction consisting of dense fibrous tissue, epithelioid cells, and a few giant cells. Small crystals (not visible at this magnification) are scattered throughout this section. (×98.)

present. Many of the nodules contain particles of unstainable crystalline material which is birefringent and which in size and shape resembles talc" (figs. 2 and 3).

On October 14, 1947, the conjunctiva was reflected and both masses were surgically excised. The pathologic report was: "The findings in this specimen are similar to those of the previous specimen except there is some lymphocytic infiltrate associated with the epithelioid nodes. The pathologic changes

* We are indebted to Dr. Hermann Pinkus, Monroe, Michigan, for preparation and interpretation of the histologic specimens.

resemble those found in sarcoidosis, but apparently represent a tissue reaction to the foreign crystalline material which is probably talcum powder."

Following surgery, convalescence was un-

Fig. 3 (McCormick, Macaulay, and Miller). This section shows a large giant cell enclosing a talc crystal. (×330.)

eventful and the wounds healed promptly. Follow-up examinations at 2 and 6 months showed no recurrence. A slight roughness persisted at the excision sites.

DISCUSSION

This case is of interest from several standpoints. Although talcum powder has been known to produce foreign-body granulomas in almost all tissues of the body, this is the first recorded case of such a lesion occurring in the eye. There are several reasons why this apparent rarity may be valid. The operative field in ocular surgery is small. The manipulations are minute. Instruments provide accessibility. The possibility of the accidental implantation of talc in eye surgery is considerably more remote than, for example, in abdominal surgery.

On the other hand, missed diagnosis may in some degree account for the rarity of this lesion in the eye. It must be admitted that the medical profession as a whole is still not entirely aware of the dangerous potentialities of talcum powder in surgery. It is known that many talc granulomas found

elsewhere in the body were originally diagnosed as tuberculosis or some other disease, and only after restudy was the true nature of the lesions disclosed. It has been suggested[2] that the granulomatous masses often seen for many weeks at the site of eye muscle surgery might conceivably be foreign-body granulomas due to talc. These lesions should be investigated histologically.

The fact that some of these tumors may assume a sarcoidlike structure microscopically has already been pointed out by German.[5]

A most unusual feature in this case is the prolonged interval (14 years) from the original eye muscle surgery (the year of Antopol's first report) when talc presumably was implanted to the first signs of growth of the granuloma. In analyzing 37 cases of talc granuloma, most of which developed following abdominal operations, Eiseman and others[3] pointed out that the time interval between the original operation and the appearance of symptoms varied from the immediate postoperative period to 10 years. German's patient[5] first developed signs of activity 14 years after the original wound. Lichtman and others[7] reported that a nodule which first appeared in a scar on the forehead 36 years after the original laceration was found microscopically to contain talc. Hence, although one may expect symptoms of talc granuloma to appear in early weeks or months following implantation of the crystals, such is not always the case. The spontaneous appearance of both lesions at the same time is also impressive.

It is interesting to note that in 1945 Chamlin[2] conducted a series of experiments in which he introduced talc into portions of rabbits' eyes. He was prompted by curiosity to learn if a talc granuloma could actually be produced in the eye since none had been reported. The experiments were planned to simulate the accidental introduction of talc during accepted ophthalmic operations, such as trephination of the anterior chamber, iridectomy, and eye muscle surgery. In most cases typical talc granulomas were produced. Chamlin realized that in eye muscle surgery the operative field is widely exposed and vulnerable to talc contamination in contrast to intraocular operations. He intimated that a talc granuloma of the human eye, when discovered, would most likely be at the site of such an operation. His prediction is fulfilled.

SUMMARY

A case is presented in which talc granulomas developed at the sites of eye muscle surgery 14 years after the original operation.

This is apparently the first recorded instance of such a lesion occurring in the eye.

Marshfield Clinic.

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THE HANDLING OF THE AMBLYOPIC PATIENT*

MAYNARD C. WHEELER, M.D.
New York

When Dr. Post asked me to take part in this symposium, it occurred to me that a description of how we handle the amblyopic cases at Vanderbilt Clinic might be of general interest and should provide the basis for discussion.

HISTORY

The history is of particular importance in the handling of the amblyopic patient. It is amazing how many ophthalmologists seem to feel that a history is not work taking, at least if one can judge from many clinic records. The date of onset, while often unreliable, is still worth recording as accurately as possible. There is general agreement that the earlier the squint develops and the greater the proportion of the patient's life it has been present, the longer it will take to restore vision.

It has surprised me that frequently the parents are not sure which eye is turning and frequently will name the wrong one. This may become important when asking for intelligent coöperation in carrying out the treatment. It is vital to know which eye they think turns when surgery is being performed, to avoid a misunderstanding. Usually, however, this information is given reliably. The history of a weak eye in several members of the family is frequently volunteered.

The story of previous treatment should be recorded carefully, with any comments as to the results.

VISION

Anyone who has seen the bizzare and completely fantastic visions written on the clinic charts, in good faith, by trained nurses, will realize that it is not the simple, routine task that it may seem. One must be on guard particularly in children with one poor eye.

The desire to cover up a defect and to make a good score is strong; so that peeking, memorizing, and guessing must be carefully guarded against.

In our clinic, we are satisfied with the results that we get with separate E's mounted on white plastic squares. We know that we get better visions than with the Snellen cards but, as it is the comparison of the two eyes that is really important, this is not a serious criticism. Careful technique will rule out peeking and memory. Guessing can only be detected by an alert examiner.

Most children aged four years, can be taught the "E game" and they love to play it. A recent writer has advised excluding other children, and the parents, from the examining room. I strongly disagree. Watching others play the E game has melted the resistance of many of our children. It shows them how it is done, it gives them confidence in us and probably stimulates them competitively. We find it worth while to have the mother start the little ones at home, although we have not bothered with records of visions taken at home.

It must be apparent to everyone who has worked with these youthful squint cases, that it is not necessary to wait until the vision can be reliably tested to know that the child is amblyopic. If any youngster uses one eye habitually, the deviating eye will surely be amblyopic. With experience one can tell by the expression of the squinting eye, and the child's behavior, when the fixing eye is covered, that it is amblyopic. Conversely, if there is alternation, even in just one field, you can be fairly sure that there will be good vision in both eyes. This information is reliable enough to enable us to proceed with treatment with confidence, as will be discussed later.

REFRACTION

The most interesting feature of the re-

fraction is the inequality in the two eyes. The amblyopic eye is almost always the one with the greater error. If the reverse is true, one should be very suspicious that it is not an amblyopia from disuse. I know of no way to tell how much anisometropia is compatible with binocular single vision, but this must be considered. I am convinced that occlusion is wrong in extreme cases of anisometropia. Aniseikonia may be important as an obstacle to binocular single vision, but our ideas on this are largely theoretical because of the lack of an adequate means for measuring it in squint cases.

FUNDUS EXAMINATION

The necessity of a thorough fundus examination, before occlusion, should be evident. I believe this to the degree that I demand an examination under general anesthesia if the child will not coöperate for at least a satisfactory inspection of the discs and maculas. Recently this belief was strongly reinforced when a five-year-old boy was brought to me with an advanced retinoblastoma in his right eye. Two years previously, this child had been treated with occlusion of his other eye, unsuccessfully.

TYPE OF AMBLYOPIA

The diagnosis of the type of amblyopia is of great interest but this is largely academic because of the young age of most of these patients. I have no quarrel with the writers who classify these cases by means of their scotomas, but I want to treat these children long before these scotomas can be satisfactorily plotted.

The cases with gross pathologic conditions are easily classified. But there is a group with normal-appearing eyes who do not improve after adequate occlusion. I call this "pathologic amblyopia" and visualize some small lesion in the retina or optic nerve, possibly from birth trauma, that cannot be seen with the ophthalmoscope. I know of no way to separate them from the amblyopias of disuse except by a trial period of complete occlusion. If any case fails to show improve-

ment, or the younger ones fail to switch fixation after two months of complete occlusion, I am inclined to call it "pathologic" and abandon further treatment.

DEVIATION

The examination of the deviation, in the presence of amblyopia, raises special problems. I am referring here particularly to those patients who lack reliable fixation in one eye. Of course, the cover test cannot be used. Simple inspection can be of great value, particularly when the observer is apparently not paying more than casual attention to the child. Talking to him, while playing with a toy dog whose eyes light up, may enable the examiner to note the displacement of the corneal reflex in the squinting eye. Using the same toy-light, and considerable patience, the excursions may be elicited.

But here a word of caution is necessary: when trying to bring out abduction of an amblyopic eye, it is very easy to be misled into the conclusion that there is a weakness of the external rectus. The child follows the light with his fixing eye until the bridge of his nose intervenes, then movement in that direction stops. He sees the light just about as clearly with the peripheral retina of the amblyopic eye as he does with the macula, so there is no incentive to abduct it farther. A day or two of occlusion will usually demonstrate his ability to abduct the eye fully.

With the very young patient, this may be all of the information that can be obtained. The angle of deviation must be estimated by the displacement of the corneal reflex, after the method of Hirschberg. This is only an approximation and unsatisfactory, but if that is all that we can get we must proceed.

Soon after the age of two years, in many cases, a prism can be slipped in front of the fixing eye (base out in esotropia) while the patient is watching a light held on the examiner's nose. This will cause a shift in the fixing eye toward the apex of the prism and a corresponding movement of the squinting eye. When the prism is found that corresponds to the angle of the deviation, the

reflex will be centered in the cornea of the amblyopic eye. This is the prism reflex test, described by Krimsky, which I believe to be both the most convenient and the most accurate method for measuring the deviation for "near" in amblyopic cases. I believe that it is proper to assume that the angles Kappa are symmetrical in the two eyes and to make an allowance for this. A vertical deviation can be measured at the same time by placing a vertical prism before the fixing eye with apex in the opposite direction.

The perimeter still offers the best method that I have found for measuring the deviation for distance, in these cases. Unfortunately, our perimeters are not usually conveniently placed for this purpose and I am afraid that most of us get along without distance measurements. Theoretically at least, measurements can be made in the cardinal directions with the perimeter but this offers great difficulties and is probably rarely done. A careful study of the excursions, comparing the two eyes, should be part of every analysis, however.

TREATMENT

There is general agreement, I believe, on the principles of the treatment of amblyopia. The earlier occlusion is instituted, the more quickly will the result be obtained. Frequently a very young child will accept an occluder more readily than an older one. In most cases the important thing is to take time to explain to the mother what is being attempted; how vital it is; and that it will become more difficult with each delay. The mother's coöperation is absolutely necessary and I have rarely failed to get it when the problem was adequately explained. With a few exceptions, occlusion should be begun with an adhesive bandage, worn continuously. As already stated, a trial period of two months is considered adequate to differentiate amblyopia of disuse from the pathologic type. However, after two weeks of satisfactory, complete occlusion, if the eye fails to fix centrally, I am inclined to stop the treatment. Any visual improvement is an indication for continuing occlusion and I favor keeping it up until there is no further gain over 2 to 4 weeks.

There is no fixed point at which the bandage can be abandoned for less drastic measures. This varies with the age, the refractive error, and the season of the year, as well as the progress of the vision. In recent years, I have used the various types of occluders much less and have relied largely on atropine in the fixing eye, and paper on that spectacle lens. Many mothers are able to regulate the use of atropine, putting in a drop when the child starts to look over the glasses, that is every week or 10 days. Once equal vision is achieved, intermittent occlusion, 1 month out of 3, has been the most satisfactory method of maintaining the vision.

A question that is frequently heard is: why all of this bother when the vision usually slips back as soon as the treatment is stopped? True, if no further attention is paid after the original course; but that is not enough. I am well aware of how difficult it is, but we must strive to maintain the vision, by intermittent occlusion, until the child is at least six years old. I cannot prove it, but it is my belief that if the vision slips after this age, and it frequently will, it can be regained later if ever needed.

Another difficult question is: at what age is occlusion no longer effective? Various answers can be found in the literature and there is no doubt that visual improvement has been obtained in individuals, aged 20 years or more. But there is also no doubt that the task becomes increasingly difficult with added years and that the practical obstacles are formidable. Both in my practice and in the clinic, we rarely recommend occlusion after the age of seven years.

I have made no attempt to discuss the part that an orthoptic technician can play in handling these cases as I have not had the benefit of such assistance. There is no doubt that a technician can shorten the treatment period in many instances, and might succeed at times when I have failed. Valuable aid

can also be rendered at home with drawing, coloring, and games that stimulate the desire to see while using the hands. Home movies have always seemed worth while. Maybe this would even be an argument in favor of television.

Occlusion should always be carried out before surgery, if possible. Waiting for surgery causes an undesirable delay. Psychologically, for parents, it works out better. A course of occlusion helps to prepare them for surgery, while on the other hand, after recovering from the emotional upset of an operation, it is human nature to want to forget about the whole thing. Of course, this may not be possible because in the young ones who do not acquire binocular single vision or alternation, intermittent occlusion may be necessary for a long time, but at least the tedious part is out of the way. Another feature that must be mentioned, although I am unable to explain it, is the recurrence of the squint that occurs occasionally during postoperative occlusion. This is not a strict contraindication but should make us proceed with caution.

As soon as the vision has been equalized, or fixation switched, operation is indicated, unless orthoptic exercises are to be employed. Speed is of the greatest importance, here, if one is to take full advantage of the new condition. The eyes should be made as straight as possible in the hope that binocular single vision will be acquired.

When occlusion fails, a cosmetic correction is all that can be hoped for. A surgical undercorrection should be sought because these are the eyes that tend to turn out later.

In an attempt to see what sort of results I was obtaining, I looked over the records of the last 40 patients in my private practice, for whom occlusion had been prescribed. I considered that a serious effort to carry out the treatment had been made in 33. My criteria of success were: (1) In the young children, shifting of fixation to the other eye; (2) improvement of vision to within one line of the other eye. On these criteria, 21 of the 33 cases were successful. The series is too small to make further analysis worth while. No significant difference could be found between the two groups to explain the failures.

Considering the failures, one aspect stands out. I am sure that we have all been impressed by the emotional resistance in the unsuccessful cases. It is not easy to see beyond the intensity of this reaction for the explanation that very possibly is but the normal reaction of a youngster who is forced to have his only useful eye covered. In other words, these obstreperous ones frequently have a pathologic amblyopia and are truly tortured by occlusion. Unfortunately there is no easy way to be sure. Because of this possibility, I tend to give the child the benefit of the doubt.

CONCLUSION

I have tried to select the points that are peculiar to or of special importance in the examination and treatment of children with amblyopia.

30 West 59th Street (19).

DISCUSSION

F. ELIZABETH JACKSON, M.A.

Erie, Pennsylvania

Dr. Wheeler has already discussed very completely and ably the problems presented by the amblyopic patient and procedures in office treatment of this condition. The handling of the amblyopic patient at an orthoptic clinic is merely a relegation of duties to the technician during the early stages of occlusion and visual development. The problems and methods are the same and are met with the same point of view.

The close correlation of the results of visual achievement in Dr. Wheeler's series of 40 cases with those in a group of 50 cases treated at the Erie Orthoptic Clinic would certainly seem to indicate similarity in treatment. In Dr. Wheeler's group, 21 out of 33 cases, or 64 percent, were successfully treated. In the Erie Clinic group, 32 out of 50 cases, or 64 percent, attained 20/30 vision or better which would seem to be comparable to Dr. Wheeler's criteria of success.

Dr. Wheeler mentions the difficulty of maintenance of vision in the amblyopic eye once it is obtained. It is at this point that the orthoptic technician can make her original and most important contribution.

In this same series of 50 cases with original vision of less than 20/50 in the amblyopic eye, the vision developed by occlusion and supplementary exercises was maintained in 21 cases, or 42 percent for a minimum period of six months. Table 1 shows maintenance in relation to highest vision obtained.

MAINTENANCE OF VISION

Further analysis shows that three factors in particular have an important bearing on maintenance of vision: (1) Length of occlusion; (2) conversion to alternation; and (3) development of fusion and parallelism.

LENGTH OF OCCLUSION

An analysis of length of occlusion in this series shows that, in general, best results were obtained in those cases which were occluded for longer periods. The majority of cases were occluded from 4 to 12 months. Maintenance in the 12-month group was 100 percent as compared to 27 percent in the 4-month group.

This might seem to be the solution to our problem except for the coöperational difficulties involved in long occlusion, especially in older children. When the child is first patched and forced to use his amblyopic eye, with vision usually of 20/200, the parent is sufficiently impressed with his obvious visual difficulties to coöperate completely. During early stages where visual development tends to be rapid, the child himself is pleased with his progress. But later, when vision is improved, the patch gets to be an "old story," and when it can come off part time, its partial use is apt to become slipshod. Too often, everyone becomes discouraged, and the original effort is wasted.

The technician who is giving fusion training during this period of partial occlusion is at an advantage. Frequent clinic visits maintain emphasis, if not always interest. Monocular exercises can be assigned for periods when the patch is on, binocular exercises for periods when it is off, thus making the spacing of occlusion logical rather than arbitrary.

CONVERSION TO ALTERNATION

Dr. Wheeler mentions shift in fixation as a criterion of successful treatment. It is indeed, for a patient with amblyopia of long standing may continue to fix with the originally good eye, although, after long occlusion, its vision is lower (for the time being) than that of the amblyopic eye.

When spontaneous alternation of fixation can be developed, no loss of vision occurs after occlusion is discontinued whether or not fusion and parallelism are achieved. It has been our experience that development of such ability is possible only in the very young child where the deviation is necessarily of short duration. Four cases only of the 50 studied became natural alternators after oc-

TABLE 1

MAINTENANCE OF VISION IN RELATION TO HIGHEST VISION OBTAINED*

Highest Vision Obtained	Number of Cases	No. Cases Vision Maintained	Percent Maintained
20/20	4	1	25
20/25	12	4	33
20/30	16	8	50
20/40	7	3	43
20/50	7	5	71

* In those cases in which final vision of 20/50 was obtained, the original vision was 20/100 in 1 case and 20/200 or less in 6 cases.

clusion and orthoptics. Their ages when treatment was begun ranged from 2½ to 4 years. Thus, may I add another reason to Dr. Wheeler's in his insistence upon early occlusion.

DEVELOPMENT OF FUSION AND PARALLELISM

Of the 21 cases in our series who maintained all of their visual improvement, 4 cases (as previously mentioned) achieved alternation, 3 were occluded for 12 months or longer, and 14 attained parallelism with fusion—that is, they developed the ability to hold their eyes straight in daily life and had fusion under some conditions of distance, size of object of regard, and amount of effort involved. Thus it would seem that achievement of parallelism with fusion, whether by surgery, orthoptics, or both, is the largest factor in maintaining vision. There is nothing startling in this finding. Both eyes are being used; disuse is not present; therefore, one would not expect loss of vision.

However, 11 cases did not maintain total visual improvement by achieving parallelism and fusion. Seven cases dropped to 20/50 still maintaining binocular ability; 4 cases dropped to 20/70 or less with loss of parallelism and fusion. In those cases where loss of parallelism and binocular function occurred along with loss of vision, we can conclude that, although possible, fusion required too much effort to become established as a daily habit, or that coöperation and persistence were not equal to the task, or that the case was dismissed prematurely. But in those cases where binocularity remains in spite of visual loss, we must consider the nature of the binocularity present and look for deficiencies in that function. It is apparent that binocularity will insure maintenance of vision at the 20/50 level, but not necessarily above that.

CRITERIA FOR CLASSIFICATION

Criteria for classification of parallelism and fusion were: (1) Phoria only on cover test; (2) fusion on small targets on synopto-

phore at zero setting; (3) fusion on Worth-4 dot; (4) fusion on fixation light with red cover before dominant eye; (5) appreciation of physiologic diplopia.

DEFICIENCIES IN BINOCULARITY

None of the 50 cases studied showed true stereopsis as tested on Keystone diagnostic slides DB6 and DB60. Some of the patients were too young for this test. Many patients were able to fuse synoptophore targets with parallactic displacement, and many gave accurate responses of depth perception. However, we have found that familiarity with the targets may make this possible by monocular criteria, and does not prove the presence of accurate depth perception.

In some cases, although physiologic diplopia was appreciated, indicating the use of both eyes, certain deficiencies appeared. Some patients were unable to localize one or both diplopia images correctly. Frequently, when the images could be properly spaced by movement of the bar to and from the nose, bar-reading remained an impossibility because the bar-image of the amblyopic eye remained solid, although the second shadowy bar was clearly present.

How are we to explain these deficiencies? The most obvious explanation is continuance of suppression of the macular area of the amblyopic eye in spite of peripheral binocularity. This, of course, would preclude stereopsis and explain inability to bar-read.

Another explanation is malprojection of the amblyopic eye. This theory was recently presented by Dr. Lazisch.[1] He believes that "amblyopia ex anopsia is poor vision due to malprojection of the affected eye so that the visual ray is directed eccentrically to the fovea."

Although time has been insufficient to test much of Dr. Lazisch's evidence, some phenomena have appeared during the course of treatment which favor his point of view. Dr. Wheeler mentioned the fact that better vision is obtained when single E's mounted on white squares are used than with Snellen cards. We have found this to be true in-

variably. It also occurs with the use of the Project-O-Scope when any chart letter is exposed singly. The difference in visual acuity when tested by single letter and row of letters varies with the individual tested, but may be as much as four lines.

Another related phenomenon is noted when the examiner stands at the chart and points to the letters. The child will often read correctly and without hesitation the letter next to (usually to the right of) the one pointed out. He will sometimes read two lines further than the correct vision recording in this fashion. This would seem to be a deficiency in fixation or in interpretation of position rather than in acuity itself.

When the amblyopic child is asked to place thumb tacks in the centers of round discs or other geometric figures of varying sizes with the good eye occluded, he will persistently err, and in the same direction—toward the good eye, regardless of the size of the disc. This is interpreted by Dr. Lazisch as evidence of "malprojection of the visual axis," and continued practice in centering as "relearning eye-hand coördination."[2] This phenomenon seems to me to admit of a simpler explanation, namely, directional judgment based on the child's customary monocular usage and coördination of hand with the good eye.

Whatever the explanation, improvement in the patient's ability to center occurs rapidly with daily practice and, although this particular phase of treatment has been tried only recently in our clinic on an experimental basis and with patients whose vision was 20/70 or better, in most cases one line of visual improvement has occurred, and in all cases more stability of fixation has been noted on the synoptophore. It is too soon to judge whether this initial improvement will continue or be maintained.

Whether we explain the binocular de-

ficiences of the amblyopic patient on the basis of macular suppression, malprojection, or a pathologic dominance of the better eye, treatment must be directed toward correction of these deficiencies. They are as much a part of the syndrome as loss of acuity.

Dr. Wheeler has mentioned the use of drawing, coloring, and games that stimulate the desire to see while using the hands. I heartily endorse this procedure and suggest that the element of correct spatial judgment can easily be incorporated into these monocular tasks.

Emphasis in treatment should always be placed on developing ability to fix with the amblopic eye, to alternate fixation at will, and to appreciate diplopia under as many conditions and in as varied visual situations as possible.

Discernment of minute, centrally spaced details with the amblyopic eye should always be insisted upon in training with haploscopic devices. We must aim at the macula to develop acuity. Excellent results in treatment of amblyopia by rhythmic illumination have been reported by Miss Helen Cotter.[3]

I am certain that we have all wondered during the prolonged course of treatment of the amblyope whether our efforts are justified. To persist in treatment in the individual case when no improvement is noted within reasonable limits is certainly futile. We must recognize and accept the variable limitations of the individual case.

Our tabulations of results show 64 percent of cases with satisfactory visual acuity atttainment, maintenance of vision in 42 percent of these, and imperfection in the binocularity of those who attain fusion and parallelism (notably, lack of stereopsis). Although this achievement justifies the effort entailed, still it is a dubious laurel upon which to rest in smug complacency.

St. Vincent's Hospital.

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NOTES, CASES, INSTRUMENTS

ESSENTIAL (PROGRESSIVE) ATROPHY OF THE IRIS

PAUL WINSLOW TISHER, M.D.
New Britain, Connecticut

Eighteen months ago this patient was examined in the office and showed early signs of essential iris atrophy which was not recognized as such. At that time the vision of each eye was 20/20 with small hyperopic correction, and her main complaint was that of burning, twitching, and tearing of both eyes and some difficulty with close work.
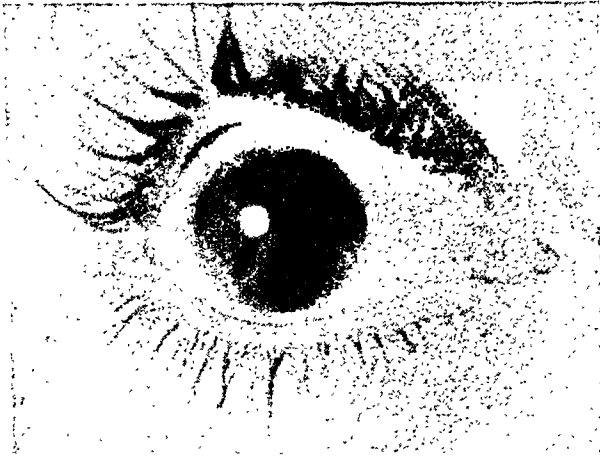
Fig. 1 (Tisher). Essential iris atrophy.

Muscle balance was normal except for convergence weakness.

The left eye showed no change, but the right eye showed a slight tucking effect in the upper nasal area. This appeared as if an injury at the limbus had caused a slight drawing up of the iris into a break in the periphery of the cornea. The patient gave no history of direct injury to the eye, but did mention that she had fallen two years before and had struck her head in the occiptal region with sufficient force to cause loss of consciousness for a short time.

There was no evidence of inflammation either outside or inside the eye. The fundus appeared to be normal. The slitlamp showed no floaters or keratic precipitates, and the iris stroma appeared perfectly normal except for the bunching, drawing up effect at about the 2-o'clock position. Routine perimeter readings were normal and tension was normal to fingers. Glasses were prescribed and the patient was asked to return in one month for reëxamination. There was some doubt concerning the diagnosis, but the findings were noted as probably being the effects of an old injury.

The patient did not return until 18 months later at which time she stated that she had had no difficulty until two months previously when she began to notice spots before the right eye and extreme photophobia. She also had occasional headaches relieved by aspirin.

The findings in the left eye were unchanged but the picture in the right eye was markedly different. Routine examination of fields and fundus showed no changes from the previous examination. The cornea was clear. Finger palpation, however, showed a hard eyeball. Tension at this time was 90 mm. Hg (MacLean). The anterior chamber was deep and the iris was displaced. The pupil was pulled up and irregular so that the lower edge was above the middle; the upper edge was at the limbus. There was a large atrophic hole in the lower portion of the iris about 2.5 mm. in diameter, with some strands, stroma remnants, extending vertically at the temporal edge of the hole. There was an almost equally large area of atrophic stroma temporally and another smaller area in the lower temporal aspect.

The stroma was also atrophic in other areas, the stroma layer being definitely more atrophic than the posterior pigment layer. At the upper limbus and also in the upper temporal aspect of the iris, the root of the iris appeared to be definitely thickened. It almost appeared as if this area in thickening and shrinking had pulled the pupil up and that the pull had caused the opposite portion of the iris to become atrophic.

Repeated doses of miotics of various strengths brought the tension down to be-

tween 50 to 60 mm. Hg (MacLean) and 28 to 32 mm. Hg (Gradle-Schiøtz). This seemed to relieve the patient of pain and ocular difficulty. Discontinuance of the medication caused immediate rise in tension and return of symptoms.

Duke-Elder describes this condition as a unilateral disease of unknown etiology, characterized by a slowly progressive atrophic change in the tissues of the iris, which leads to the complete disappearance of large portions of the tissue and ultimately ends in blindness from absolute glaucoma. He further describes it as coming on in early adult life with the development of an eccentric position of the pupil, which becomes distorted and displaced to the side. Usually the pupil shows an ectropion of the pigment epithelium and, finally, merely a shriveled remnant of the iris connects it to the ciliary body. On the opposite side, large holes appear in the iris. These enlarge and coalesce so that the entire tissue atrophies until only a few strands of stroma remain, with large apertures between. Eventually, after some years, when most of the iris vanishes, the tension rises and the first clinical symptoms become conspicious.

The glaucoma that develops shows little response to miotics and can rarely be operated with success. The common end result is blindness. As far as can be learned, all cases reported have been unilateral.

99 West Main Street.

RETINAL ANGIOSPASM*

The fundus in diffferent stages of an attack in the left eye

Ursula Rexed

Stockholm, Sweden

A number of cases of retinal angiospasm showing attacks of temporary blindness have been described in the literature (Duke-

Elder: Textbook of Ophthalmology, v. 3, 1945). However, it is seldom that such attacks have been photographed. I am showing here a series of photographs of the fundus taken during an attack.

CASE REPORT

History. The patient, a business woman, aged 40 years, had often shown signs of vasolability with blushing, palpitation, and a general sensation of warmth. She had occasionally had a slight feeling of numbness in her fingers, otherwise she had had no symptoms of circulatory disturbances or endocrine trouble. Three years earlier she had had an attack of blindness of the left eye which lasted for 2 to 3 minutes and which did not recur. She had had no more attacks between this time and the time when she was observed at the clinic.

She arrived at the ophthalmic clinic one evening in October, with an acute attack of blindness of the left eye caused by retinal angiospasm. This attack lasted for a couple of minutes and was followed by a series of similar attacks in the left eye, each attack lasting for about 10 minutes. The patient was extremely nervous and agitated and showed palpitation and blushing cheeks.

The pulse rate and blood pressure showed an increase during the attacks. In one attack the pulse rate rose from 104 to 120 and the systolic blood pressure from 130 to 150 mm. Hg.

The visual acuity of the left eye was 0.8 between the attacks and diminished to perception of hand movements during an attack. In the left eye the perimetric field was being measured when an attack occurred. The field was rapidly diminished from without inwards. Between the attacks the field was normal and showed no scotomas.

The patient was given vasodil subcutaneously and by mouth and luminal tablets and put to bed. The attacks continued during the night but had practically ceased by the next morning. Only a couple of stray attacks occurred during the day, one of which was

Fig. 1 (Rexed). The normal fundus of the right eye.
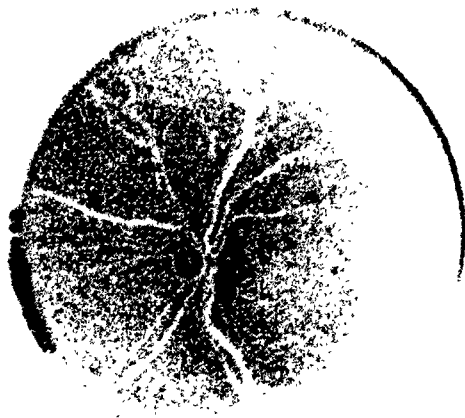
Fig. 2 (Rexed). The normal fundus of the left eye.
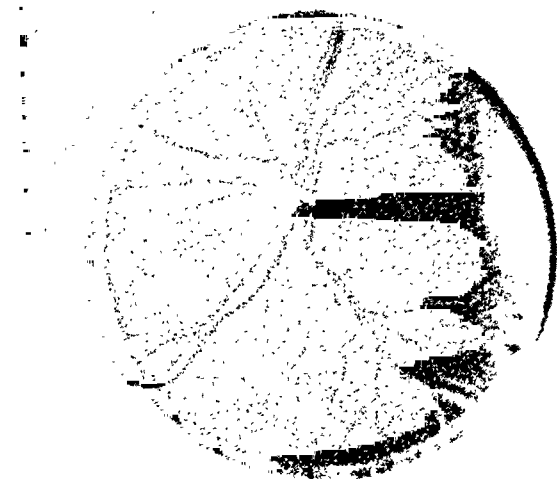
Fig. 3 (Rexed). Fundus of the left eye taken between attacks of retinal angiospasm, three hours after a preceding attack and about 10 minutes before the photographs (figs. 4 to 8) of different stages of an attack.

Fig. 4 (Rexed). Fundus of the left eye during an attack of retinal angiospasm taken about one minute after the attack had started. The arteries have contracted, several of the smaller arteries can no longer be seen (the small artery at the 9-o'clock position and the smaller arteries between the 3- to 6-o'clock positions). The veins have also contracted and the color of the fundus is paler than in Figure 3.

the one photographed. After this, no more attacks occurred, although the patient stayed at the clinic for over a week.

A thorough general examination was made of the patient with a view to finding the etiology of the attacks. The electrocardiogram showed a sinus tachycardia with a rate of 120. The arteries of the legs and feet were examined by oscillometry, and the skin

temperature was recorded after vasodilatation. The results seemed to show a certain lability of the arterial tonus.

All other investigations were negative. Heart and lungs were normal. Neurologic examination was normal. Gynecologic exam-
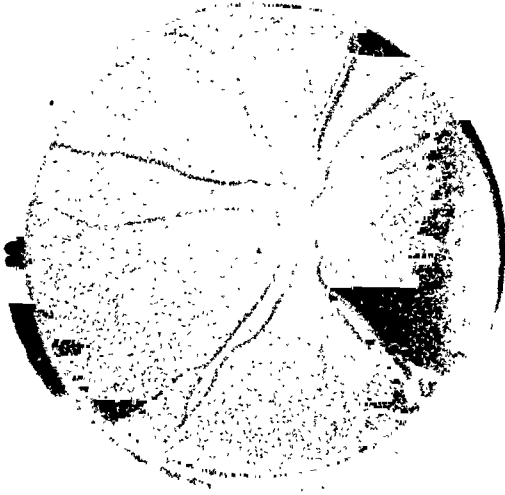
Fig. 5 (Rexed). The arteries are now extremely narrow and this is seen especially upward in the picture. There is a segmentation of the blood column in some of the veins. The color of the fundus has become still paler. (Taken 15 to 20 seconds after Figure 4.)

Fig. 6 (Rexed). A different part of the fundus, showing the macula. On the optic disc the arteries are seen to be empty. This was a phenomenon that occurred toward the end of each attack as the spasm reached its maximum, and which was followed by a sudden filling up of the vessels, as seen in Figure 7. A slight cherry-red contrast is seen in the macula. Ophthalmoscopically, a slight edema was observed. (15 to 20 seconds after Figure 5.)
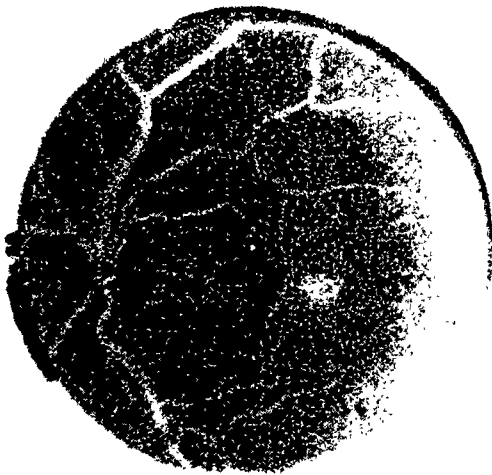
Fig. 7 (Rexed). In this view, most of the vessels have filled up. Some of the arteries are, however, still empty and are seen near the disc as thin white lines. The veins are engorged. The fundus has started to regain its color, especially in the periphery. (15 to 20 seconds after Figure 6.)
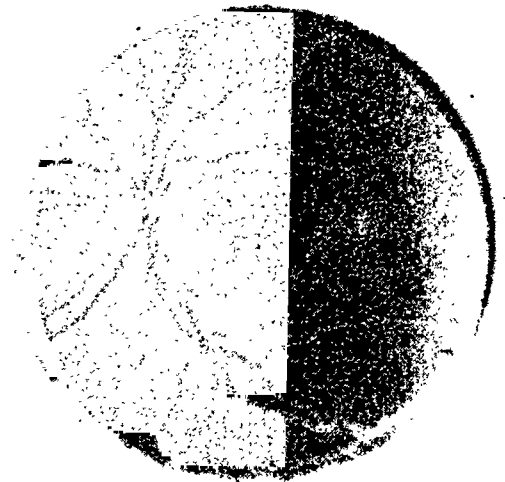
Fig. 8 (Rexed). All of the arteries are now filled up. The veins are still engorged. The fundus is redder. (15 to 20 seconds after Figure 7.)

ination was normal; the patient had never had any disturbances of menstruation. The basal metabolism rate was a plus 11. An electroretinogram, taken between the at- tacks, gave normal findings. It was not possible to provoke an attack during the registration.

Banèrgatan 33[4].

Fig. 1 (Weston). Motor used for the electrical control of revolving astigmatic cross.

AN ELECTRICAL REMOTE CONTROL FOR THE REVOLVING ASTIGMATIC CROSS

HORACE L. WESTON, M.D.

Detroit, Michigan

The revolving astigmatic cross has been recognized for years as a useful aid in the measurement of ocular astigmatism, particularly with regard to the strength of the correcting cylinder. However, since the cross is of little value unless it can be turned to the appropriate axis for each eye, it has been necessary to devise remote controls in order to eliminate the inconvenience of direct hand adjustment.

Remote control has usually been achieved by the use of strings and weights or by the use of a gear box and reversing motor. The former method accomplishes the purpose well but frequently necessitates the use of unsightly strings. The latter method is more modern in appearance but too slow in operation.

For the past year, I have been using an electrical remote control which is practically instantaneous in action and is accurate to within one degree. The astigmatic cross which is mounted near the Snellen test chart is synchronized with the dial on the control box by the use of a pair of selsyn generators. These "generators" or "motors" were obtained from war-surplus stock (frequently advertised in popular science and radio magazines). The motors in use (fig. 1) were

designed to operate on 115 volt-400 cycle A.C. but work well on 24 volt-60 cycle A.C., as obtained from an ordinary furnace control transformer.

The control unit (fig. 2) is mounted in a box on top of which are push-button switches for the primary circuit and for a muscle light. The primary circuit is turned on only when the dial is being rotated, in order to eliminate hum. An 8-wire radio battery cable leads from the control box to the chart box.

In present operation, reverse charts are employed for use with a mirror. For operation at 20 feet one needs only to use a longer cable and to reverse two of the control wires so that the generators will turn in opposite directions. The driving generator and the muscle-light mounting are located behind the face of the box. Storage space for other charts is located in the upper half and is reached through a slot in the side.

In addition to affording an excellent test object for the finer measurement of cylinder strength the single-line cross is useful when used in connection with the cross-cylinder in the highly sensitive axis test reported by Crisp and Stine.* To facilitate this test small marks have been added to the control dial at the 45° and 135° positions.

703 Stroh Building (26).

* Crisp, W. H., and Stine, G. T.: A further, very delicate test for astigmatic axis, using the cross cylinder with an astigmatic dial and without use of letter charts. Am. J. Ophth., 32:1065 (Aug.) 1949.
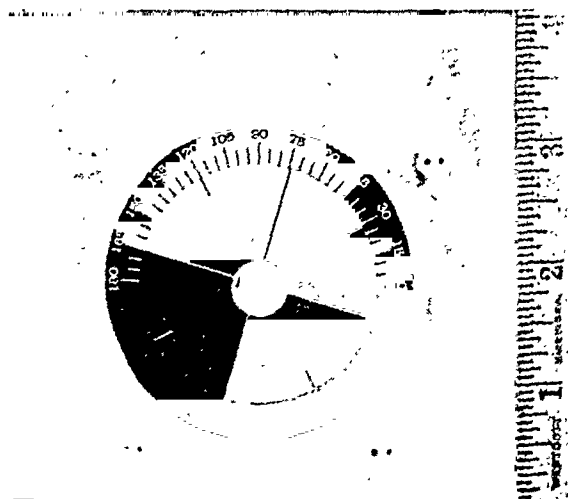
Fig. 2 (Weston). The control unit.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

SECTION ON OPHTHALMOLOGY

October 21, 1948

DR. PERCE DELONG, *chairman*

OPTOCHIASMATIC ARACHNOIDITIS

DR. MORGAN B. RAIFORD (by invitation) presented an 8-year-old white boy, who was admitted to the Graduate Hospital of the University of Pennsylvania on June 15, 1948.

The chief complaint was that of poor vision in both eyes which was first noted in December, 1947. He had no history of any intercurrent disease, either ophthalmic or systematic other than a fall in October, 1947, which resulted in a contusion of the forehead without any noticeable effects.

When returning to school after the Christmas vacation, he noticed that he was unable to see the blackboard. There was no pain or redness or any other symptom. He was hospitalized from the middle of February to mid-April, 1948. The diagnosis at that time was optic neuritis. He had had spinal-fluid examinations, six typhoid injections, and multiple vitamins. These studies were repeated in another hospital and confirmed. The patient's visual defect gradually increased, however, up to the time of hospitalization (mother's statement) of June of this year. The parents have been in excellent health, and the boy's one sister, is normal.

Systemic review. Tonsils had been removed at five years of age. The patient had complained of transitory frontal headaches that were noticeable by his mother in November and December, 1947. They were dull and diffuse in character. He had suffered with no headaches since that period.

Neck, negative; heart and lungs, negative; appetite good, abdomen and bowel function normal—no history of nausea or vomiting; genito-urinary system, negative; extremities, negative; skin, negative. The patient had no physical abnormalities other than the ocular defects.

Eye examination. There was no exophthalmos, ptosis, nor nystagmus. Pupils were round, central, reacted equally to light and accommodation, and consensually. Tension was: O.D., 17 mm. Hg (Schiøtz); O.S. 19 mm. Hg. Extraocular movements were normal and full. Lids and lacrimal apparatus were normal. Vision was: O.D., 2/60; O.S., 2/60.

Refraction under atropine cycloplegia on June 17, 1948, was: O.D., +0.5D. sph. = 2/60; pinhole, 2/60. O.S., +0.5D. sph. = 2/60; pinhole, 2/60. The patient complained of his vision being smoky.

Visual fields on June 18, 1948, showed concentric contraction of both the peripheral and central fields with slight enlargement of the blind spots. No scotoma was present. Could not see less than 5-mm. white test object clearly. Sclera and cornea were normal; lenses were clear and normal; vitreous was clear.

Fundus examination showed that the discs were pale and both outlines were hazy. A binocular ophthalmoscopic examination was done, and no evidence was present that suggested old papilledema. The blood vessels were normal with an arteriovenous ratio of 2 to 3. The macular areas revealed slight pigmentation. The periphery were clear. No hemorrhages or exudates were present.

A neurologic examination by Dr. Joseph Yaskin did not reveal any other abnormalities.

On June 18, 1948, X-ray studies of the skull, orbits, sella, and optic foramina were negative.

A ventriculo-encephalogram was done June 29, 1948, by Dr. Finkelstein and the following reported: "Only a small portion of the third ventricle is visualized and this is normal in size. The fourth ventricle is not

visualized. No air can be seen in the basal cisterna or the subarachnoid pathways. We are, therefore, unable to exclude the presence of a posterior fossa lesion, such as a tumor or basal arachnoiditis."

Operation. In veiw of these findings, a right frontoparietal craniotomy was done by Dr. Robert A. Groff on July 6, 1948, and a chronic arachnoiditis was found around the optic nerves and chiasm. These fibrous bands and adhesions were incised and the optic nerve freed.

The patient made an uneventful recovery, and was discharged on July 13, 1948.

The patient was last seen on September 15, 1948, at which time the visual acuity was: O.D., 6/30; O.S., 6/7.5. The visual improvement has been quite noticeable to the patient, and he has been able to read without any difficulty.

Discussion. Dr. Robert A. Groff: There is one contribution I should like to make, and that is that there are other cases which have been verified by operation. However, I do not believe there are any so young verified by operation in the literature. Arachnoiditis is a definite entity. It occurs primarily around and near the chiasm, and secondly about the cisterna magna in the posterior fossa, in both instances frequently simulating tumor. This is in the literature, and was referred to by Dr. Frazier as pseudotumor.

The diagnosis is extremely difficult and, to me, is only made at the operating table. I do not believe that the diagnosis can be made clinically with certainty, but it can be suspected, and then confirmed at operation. It is very difficult to make a decision to operate on such an individual, because the operation is rather serious. However, one weighs that against the fact that vision is extremely important to the patient. The entire matter has to be put before the family with the idea that we may be able to do something for the vision of the patient or not, depending on what we find. In this patient we were very fortunate in finding a definitely thickened

arachnoid, which was removed from the region of the chiasm. The subsequent course showed that the arachnoiditis had been the cause of the visual effect.

SECONDARY FUNCTIONS OF INFERIOR OBLIQUE

DR. WILLIAM E. KREWSON, III, briefly reviewed the literature with its confusion regarding the manner in which the inferior oblique muscle moves the eye. Perspective drawings portraying the muscle plane and the location of the muscle were shown for various positions of rotation.

The action generally attributed to the inferior oblique muscle is primarily that of extortion, which increases as the eye is externally rotated, together with the secondary or subsidiary functions of elevation, which increases as the eye is turned inward, and external rotation, which increases as the eye is rotated outward. Based on the anatomic data of Volkmann, variations in these generally accepted actions apparently exist.

Both the primary function of extortion and the subsidiary action of elevation can be shown to have their maximum effect when the eye is turned outward seven degrees, while at this position the horizontal rotating effect is nonexistent. As the eye is turned outward beyond this position, the inferior oblique muscle becomes an external rotator and, as the eye is turned inward from this position, the muscle acts as an internal rotator.

The manner in which the muscle actually functions depends upon its angular attachment to the globe. Probably these opposing views can be reconciled on the basis of the marked variation which is known to exist in the anatomy of the extraocular muscles.

Discussion. Dr. Francis Heed Adler: This careful study by Dr. Krewson is about the best argument we have for abandoning the old conception of a primary, secondary, and tertiary action of each of the ocular muscles. This may have been a convenient way of teaching the various components of

pull of each of the muscles, but it leads to false conceptions.

These studies show that the inferior oblique has one action in one position of gaze, and in another position a diametrically opposite action. The same is true, not only of the inferior oblique, but of the superior oblique and both the superior and inferior recti. We think of the superior rectus as an adductor, and it is, in the primary position of gaze, but, when the eyeball is abducted 23 degrees from the primary position, it loses its adduction as one of the components of its pull, and, when the eye is rotated outward beyond that point, it then becomes an abductor.

I think we must accept the studies that have been made which show that there is no center of rotation of the globe. The studies of Park and Park and of Verrijp and others have proved conclusively that we do not have such ideal conditions as a point center of rotation about which the eye moves.

The eye makes transitory movements laterally, forward and backward, and up and down, and the centers of rotation cover an area of some few millimeters. For this reason, it is extremely difficult to make calculations which decide in just what position the inferior oblique becomes an adductor instead of an abductor.

There is a point in muscle physiology, which is often overlooked, and that is that in all ocular movements, more than one muscle is contracted. In the lateral versions, for example, five muscles are co-contracting in each eye simultaneously. In dextro-version, the lateral rectus of the right eye acts sufficiently as an abductor at the start. In this position it has a long arc of contact, and is working at a mechanical advantage. The superior and inferior recti in this position co-contract, and keep the eyeball from moving up or down. They also act as adductors in this position, but this adduction is balanced by the co-contraction of the two obliques which keep the vertical meridian erect and by their abducting effect counterbalance the adducting effect of the superior and inferior recti. As

the movement progresses, the lateral rectus acts to a greater and greater disadvantage.

When the eyeball has passed 23-degrees abduction, the superior and inferior recti become abductors, and they, together with the obliques, are largely responsible for the further abduction of the eye. This fact explains the modus operandi of the Hummelsheim operation, and probably all operations which are modifications of this. By transplanting part of the superior and inferior recti to the attachment of the lateral rectus, we make these muscles abductors by their co-contraction, and this abduction takes effect at the very beginning of dextro-version.

These studies by Dr. Krewson are of vital interest, and should eradicate from textbooks the idea that each ocular muscle has three separate functions.

Dr. Krewson, (closing): I want to thank Dr. Adler for his informative discussion. His criticisms are well taken, and quite justified. It is true that there is no fixed center of rotation, and that this center is not identical with the anatomic or geometric center of the globe. Also, variations due to the check-ligaments, Tenon's capsule, and the like are factors, but probably none greatly affect the overall picture.

It is also true, as I intended to mention but omitted because of limited time (but will include in published manuscript), that no one muscle acts on the globe independently or at any one time. I did not wish to imply that the muscle, the inferior oblique in this case, actually and independently turned the eye to the positions indicated; rather, the analysis is to show how the energy of the muscle is expended on the globe, or how the muscle really acts, when the eye is already rotated in the various positions mentioned.

SYPHILITIC PRIMARY OPTIC ATROPHY

DR. JOSEPH V. KLAUDER, DR. GEORGE P. MEYER, and DR. BENJAMIN A. GROSS (by invitation) gave a brief resume of the reports on the frequency of syphilis as a cause of blindness. They said that 10 to 15 percent

of blindness is due to syphilis. The importance of this in the United States is shown by the fact that there are between 20,000 and 30,000 cases of blindness due mainly to syphilitic optic atrophy.

A report was presented on the study of 397 cases of syphilitic primary optic atrophy, 20 of which were of congenital syphilitic origin, the remainder acquired. The authors discussed (1) Relationship of age, sex, race, and type of disease; (2) character of antisyphilitic therapy before onset of optic atrophy (treatment was shown to be deplorably inadequate); (3) visual acuity, time of admission to clinic (61 percent were industrially blind or worse); (4) pathogenesis —generally accepted view is the inflammatory origin; (5) symptomatology—stress was laid upon diplopia and leg pains as prodromal, and loss of vision and field changes as early symptoms, accompanying neurosyphilitic signs are also present; (6) diagnosis—probably the earliest sign is a field defect, loss of central acuity and pallor of disc usually occur later and indicate further advanced and usually irrevocable changes.

The authors' comments were: (1) Syphilis is a very frequent cause of blindness, approaching cataract and glaucoma in importance; (2) ophthalmologists are urged to be alert to the early diagnosis of this condition, for early diagnosis holds the only promise of amelioration or arrest.

Discussion. Dr. Joseph V. Klauder: In addition to the rather pessimistic figures presented by Dr. Meyer in the forepart of his presentation, one could make rather similar deductions from the following. Before the war, the incidence of new cases of syphilis in the United States as calculated by the U.S. Public Health Service was about one-half million per year. That decreased until shortly after the war it slightly increased, and it is estimated now that there are about one-fourth million new cases of syphilis arising each year. It is thought that, of new cases of syphilis, about 5 percent, if untreated or inadequately treated, will later develop

tabes dorsalis; of these patients, 10 to 15 percent will develop optic atrophy. This estimation applies only to patients with tabes dorsalis, and does not apply to about 40 percent of patients with optic atrophy associated with neurosyphilis other than the tabetic form.

Dr. Meyer has presented our rather unfortunate experience in early diagnosis of optic atrophy at Wills Hospital. The figures he presented—61 percent of patients when first seen were industrially blind—are certainly not gratifying.

What can we do about it? I think the importance of syphilis as a cause of blindness needs no emphasis. It is worthy of attention of every physician who treats syphilis. The ophthalmologist is particularly concerned in syphilis as a cause of blindness. We appeal to ophthalmologists for more interest in syphilis as a systemic disease, in its public health aspects, its treatment, and in the early diagnosis of optic atrophy. We believe that was the implication in Berens and Goldberg's report (Syphilis in relation to the prevention of blindness: A study of 100,000 case records. J.A.M.A., 109:777-781 (Sept.) 1937) in which it was stated that frequently insufficient attention was given to the history, examination, serologic tests, and treatment of patients whose ocular disease was syphilitic in origin.

Optic atrophy occurs in patients whose neurosyphilis usually pursues a silent form. It is infrequently associated with the classical symptoms of tabes dorsalis—dysuria, ataxia, and severe leg pains. In our study the two most frequent symptoms preceding subjective loss of vision were diplopia and leg pains. Diplopia was usually transitory and preceded, frequently by years, loss of vision. Leg pains were usually mild and elicited only by direct questioning. Optic atrophy predominantly occurs in patients who are unacquainted with their infection and who have had no antisyphilitic treatment. Unfortunately, the major symptom that leads to diagnosis is impaired vision.

Ten years, at least, elapses after infection

for optic atrophy to develop, the usual interval is 18 years. There must be a period in which early perimetric field defects are present preceding pallor of the nervehead and impairment of visual acuity. From our study, we believe that that period may range from a few months to several years. We would stress that interval as a propitious one for early diagnosis of optic atrophy. To accomplish this, routine ophthalmoscopic examination is necessary on every patient with syphilis of more than 10 years' duration, certainly on every patient with neurosyphilis. It is to be recalled that pupillary abnormalities are common symptoms of neurosyphilis, appearing early and constituting "short cut" in clinical diagnosis.

Bruetsch observed basilar meningitis as part of optic atrophy existing in the absence of other evidence of neurosyphilis. Clinical diagnosis of syphilitic optic atrophy is, therefore, justified in a syphilitic patient without evidence of neurosyphilis. In our experience, however, this occurrence is rare.

To facilitate early diagnosis of optic atrophy, ophthalmologists and all physicians who examine patients with syphilis should have a high degree of awareness of the optic nerve. In records of private, ward, and clinic patients, too infrequently no mention is made of examination of the optic nerve unless the patient complained of visual loss. The ophthalmologists are admirably situated to exclude optic atrophy in every patient examined, who has had syphilis of some years' duration, at least in patients with pupillary abnormalities.

The ophthalmoscope and the perimeter should be added to the lists of instruments— dark field microscope, lumbar-puncture needle, roentgen ray, and electrocardiograph —of vital importance in the diagnosis of syphilis.

Dr. Louis Lehrfeld. In the year 1937, there was prepared from data at the Wills Hospital a survey on optic atrophy due to syphilis. This survey covered a period of years, 1926 to 1937 inclusive. There was a total of 522 patients studied. All of these patients had some degree of optic atrophy. It is gratifying indeed to find that the present investigators have found statistics that are quite comparable with those that were reported by me in 1937. That survey aimed to find out what happened to patients with optic atrophy. Did they get well? Did they get worse? And was our treatment effective in controlling optic atrophy?

I am reminded in reading Duke-Elder tonight of the statistics in which he quotes me: "Of the untreated cases, 74 percent were blinded in a period of three years; all of them were blind in five years. Of those treated by the well-known methods of antiluetic treatment at the time, 24 percent of the optic-atrophy cases became blind in a period of five years, and all of them were blind in a period of eight years."

This was very damaging evidence, pointing out that the method of treatment at the time was not sufficient to control optic atrophy due to syphilis, to cure it, or even to arrest it. I had hoped that the essayists tonight would give us some information along those lines. Despite the fact that we preach early diagnosis of optic atrophy, it is true that our methods of treatment today are insufficient and inadequate. What suggestions do the essayists have in the way of modifying our methods of today to bring about a control of optic atrophy, or at least to reduce the incidence of blindness from this disease?

I wish to call your attention to an article published in Science of November 7, 1947, by Dr. Knisley of Chicago. In that article he speaks of blood sludging occurring in various diseases. He speaks of the red cells in the blood becoming sticky, and agglutinating in malaria and various inflammatory and infectious diseases. Dr. Knisley has probably opened up an entirely new field of pathology in the case of optic atrophy due to syphilis, namely the blood sludging occurring in the end arteries of the retina. Sludging means that the blood vessel caliber is

closed, the nutrition of the part ceases, and progressive optic atrophy develops. The question I wish to point out to the investigators tonight is this. Do we have anything to control optic atrophy even if it is diagnosed early? Are the methods used today —the use of penicillin, the use of heavy metals—sufficient to control optic atrophy, or are we going to lean upon Dr. Knisley for another suggestion so as to prevent blood sludging, and thereby prevent optic atrophy?

I wish to congratulate the authors of the article just presented, and I know they have some very valuable information for us in rebuttal.

Dr. Joseph V. Klauder (closing): One cannot answer Dr. Lehrfeld in an arbitrary manner, because there is so much variability in the course of syphilitic atrophy. We are all familiar with the rapidly progressive cases that pursue a downhill course regardless of treatment, and are blind in one year or less. In the slowly progressive cases, the prognosis is more favorable. If we exclude the rapidly progressive cases, we do not believe the inevitable result is blindness. We have a number of patients in the clinic whose optic atrophy has remained stationary for periods of observation ranging up to 18 years. We observed this in patients who had received different methods of treatment.

Certainly one is justified in being less pessimistic about prognosis than years ago; that era, for example, when the disease was treated with strychnine. There has been considerable addition to the therapeusis of the disease. Fever therapy, especially malaria, is to be stressed. The status of penicillin awaits evaluation.

Dr. George P. Meyer (closing): If you read the program, it says, "Syphilitic primary optic atrophy as a cause of blindness and importance of early diagnosis." I think we have shown tonight the importance of early diagnosis, because with a well-advanced optic atrophy the outlook is pretty poor. I remember when Dr. Lehrfeld's article came out in 1938 I felt depressed about it. I hap-

pened to have at that time a patient who had neurosyphilis and beginning optic atrophy, and I went to one of the local syphilologists in Jersey, and asked him to undertake the treatment of syphilis. He just shrugged his shoulders, and said, "Oh well they all go blind anyway," and he was associated with one of our larger teaching institutions in the city.

The patient was subsequently referred to Dr. Klauder, and he still has vision. Dr. Klauder did not have the pessimistic outlook as far as therapy was concerned. I think the first bright note was struck by the Baltimore investigators. I do not remember the figures exactly, but there is a direct ratio between the good prognosis and the amount of vision that was retained when a patient first reported for treatment. If a patient first reported for treatment industrially blind, the outlook was pretty poor. So it is you get figures like those of Dr. Lehrfeld and Duke-Elder who report that, within eight years, all patients become blind. That certainly is not the experience in our clinic for there are many patients who still have useful vision 8 or 10 years after the diagnosis of optic atrophy was made, and I think the first person to whom we have to point that lesson is the pessimistic ophthalmologist. Get him to feel that if he is alert enough to make an early diagnosis, very valuable vision may be saved for a patient.

M. Luther Kauffman,
Clerk.

CHICAGO OPHTHALMOLOGICAL SOCIETY

October 18, 1948

Dr. Arlington C. Krause, *president*

Clinical cases were presented by the Department of Ophthalmology, Veterans Administration Hospital, Hines, Illinois.

DISCIFORM DEGENERATION OF MACULA

R. D., a 29-year-old white man, entered

Hines Hospital on February 26, 1948, complaining of defective vision in both eyes for six months. He stated that on routine examination overseas in October, 1943, vision was: R.E., 20/40; L.E., 20/20. He had no complaint at that time. He received a medical discharge from the Army in 1943 because of rheumatic fever. In August, 1947, he was seen by an ophthalmologist who noted vision to be: R.E., 20/400; L.E., 20/70. He gave a past history of two attacks of bronchitis and one of probable rheumatoid arthritis.

When examined, his general physical condition was normal. Vision was: R.E., 20/300. Anterior segment, media, and lens were normal. Fundus showed a slightly elevated, sievelike, spongy gray mass, well circumscribed, oval in shape, occupying the macular area and containing red pinpoint spots; lateral to this was a small similar gray patch. Disc and vessels appeared normal.

Vision was: L.E., 20/30−2, correctible to 20/30+3. Anterior segment and media were normal. The lens showed a thin opacity of posterior lens capsule. The fundus revealed a mass in the macular area similar to that in the right eye, with a few small patches laterally. Within the large porous mass was a central red spot which suggested remaining normal macula.

Peripheral fields were normal; central field, right eye, showed a central scotoma surrounding the upper half of the fixation area for a distance of 5 degrees, including the fixation point. The left eye showed a pericentral doughnut-shaped scotoma circumscribing the fixation point and leaving 1 to 2 degrees free at the fixation point.

All laboratory tests revealed normal findings. A tentative diagnosis of disciform degeneration of the macula, bilateral, was made. Treatment consisted of nitrosclerin, vitamin-B complex, and thiamin.

The patient was discharged on March 19, 1948, but returned 10 days later because of sudden decrease in vision in the left eye. The lesion appeared to be the same as on previous admission except that the small area in the center of the macular area, which previously suggested normal retinal tissue, now appeared pale and degenerated. Vision was: L.E., 20/200.

Stereocampimeter showed definite central scotomas involving the fixation area bilaterally. He was given typhoid and nitrosclerin intravenously, as well as rutin and vitamin-B complex. Twenty-four days later the vision returned to 20/30+3, 5 point. He was discharged a few days later, and now returns with vision: R.E., 20/400; L.E., 20/300.

Final diagnosis: Disciform degeneration of the macula, bilateral.

DISCIFORM MACULAR DEGENERATION

J. E. A., a 32-year-old white man entered Hines Hospital on April 10, 1948, complaining of a small blind area in the right eye of two weeks' duration. The scotoma was located just below the fixation object and moved in the same direction as the eye. In 1943, he suffered loss of central vision in the left eye over a six months' period; there was no associated pain. He received a medical discharge in 1945. Past general history was negative except for an abscess in an upper incisor tooth.

General physical examination was normal except for an atrophic testis on the right side.

Examination of the eyes showed: R.E., vision 20/20, anterior segment, media, lens, normal; fundus showed a normal disc but the macular area appeared edematous and contained 4 or 5 hemorrhagic spots, mostly deep and round, and one superficial flame-shaped hemorrhage. A small dot of exudate was present.

L.E., vision, large objects only, not correctible; anterior segment, media, and lens normal.

The fundus revealed a normal disc, but temporal to the disc and overlying the macula was a white circumscribed elevated fibrous mass, about 3 disc diameters across. The

retinal vessels rose about 2 diopters to cross over it. The mass was fairly round but had a pseudopod in the upper aspect, and contained a slight amount of pigment. Temporal to the mass was a small circumscribed pigment patch. The retina was pale, suggesting change of a glial nature. The central field, right eye, showed a round scotoma about 10 degrees in diameter, situated just below the fixation point.

All laboratory tests and X-ray findings were within normal limits. Genito-urinary examination showed a mild chronic prostatitis, which improved under treatment. Dental examination revealed evidence of pyorrhea and three teeth were extracted.

The patient was put on rutin and thiamin therapy and one small injection of typhoid, intravenously.

Shortly after admission, more small hemorrhages together with waxy edema of the right macula became apparent. Vision decreased rapidly; on May 10th, it was 20/100 and the scotoma included the fixation point. There was a suggestion of a macular star. About 4 disc diameters from the disc at the 7-o'clock position was a small round gray exudate. Another oval gray patch of choroiditis was seen at the 1-o'clock position.

On May 17th, a small, round, blue exudate appeared 2 disc diameters from the disc at the 10-o'clock position. On May 18th, vision in the right eye improved to 20/70, and the scotoma appeared to be smaller. However, the vision continued to fall and by June 1st, it was 20/400; today it is 5/400, not correctible.

Final diagnosis: (1) Disciform degeneration of macula, bilateral, progressive on right, unchanged on left; (2) prostatitis, chronic, mild, improved.

IRIDOCYCLITIS, CHOROIDITIS, AND GLAUCOMA

S. G., a 34-year-old white man, entered Hines Hospital on March 19, 1948, complaining of progressive blurred vision and aching in the right eye of three days' duration, together with a feeling of "pressure," slight redness, but no discharge.

In January, 1943, he noted a spiderweb appearance over the right eye which lasted for three weeks. This recurred three months later and then cleared with vision of 20/20. The left eye was normal. He had a similar episode in 1944.

In January, 1946, he entered the hospital with the same complaints. At that time eye examination showed visual acuity: R.E., 20/100; not correctible; lids, sclera and lens were normal; 1+ mixed bulbar injection; iris muddy; pupil dilated to 5 mm. under atropine; slitlamp showed 2+ aqueous flare with many cells present, numerous keratic precipitates in delta configuration in lower third of cornea; the fundus revealed a faint red reflex but no details were visible.

The left eye was normal. A diagnosis of iritis, acute, recurrent, was made and he was discharged in six weeks. Vision: R.E., 20/20−3; L.E., 20/20. The family history was essentially negative. The patient had had usual childhood diseases and malaria in 1943, with eight recurrences.

General physical examination revealed some carious teeth and was otherwise negative. Examination of eyes: R.E., atropinized, vision was 20/40−1 with pinhole; lids normal; questionable pericorneal injection. The cornea showed some endothelial bedewing in lower inner quadrant. One minute pigment particle was noted on endothelium; 1+ aqueous flare, and few cells seen. The lens revealed a clump of pigment in lower half of anterior lens capsule. Vitreous floaters were present. The fundus showed a discrete circumscribed small bluish exudate, one disc diameter from the fovea. Tactile tension was normal. Left eye, vision 20/15, essentially normal.

All laboratory and X-ray tests, including smears for malaria, were negative.

Treatment was started with atropine solution and hot, wet dressings to the right eye, and a course of typhoid injections was given. Nose and throat and genito-urinary

consultation gave no significant findings. Brücellergin skin test, Volmer patch test, and first strength P.P.D. were negative. The vitreous floaters appeared to be decreasing on the 5th day of hospitalization, and vision was: R.E., 20/25; the peripheral field was slightly constricted, the central field normal. Second strength P.P.D. was positive, and old tuberculin was started.

On April, 18th, an increase in vitreous floaters was noted and the fundus was hazy. Old tuberculin was discontinued after five injections of 1:100 dilution in gradually increased doses. Vision was: R.E., 20/40 on May 1st, and decreased to 20/50—3 by May 3rd. The fundus appeared more cloudy.

One carious tooth was extracted and a slight ache developed in the right eye; the following day the tension rose to 65 mm. Hg (Schiøtz,); vision was 20/100. Retrobulbar injection and typhoid serum were given, with reduction of tension to 48 mm. Hg.

On May 11th, a paracentesis was performed. May 18th, the tension remained controlled; vision, 20/200; fundus, hazy and numerous keratic precipitates present.

On June 9th, the vessels in the fundus could be distinguished; a large yellowish-white exudate was seen in the superior nasal region, about 3 disc diameters across and about 5 disc diameters above the disc. This was suspected to be a tubercle.

On June 24th, the vision was 20/50 and the patient was dismissed for two weeks. On his return, vision was 20/30+2; tension, 26 mm. Hg (Schiøtz). The cornea was clear except for the paracentesis scar at the 7-o'clock position. The small discrete exudate area near the fovea was unchanged, as was the tubercle, and he was discharged.

Diagnoses: (1) Iridocyclitis, acute, recurrent, right eye; (2) choroiditis, acute, right eye, on tuberculous basis; (3) glaucoma, secondary to uveitis, right eye.

FAMILIAL CORNEAL DYSTROPHY

R. R. L., a man, aged 51 years, complained of progressive loss of vision since 1933; inability to wear glasses for more than a few minutes for near; intermittent redness of eyes and discharge in morning.

Eye examination was recommended when the patient was in third grade in school, but was not obtained. Repeated eye examinations since the age of 21 years revealed diminished vision. He was inducted into the Marine Corps, but not given target practice. He had had intermittent attacks of bilateral conjunctivitis, which improved with argyrol and warm boric-acid soaks. Corneal opacities were diagnosed in 1933 and glasses were prescribed, but the patient preferred 5- and 10-cent store reading glasses.

Family history revealed that his father died at the age of 61 years of a stroke. There was a history of special eye examinations. His mother died at the age of 67 years of diabetes. One eye had been enucleated; vision was poor with glasses. Four brothers had good vision. One brother had had one eye enucleated (traumatic). The other eye has "lattice-type dystrophy," and this man has been a patient of Dr. Fitzgerald. One sister has some eye trouble.

R. R. L. was first seen at Hines Hospital in 1931, at which time he was admitted for an injury. At that time vision was O.U., 20/50 correctible to 20/30. In 1933, the vision was unchanged, although the examiner described "fine stippling opacities of the cornea with clear centers seen bilaterally with slitlamp." In 1936 and 1946, vision had deteriorated to 20/100 and 20/200 respectively. At present:

	Searchingly	P.H.	Mydriatic
O.D.	20/50	20/50	20/70
O.S.	20/30	20/30	20/70

Own Glasses

2.5D sph., 20/60
4.0D. sph. ⊂ 2.0D. cyl. ax. 180°, 20/30

Examination of both eyes showed tactile tension to be soft; pupils equal and reacted to light, directly and consensually, and to accommodation; moderate chronic injection

of palpebral conjunctiva; marked anesthesia of corneas, which grossly had appearance of glass eyes badly scratched through the central areas; lens, media, fundus, negative.

Slitlamp examinations showed both corneas to have multiple discrete and confluent gray-white lesions of varying size and shape through all layers, confined to the central 6 mm.; pupil zones relatively clearer, with fewer lesions. The lesions themselves appeared like clumpings of a snowflakelike substance, in solid nodes and complete and incomplete doughnutlike rings. The overlying epithelium was irregular and the majority of the lesions were in the superficial stroma. The periphery was not entirely clear but had what appeared to be a gerontoxin in the inferior one half.

Discussion. Dr. James E. Lebensohn said that all these patients show the juvenile type of disciform degeneration of the macula. Three very similar cases were illustrated by Adler, in 1944, and, although the senile form of disciform degeneration of the macula is more commonly seen, the first cases reported were also of the juvenile type. The abiotrophies are generally not restricted to one age level. Amaurotic family idiocy has both infantile and juvenile types. Hereditary macular degeneration can be classified by age incidence into 4 of 5 groups. There is as yet no treatment for the condition. Although temporary remissions may occur, the inevitable end is poor central vision.

Dr. Charles A. Bahn (New Orleans) felt that these cases represent the ophthalmic condition we are most frequently called upon to diagnose and treat—atypical senility. Unfortunately, few people are like the one-horse shay of Oliver Wendell Holmes; some of the billions of cells which constitute the body are dying and being reborn every minute. The constitutional death and replacement rate varies widely in different tissues in different persons, and at different periods of life. In the retinal neuro-epithelium, for example, there is practically no replacement after birth. Hence, if these cells

have a constitutional predisposition to senility, function becomes permanently lost before death. If this process takes place in childhood, it is called Best's disease; in adolescence, Stargard's disease; and in middle life, Behr's disease. These are essentially the same condition, varying only at the time at which presenility actually manifests itself. The macula is usually first involved because it is phylogenically the oldest part of the retina and more highly specialized. The absence of repair is illustrated in the lack of new blood-vessel formation.

The younger ophthalmologists especially would do well to obtain a better understanding of the structural and functional evidences of normal and abnormal senility in all parts of the eye because of their diagnostic importance.

Dr. Homer Field said that the third case demonstrates the fact that, when there is posterior uveitis and glaucoma, it is hard to see what is left of the fundus. Solitary tubercles of the fundus and choroid are not too rare, neither are they common. Usually they occur in the choroid in the region of the posterior pole, or at the equator, and may be quite elevated, or under the layers of the retina and fairly flat. Sooner or later detachment occurs, which may be prominent or fairly flat. The tubercle tends to show a considerable amount of pigment. In this case, the fact that there was little disturbance of pigment is noteworthy, and it is a question whether this is a solitary tubercle or a case of posterior uveitis on a possible tuberculous basis.

The relationship between extraction of the tooth in this case and exacerbation of the condition of the eye is interesting. It demonstrates that, in differential diagnosis, one must not lose sight of more rare conditions such as Boeck-Schauman's disease which can cause considerable posterior involvement of the eye and yet does not produce too much acute inflammation. Toxoplasmosis must also be considered. In the absence of other positive findings, this could well be a solitary

tuberculous lesion; however, there are evidences of older, smaller lesions, which may or may not have been the same type. It is always interesting to think in terms of miliary tuberculosis when a solitary tubercle is found. The general condition of this patient does not speak for any great amount of tuberculous involvement.

Dr. Cyril Crane said that the fourth case was selected because it was felt that it represents a classical clinical picture of familial corneal dystrophy, first described by Grünow in 1890. It is obvious that there are many similar disease processes described under various names which are essentially the same clinical entity, probably with minor differences in morphologic detail.

Familial corneal dystrophy is an hereditary degenerative process occurring usually bilaterally, the symptoms first becoming manifest at about the age of puberty with insidious loss of vision; it is characterized by deposition of hyalinlike material in the layers of the substantia propria of the cornea, particularly the central portion thereof.

The first type described in the literature by Grünow was of this type; he later elaborated on the description by giving the histologic findings, in 1898, and, about 1917, was able to report on transmission of the disease through three generations; in 1933, he reported on four generations, all the cases having been examined by him personally.

This patient, so far as can be determined from the history, had some difficulty even prior to the age of puberty. Several cases have been reported in which it was thought that, biomicroscopically, the findings could be detected before the age of puberty. Obviously the loss of visual acuity here was so insidious that little attention was paid to it until about 1931. However, the patient was obviously otherwise physically well qualified, inasmuch as he was selected for the Marines in World War I; the qualifications for that service have always been high. He was never at any time put on the rifle range, which is an important part of the Marine Corps, so

it must be assumed that at that time, when he was 19 years old, there must have been considerable loss of visual acuity.

Thirteen years later, when seen at Hines Hospital, in 1931, he showed the early slit-lamp findings of pearly white dotlike lesions occupying principally the anterior third of the substantia propria in the central area. At the present time, at the age of 51 years, the patient's visual acuity has been markedly reduced and he now has variable types of lesions in all layers of the substantia propria, some of which could be described as of the reticular variety. However, the lesions predominantly are nodular as described by Grünow, varying in size and shape, many with a rather characteristic doughnut or ringlike appearance and, for the most part, in the peripupillary zone, which is also rather characteristic.

Dr. J. Robert Fitzgerald mentioned that the younger brother of the fourth patient reported had lost one eye due to trauma many years ago. The corneal changes started some time during adult life and there was a corneal stippling similar to that seen in the older brother. The opacities were primarily in the axial portion of the cornea with a perfectly clear periphery. When last seen, about a year ago, the lesions were comet-shaped and clublike, alphabetical, and interlacing, with a rather lattice-shaped pattern in the central portion of the cornea. The opacities were much more prominent, although the visual level was apparently about the same as that of his brother. The opacities were of such density that they could be seen at 4 or 5 feet with ordinary room illumination; whereas, in this patient, they were visible primarily with retro-illumination.

NEUROFIBROMATOSIS OF THE EYELID

Dr. Max M. Kulvin spoke on the surgical repair of neurofibromatosis of the eyelid and reported on two cases. His paper is published in full on page 1231 of this Journal.

Discussion. Dr. James E. Lebensohn said

that, at first glance, one is discouraged from working on these cases because everything seems so disorganized. However, although the final result leaves much to be desired, it is, nevertheless, better than either the surgeon or the patient anticipated. All the patients were well satisfied with the results.

Dr. Homer G. Field stressed the use of the sliding flap with the tarsal plate in reconstruction of the eyelids. In these two cases there was marked destruction of the eyelid and, in one, there was absolutely no tarsus left—the conjunctival surface was completely obliterated. It is simple to make a tarsal conjunctival flap and slide it into position in the upper lid. The technique was designed originally by John Wheeler and later modified considerably by Wendell Hughes.

In this case the technique was actually a Wheeler-Hughes operation in reverse; instead of bringing the upper tarsal plate down to the lower lid, the lower tarsal plate was brought to the upper lid.

For overcoming ptosis any suspension procedure may be used, as a fascia lata suspension from the superior rectus; where there is so much redundant tissue, however, suspension from the brow margin is probably a better procedure.

Reconstruction of an eyelid is sometimes a problem. Where there is a large tumor mass, with complete destruction of the functioning portion of the lid, it is difficult to preserve or restore function. If ptosis is permitted to remain complete, a functioning result is not obtained.

Dr. Max M. Kulvin (closing) said that in one case the final result so far as vision is concerned is poor. Some complication developed which caused corneal scarring and not much vision was obtained, but the patient had had none for so long that he was not concerned about that.

SURGERY OF ORBITAL IMPLANTS

DR. NORMAN CUTLER (Wilmington, Delaware) discussed the ideal implant which should accomplish certain objectives

such as permanence, motility, and a good cosmetic result. The integrated type implant is being improved in every respect until it now merits serious consideration by all ophthalmic surgeons. The only factor still to be determined is the one of permanence. This, of necessity, will require more than the few years so far available. The cosmetic result and motility are uniformly good. The operation has been simplified and shortened and the possibility of postoperative complications has been greatly reduced or eliminated. Although the present advances are due to the discovery and use of the plastic artificial eye, this material is still not ideal from the aspect of minimal tissue reaction.

The subject was discussed under the general headings of: (1) Types of implants—their advantages and disadvantages; (2) evisceration versus enucleation, with indications for each; (3) illustrations of operative procedures; (4) possible complications; (5) possibilities in reimplantation procedures; (6) a general discussion of statistics.

It is believed that statistics can be overemphasized in either advocating or condemning any procedure. They may be particularly misleading when constant experiment and development of a procedure is taking place and when these procedures must, in the nature of things, be carried out on human subjects.

Discussion. Dr. V. M. Leech asked whether Dr. Cutler had discarded ring implants in favor of those that have tantalum mesh only. Also, some surgeons used charred bone balls instead of glass and other smooth materials, and he wondered whether Dr. Cutler had had any experience in removing such implants in order to insert the more modern ones of which he spoke.

Dr. Cyril V. Crane asked how selection is made for reimplantation in the absence of previous history or record as to the original operative procedure, and what criteria are used to determine the presence of adequate healthy conjunctiva for reimplantation.

Dr. J. Robert Fitzgerald asked whether

Dr. Cutler had any operative technique that he feels may prevent granulomatous changes around the neck of the implant. Many times there is bleeding for a considerable period after the prosthesis has been implanted.

Dr. Norman Cutler (in closing) said that the ball and the ring implant is not being used. In his opinion, over a period of years tissue which has formed around a ring will gradually erode through. A number of his cases had been under observation for more than three years, but he felt there is a tendency, as the tissue stretches over a hard surface, for it to gradually wear thin. The principal advantage of the ring implant is that it is a space-developing implant when it turns;

however, because of the difficulty of insertion it will probably not be used. He had not removed any bone balls to put in implants. One would probably have to cut the tissue off with a knife.

When a reimplant is put in, more conjunctiva is available in the fornix. The only criterion is movement in the stump. If there is no movement, there will be no improvement. Most do have quite adequate movement, but some do not.

The problem of granulomatous tissue cannot be answered as yet. He had cauterized it on occasion, but had felt that if it did occur it would not be a permanent problem.

Richard C. Gamble,
Secretary.

OPHTHALMIC MINIATURE

I have lately seen two cases in which there was a paralysis of all the parts supplied by the nerves of the third pair, viz. three of the recti muscles, one of the obliqui, and the levator palpebrae superioris, so that the upper eye-lid could not be elevated, and the globe was drawn outwards by the external straight muscle. In both instances the pupil was largely dilated. It may, perhaps, be suspected that the optic nerve was insensible; but this was not the case, for when the patient looked through a minute opening in a card, producing what may be called an artificial contracted pupil, vision was perfect. I mention these facts, because they may assist in the investigation of the subject, for further inquiry is undoubtedly necessary. If a perfect state of motion can subsist in the iris when the retina is perfectly insensible, the changes in the pupil cannot be referred to the effect of light upon the optic nerve. To what, then, it may be asked, are we to refer them? How are they to be explained? I confess that I cannot explain them.

Sir William Lawrence, *A Treatise on the Diseases of the Eye*, 1833.

AMERICAN JOURNAL OF OPHTHALMOLOGY

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RECENT TRACHOMA STUDIES

In reviewing wartime trachoma studies for the two volumes of *Ophthalmology in the War Years*, edited by Dr. Meyer Wiener, I was impressed by the dearth of significant reports on the disease still considered by many to be the eye disease of greatest worldwide importance. Since the war, however, a number of significant studies have appeared, notably by Professor Mitsui and his collaborators in Japan and by Professor Bietti and his collaborators in Italy.

The Japanese studies were actually reported during wartime but only became available to English readers in 1948. They are summarized in an article by Professor Mitsui in this issue of the JOURNAL.

These investigators confirmed anew that human volunteers could be inoculated with trachoma. In their experience the average incubation period was from 5 to 6 days. The onset was always acute and Prowazek-Halberstaedter inclusion bodies were always present, in numbers proportionate to the severity of the clinical signs.

The question of the frequency of inclusion bodies in the chronic stage of the disease was reexamined. Typical inclusions were

found in 537, or 65 percent, of 823 chronic cases and in 85 percent of 392 cases with typical clinical symptoms. Tissue sections were positive for inclusions in 108, or 92 percent of 117 cases. Inclusions were demonstrated in the epithelium of the lacrimal sacs of 5 of 6 patients with early conjunctival trachoma and were noted in the canaliculi of 2 additional cases. ·

The inclusions were never found in the subepithelial tissues and the absence of trachoma virus in these tissues was proven in 10 cases of typical trachoma: subepithelial tissue, obtained in all 10 cases without penetration of the conjunctiva, was shown to be noninfective for human volunteers;· control inoculations with conjunctival tissue from the same cases resulted in typical infection. Furthermore, subconjunctival inoculation of volunteers with infective material failed to induce trachoma; whereas, a control inoculation of the conjunctiva with the same material resulted in typical experimental trachoma.

In tissue-culture experiments, the Japanese investigators were unable to obtain growth of the virus in serial cultures, although the first two cultures of trachomatous epithelium were infective. On the basis of inoculation experiments on blind infant eyes, they claim to have established an identity between inclusion blennorrhea and trachoma but their evidence on this point is inconclusive. Interestingly enough, they were able to infect the human cervix with trachomatous materials, a finding comparable to that of Braley who obtained infection of the cervix of the female baboon with trachoma virus.

The experiments of Bietti and his collaborators dealt primarily with the therapy of trachoma, although Bietti covered all aspects of the disease in a monograph entitled "Il Trachoma," published in Rome in December, 1947. In a resume of his studies on the sulfonamide and penicillin therapy of trachoma (Revue Internationale du Trachoma, 25: 115, 1948), Bietti concluded that all the ordinary sulfonamides were active against

trachoma but that he preferred paraminophenylsulfamide.

He recommended an oral dosage of 2.5 gm. daily for 10 days or longer; topical applications he found less valuable. The drug was most effective against the secreting forms of the disease and against pannus and corneal ulceration. He found that 50 percent of all cases were cured completely and that about 10 percent of the actively secreting forms and 40 percent of the chronic hyperplastic forms were resistant.

He stated that recurrences were frequent after short treatment periods and that reinfections occurred in about 5 percent of cases. He noted that about 10 percent of subjects had an intolerance to the sulfonamides but that vitamins C and B complex were useful in reducing the intolerance. He was able to show that patients on sulfonamide therapy were noninfective for monkeys and man.

Professor Bietti found that penicillin had some curative effect on trachoma but that it was less effective than the sulfonamides. He noted the disappearance of epithelial inclusions within 72 hours. The effect of penicillin on secondary infection was marked. Streptomycin also had a marked effect on secondary infection but little if any on trachoma virus itself. Tyrothricin was of no value.

Of special interest is an article by Bietti and Pasca (Boll. Soc. ital. biol. Sper., 24:82, 1948) reporting the inefficacy in trachoma of paraminobenzoic acid, a substance which is highly reactive against the Rickettsiae. The investigators concluded that this lack of sensitivity of trachoma virus to paraminobenzoic acid, combined with its sensitivity to the sulfonamides and penicillin and its negative Weil-Felix reaction, ruled out the existence of any close relationship between trachoma virus and the Rickettsiae.

These etiologic and therapeutic studies constitute important contributions to our knowledge of this still most destructive of eye infections.

Phillips Thygeson.

CORRESPONDENCE

Editor,

American Journal of Ophthalmology:

I should like to bring to your attention that the 1949 *Transactions* of the American Ophthalmological Society, published in book form, may be purchased by advance subscription.

This volume, priced at $12.00, contains the scientific papers presented at the annual meeting and the theses for membership. It may be ordered from the Editor:

Dr. Wilfred E. Fry
1930 Chestnut Street
Philadelphia 3, Pennsylvania

All orders must be received by December 1, 1949.

(Signed) Maynard C. Wheeler,
New York, New York.

PUPILLARY DILATATION BY

DATURA STRAMONIUM

Editor,

American Journal of Ophthalmology:

In the March, 1949, issue of the JOURNAL, Dr. Lucian Bauman published an interesting article on "Accidental cycloplegia by Jimson weed," in which he stated that "there are only 7 reported cases of accidental cycloplegia (by Datura stramonium) in the world literature during the past 50 years; 3 in the United States, 1 in Cuba, 1 in France, and 2 in French Morocco," and lists the references.

My name is omitted, although I observed a case of accidental pupillary dilatation due to Datura stramonium and reported it in the *Santa Fe Medical Review* (Argentine Republic) in the issue for October-December, 1940, on pages 26 and 27. In this case, accidental cycloplegia occurred while the patient was washing her hair with an infusion of leaves of the Datura stramonium and un-

thinkingly let some of the liquid run into her eyes. Experimentally, I have produced maximum mydriasis in eyes into which I instilled a filtered infusion of leaves of this plant.

In effect, the above paragraph is what I published in the *Santa Fe Medical Review,* and I believe that this summarized reminder is of interest as a marginal note to the recent work of Dr. Bauman.

I should like to avail myself of this opportunity to advocate the exchange of medical reviews with their articles summed up in several languages so that oculists of each country can know what is published abroad.

(Signed) Francisco Páez Allende,
Santa Fé, República Argentina.

USE OF WATER BATHS TO PROMOTE
WOUND HEALING

Editor,

American Journal of Ophthalmology:

I have found the following procedure for the management of ocular wounds to be most successful and to fulfill these aims: (1) early closure of the wound, (2) diminution of the scar, and (3) retention of the greatest amount of visual function.

After all visible debris has been removed, the wound is submerged in a water bath as warm as the patient can stand for three quarters of an hour, warm water being added to the bath from time to time to keep the temperature even. The patient is instructed to rotate his eye and to blink occasionally.

Following local anesthesia with novocain and adrenalin, a careful wound toilet is made. It is surprising how many foreign bodies not visible before the bath are visible after it. No tissue is trimmed for the parts not possessing vitality will be eliminated. Do not scrub or scrape the wound surface. If necessary, use sutures but do not complete the sewing for the sutures are to be used to guide the healing. Wound closure is attained by submerging the wound daily in a water bath. After the toilet is completed, the

wound is bandaged. The bandage is changed daily at which time the water bath is repeated.

As soon as possible after healing starts, remove the sutures and increase the number of water baths to 3 or 4 daily. As the scar contracts, the continued water baths bring hitherto invisible foreign bodies to the surface. It is surprising how quickly old and recalcitrant wounds respond to this treatment, bringing to mind the old Latin proverb: "Medicus curat, natura sanat."

Although I claim nothing new in this procedure for wound management, I believe it is well to point out that the fear of washing a fresh wound with water has no basis in fact. Bathing infected as well as sterile wounds in warm water once or more times daily for 30 to 45 minutes not only promotes healing but produces a more satisfactory closure.

In my opinion, the best first aid in an ophthalmic emergency is to submerge the wound in warm water. The wound bath is followed by careful dressing, the use of a sulfonamide powder, or penicillin, and bandaging. Secondary sutures are used only if necessary.

(Signed) Janos Majoros,
Kiskunhalas, Hungary.

BOOK REVIEWS

ELEMENTS OF GONIOSCOPY. By Archimede Busacca. São Paulo, Brazil, Rossolillo, 1945. 187 pages, 106 illustrations, 1 color plate, bibliography, and index. Price, not listed.

The appearance of this splendid textbook of gonioscopy has not hitherto been reviewed in these pages. It is worthy of special note for its author has contributed much original thought and information to the subject and was the first to bring together in book form the rich material on gonioscopy in the literature and from his own experience.

The book is written in French, but it is so well illustrated that it is not difficult to follow. After discussing at considerable length the technique of gonioscopy (Goldmann's contact lens and biomicroscopy), the anatomy of the iris angle and its appearance in gonioscopy, the author proceeds, in Part II, to describe the pathologic conditions of the angle as studied in gonioscopy. These conditions include anterior synechias, uveitis, after operations, in injuries, keratitis, adherent leukomas, dislocated lens, iris coloboma, glaucoma capsularis, and other forms of glaucoma.

Part III discusses experimental gonioscopy in iridectomized eyes under the effect of eserine or atropine. Eserine makes the ciliary bodies visible by traction; whereas, atropine retracts them.

The growing number of books on gonioscopy in English and French signifies the extent of its importance and interest to ophthalmologists. No representative ophthalmic library should pass up this excellent modern contribution to our science.

Derrick Vail.

LA GONIOSCOPIE. By Jules François. Louvain, R. Fonteyn, 1949. 220 pages, 156 illustrations of which 48 are in color, bibliography. Price, not listed.

This beautifully written, printed, and illustrated monograph represents the results of many years of study by the author. It is the second of its kind to appear in the French language, and was prepared at the request of the Belgian Society of Ophthalmology. It forms a welcome addition to the previously published volumes on the subject, notably those of Uribe Troncoso and Archimede Busacca.

The various chapters deal with the anatomy of the iris angle, the physiologic importance of the canal of Schlemm, the technique of gonioscopy, the normal gonioscopic aspect, congenital anomalies, ocular injuries, tumors, anterior synechias, uveitis, primary and secondary glaucoma, and postoperative gonioscopy.

Dr. François has arranged his material very well and the illustrations are eminently satisfactory, so that even the non-French-reading ophthalmologist will gain much important information just by leafing through the book. Those who read French will enjoy the fluent and lucid style of its author.

Derrick Vail.

TRANSACTIONS OF THE OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA. Volume 7, 1947.

The president's address, by Darcy A. William, is an interesting history of ophthalmology in Australia. The medical journals are important repositories of the data on which the story is based and their histories are included in the address. The *Australian Medical Journal*, the earlier of the two major roots of the present *Medical Journal of Australia*, which is one of the best of the world's weekly journals of general medicine, was founded in 1856.

H. M. Macindoe, in an essay on "Research organization and training overseas," recounts his experiences on an extensive visit to the medical centers of Europe and America.

J. Bruce Hamilton's "Further contribution to the study of dry eyes" amplifies his earlier study of keratitis sicca, Sjøgren's syndrome, and some unclassified cases. He clarifies the relations of these diseases to desiccation keratitis, mustard-gas keratitis, Plummer-Vinson syndrome, Mikulicz's disease, and iodide "mumps." He presents a follow-up study of the patients reported in 1940 and adds a further 24 cases of dry eyes.

Tostevin gives an adequate discussion of eye protection in industry and there are numerous short reports, 1 to 5 pages in length, on 15 other topics.

F. H. Haessler.

ARCHIVOS Y MEMORIAS DE LA SOCIEDAD DE OFTALMOLOGÍA DEL LITORAL (Organo oficial de la Sociedad de Oftalmología del Litoral). Rosario, Argentina, Volume 1, 1947-1948. Paper covers, 272 pages, illustrated.

The title of this volume, and of the society which it represents, furnishes a good example of linguistic idiom. Literally, or in the dictionary sense, we are dealing with the proceedings of the ophthalmological society of the coast (of Argentina). However, the actual broader significance appears to be "Ophthalmological Society of the Provinces (or outlying areas) of Argentina, the term "litoral" or "coast" being used in this greatly broadened sense.

The society's center of action is the great city of Rosario, the second largest city of the South-American republic, with a present population well over half a million, located 200 miles northwest of Buenos Aires, on the huge river Paraná, which rises not very far from Rio de Janeiro and runs 2,720 miles before reaching the sea at the estuary called La Plata.

The very progressive city of Rosario, with an important university and medical school, gave birth in 1938 to the vigorous second ophthalmological society of Argentina. That society, just now under the presidency of Enrique V. Bertotto, the vice-presidency of Arturo Reca, and the secretaryship of Juan Vila Ortiz, has already attained a membership of 67 coming from widely separated cities of the country. It has welcomed a number of foreign ophthalmologists at its periodical meetings, including two from the United States.

The present volume, the first annual volume of transactions published independently by the society, includes about 30 papers. Perhaps the most ambitious theme presented is the very painstaking effort of Bertotto to develop a machine for making mathematically photographic tracings of the anterior segment of the eye upon which to base a mold of the anterior segment in producing a contact lens. This technique he calls stereophotogrammetry.

W. H. Crisp.

ABSTRACT DEPARTMENT

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Aurell, G., and Kornerup, T. **The glandular structures at the corneoscleral junction in man and swine; the so-called "Manz glands."** Acta ophth. 27:19-45, 1949.

The object of this investigation was to clarify the conflicting data on the presence and nature of the glands described first by Manz in 1859. The material for the study consisted of a large number of specimens of the limbal conjunctiva of adult and new-born swine and man, and human embryos of different ages; most of the specimens were stained in toto. As the photomicrographs show, the structures described as the glands of Manz are only solid epithelial buds or tubules, which are rudiments of the lacrimal glands present in the embryonic limbal conjunctiva of swine. Balls of epithelium in the limbal conjunctiva of swine have no secretory function. In man there are no glands of Manz nor lacrimal glands at the limbus during any period of development. The corneal epithelium at the limbus grows into the conjunctiva as thick, often branching ridges; parts of these sometimes become isolated and form solitary epithelial balls, which may simulate glands, but which are not glands histologically, and have no secretory function. They may possibly give rise to conjunctival cysts. (17 photomicrographs.)

Ray K. Daily.

Fornes Peris, E. **The corneal innervation. Clinical considerations.** Arch. Soc. oftal. hispano-am. 9:237-244, March, 1949.

The author demonstrates with photomicrographs that the classical conception of intraepithelial corneal innervation is erroneous. There is no nerve plexus in the epithelial corneal layers, and innervation stops in the basal membrane. The patient is often unconscious of a foreign body on the cornea until the subepithelial nerves become irritated; even then he notes discomfort and lacrimation but is frequently not conscious of the foreign body, and may not seek ophthalmologic help for several days. The relief of pain when a corneal erosion is epithelialized is further clinical proof. (4 photomicrographs.)

Ray K. Daily.

Kokott, W. Functional anatomy of the choroidal membrane. Arch. f. Ophth. 148: 706-724, 1948.

The author studies isolated choroids of human eyes. To present their elastic framework some were digested with 4 percent potassium hydroxide. Further information was obtained by studying the directions along which the choroidal tissue splits most easily. It was found that the choroid and ciliary muscle represent an anatomic entity. The ciliary muscle serves as the tensor choroideae and helps to fill and empty the blood vessels of this membrane. Because of ganglionic cells in the choroid this mechanism, which controls the blood supply of the eye and the intraocular pressure, is to some extent autonomous. Ernst Schmerl.

Lopez Enriquez, M. The presence of medullary fibers in the retina. Arch. Soc. oftal. hispano-am. 9:367-389, April, 1949.

The author describes a patient with bilateral symmetrical medullated retinal fibers. The blind spot was somewhat enlarged and dark adaptation was retarded. The author critically reviews the literature on the disappearance of myelinated nerve fibers and emphasizes that their degeneration is of the descending type. A modification of Golgi-Rio-Hortega method of staining nerve tissue is described, and the course of the oligodendrial fibers described and illustrated. It is believed, on the basis of their anatomic course, that the oligodendrial fibers of the optic nerve are myelogenic, and the myelinated fibers of the retina are the result of a congenital anomalous extension of oligodendrial fibers into the retina. (11 figures.)
Ray K. Daily.

Trantas, N. G. Biomicroscopy of the zonule in normal eyes. Biomicroscopy of the ciliary body in two cases of surgical aphakia. Arch. d'opht. 9:31-38, 1949.

Trantas reports on the biomicroscopic examination of the zonule in normal eyes after full dilatation of the pupil by subconjunctival injection of 1-1000 adrenalin solution and with the Koeppe-contact glass. The zonule is examined both by direct and by retro-illumination, and detailed descriptions are given of the hyaloid membrane, the posterior fibers of the zonule, and the space between the hyaloid membrane and the posterior zonule. Trantas notes that the zonules at the equator are visible, as well as some of the most anterior ones. The triangular space (canal of Hannover) between the anterior and posterior zonule fibers is often sharply defined although traversed by a variable number of fibers from the equator of the lens. The author describes the complete illumination of the zonule by retroillumination and the visualization of the ciliary processes across the iridocrystallin space. He notes the differences in the appearance of the zonule and hyaloid membrane in myopia, in iritis, and in minimal subluxation of the lens, and stresses the clinical value of these observations.

Trantas reports two cases of surgical aphakia in which he was able to examine completely the ciliary body. He used a special flat-surface contact glass. The findings in the two cases are described in detail. The fundus of the normal eye can easily be visualized biomicroscopically up to the ora serrata and, with more difficulty, anteriorly. Phillips Thygeson.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Braley, A. E. Experimental studies of inclusion blennorrhea: isolation of a virus. Arch. Ophth. 41:151-171, Feb., 1949.

The virus of inclusion blennorrhea is similar to that of trachoma, lymphogranuloma venereum and psittacosis. Attempts were made to grow the virus of

inclusion blennorrhea by direct inoculation of chorioallantoic membrane, direct inoculation of yolk sac and in fluid tissue culture, all without success. Repeated blind passages through mice were carried out with the isolation of a virus which was considered as possibly the agent of inclusion blennorrhea. Mouse brain material containing this isolated agent produced a conjunctivitis in the baboon. The inclusion bodies could not, however, be recovered from the conjunctival scrapings of the baboon. Baboon eyes that had been inoculated with mouse brain material were immune to the inoculation with inclusion body scrapings. The agent from mouse brain grew well in the developing hen's eggs and could be transferred from the eggs back into the mice without difficulty. Detailed filtration, staining and neutralization tests were carried out. From these studies it was concluded that a new, unknown virus had been isolated; however, this new virus may represent a variant of the virus of inclusion blennorrhea.   John C. Long.

Campbell, F. W., and Michaelson, I. C. **Blood-vessel formation in the cornea.** Brit. J. Ophth. 33:248-255, April, 1949.

In a series of experiments it was determined that corneal lesions beyond a certain critical distance from the limbus produced no vascular response. At less than this distance a vascular area resulted which was in the form of an isosceles triangle. The vascular responses were quite constant in size with similar lesions, which suggest that a stimulating factor is released from the lesion. (4 photomicrographs.)   Orwyn H. Ellis.

Foss, Bjørn. **Experimental anaphylactic iridocyclitis.** Acta path. et microbiol. Scandinav. suppl. 81:1-127, 1949.

This study was undertaken to understand the unusual behavior of a patient with Behcet's syndrome characterized by extensive atrophy of the iris, retinal hemorrhage, ascending atrophy of the optic nerve, and relapsing hypopyon uveitis. The oral mucosa showed aphthous efflorescences and on the genitalia numerous superficial ulcers and blisters were seen. Cutaneous tests with tuberculin, trichophytin, staphylococcal vaccine, and omnadin showed a general hypersensitiveness. He was especially sensitive to staphylococcus vaccine. Intradermal injection of 1/1000 cc. of the usual staphylococcal vaccine caused a huge infiltration, sometimes with abscess formation, and always was followed by an attack of hypopyon uveitis in one to three days. Each injection was also followed by necrotic infiltration at the site of previous ones. After a series of blood transfusions the patient was free from attacks.

When 0.1 cc. of foreign serum or egg albumin is injected into the vitreous of healthy albinotic rabbits an iridocyclitis will appear after a constant incubation period. This reactive iridocyclitis is of an anaphylactic nature. Antigen is still present after the constant incubation period, and this antigen will unite with the specific antibodies of the uveal cells. This reaction is called primary anaphylactic iridocyclitis. Rabbits that have had primary anaphylactic iridocyclitis will react with a new iridocyclitis to intravenous or subcutaneous injection of a homologous antigen. Occasionally the iridocyclitis is bilateral. This iridocyclitis is designated as secondary anaphylactic iridocyclitis. It will develop within a few hours after an intravenous injection and within 24 hours after a subcutaneous injection, but no iridocyclitis will develop after an intracutaneous injection because the antigen is fixed to the cells and does not enter the circulation.

Animals that have received a general sensitization will develop a reactive iridocyclitis as an immediate result of intravenous injection of homologous antigen,

provided that the sensitization had occurred at least eight days before.

Rabbits that have had primary anaphylactic iridocyclitis of one eye will respond with a bilateral iridocyclitis 24 hours after an injection of the homologous serum into the other eye. This reaction is called sympathetic anaphylactic iridocyclitis; it does not correspond to the clinical form of sympathetic ophthalmitis.

Precipitation tests showed that the formation of antibodies following injection of 0.1 cc. of horse serum or egg albumin into the vitreous was considerably more marked than when the same amount of antigen was injected intracutaneously. The cutaneous reactions, too, revealed that intraocular injection of the same amount of antigen sensitizes the animal to a greater degree than cutaneous or intravenous injections. After primary anaphylactic iridocyclitis animals constantly develop local anaphylactic reactions as a result of intracutaneous injection. Even the 1 to 1000 antigen dilution caused a large infiltration with a central area of hemorrhages and necroses. The subcutaneous tissue, too, presented hemorrhages and dilated, blood filled vessels.

R. Grunfeld.

Scuderi, Giuseppe. **More about hemorrhagic allergy and the eye (experimental attempts to inhibit the Sanarelli-Schwartzman phenomenon).** Ann. di ottal. e clin. ocul. 74:512-522, Sept., 1948.

The Sanarelli-Schwartzman phenomenon is a necrotico-hemorrhagic reaction occurring when a bacterial filtrate is injected intravenously in a previously sensitized animal. Experimenting with rabbits, Scuderi found that the phenomenon could be inhibited by artificially induced fever but not by injections of antistin (a synthetic antihistamine compound). The antiallergic effect of pyrexia cannot be due to an antihistaminic action, and histamine is not a determining factor in the production of the Sanarelli-Schwartzman phenomenon. (References.)

Harry K. Messenger.

Streiff, E. B., and Cuendet, J. F. **The seasons and certain ocular affections.** Ann. d'ocul. 182:329-363, May, 1949.

Seasonal changes of temperature, moisture, and air pressure directly influence disease. Although geographic factors influence many eye diseases, the affect of season is apparently more important in numerous ocular diseases than the literature suggests. Data on the 20,000 cases used in this survey were collected from Germany, the United States, Switzerland, Italy, Russia, China and Japan.

Chas. A. Bahn.

Suurkula, Juri. **The effect of weather on some ophthalmological diseases.** Acta ophth. 27:75-88, 1949.

This study of 469 case histories and a critical review of the literature lead to the conclusion that the effect of air front changes on the occurrence of disease has been greatly exaggerated, and that the data on which the former studies of meteorotropism were made were incomplete and inadequate. (6 graphs, 2 tables.)

Ray K. Daily.

3

VEGETATIVE PHYSIOLOGY, BIO-
CHEMISTRY, PHARMACOLOGY,
TOXICOLOGY

Bonavolontá, G., and de Bernardis, E. **Effects of Filatov's tissue therapy on experimental retinal pigment degeneration in the rabbit.** Bol. d'ocul. 28:65-76, Feb., 1949.

Retinal pigment degeneration was produced in rabbits by intravenous injections of one cc. of 4.5-percent solution of sodium iodide per kilogram of body weight. Tissue therapy consisted of implantation of placenta according to the Filatov method and injections of palcental extracts and of

cod liver oil. The development of experimental retinal degeneration was inhibited in animals treated with both cod liver oil and placenta transplantation. Histologic examination confirmed the clinical observation. Controls treated with organ lysates of liver and of embryonic tissue did not respond with inhibition of the degenerative process in the retina. The mode of action of the effective materials is discussed. (References.)

K. W. Ascher.

Cibis, P., and Hochgeschurz, G. **Pressure experiments dealing with the effects of ischemia upon the retinal function.** Arch. f. Ophth. 148:752-760, 1948.

The authors used H. K. Mueller's dynamometer to produce increased intraocular pressure in man and studied visual acuity and visual fields in relation to the diastolic and systolic bloodpressure. They conclude that the diminished efficiency of the eye in diseases which have increased tension is caused by circulatory disturbances, not by primary changes of the optic nerve. Ernst Schmerl.

Cruthirds, A. E. **Sulfur metabolism and its relation to wound healing in ophthalmology and otolaryngology.** Tr. Am. Acad. Ophth. pp. 596-604, May-June, 1949.

In the treatment of many types of acid and alkaline burns of the eyes a 5-percent solution of hydrosulfosol in castor oil is recommended. Hydrosulfosol is a sulfadryl preparation and acts as a reducing agent. Sulphur is contained in many proteins and is largely deposited in the skin. In injuries and burns sulphur metabolism is disturbed. Sulfadryl apparently stimulates the production of enzymes for the synthesis of sulphur-containing animal acids. Chas. A. Bahn.

Davids, B. **Effects of quanta-irradiation upon the eye.** Arch. f. Ophth. 148: 617-642, 1948.

In this theoretical discussion shortwave irradiation is considered as a bombardment of the eye by single corpuscles. The changes seen in the cornea and the lens occur in foci. Single cells or smaller groups of cells are affected where radiation quanta impinge on vital structures, especially of the nuclei. Four groups of quanta-effects are enumerated: effects upon the cell plasma and the cell membrane, gene-mutations, inhibition of mitotic processes, and disturbance of the structure of the chromosomes. The need to visualize the microphysical nature of these effects of radiation is emphasized.

Ernst Schmerl.

Duke-Elder, S., Davson, H., and Maurice, D. M. **Studies on the intraocular fluids. II. The penetration of certain ions into the aqueous humour and vitreous body.** Brit. J. Ophth. 33:329-338, June, 1949.

Thiocyanate penetrates from the blood into the aqueous humor and especially the vitreous body more rapidly than either sodium, potassium or monosaccharides. Thiocyanate and the monosaccharides diffuse into the vitreous body from all the vascularized tissue surrounding it. Sodium and potassium enter predominantly from the ciliary region. In studying the factors of cell membrane permeability it was found that transference from the blood into the chambers of the eye takes place through cell bodies and not intercellular spaces. The concentration of salts in the intraocular fluids is greater than can be accounted for by a process of simple ultrafiltration; a process of secretion may be postulated.

Orwyn H. Ellis.

Fitzhugh, O. G., and Buschke, W. H. **Production of cataract in rats by beta-tetralol and other derivatives of naphthalene.** Arch. Ophth. 41:572-582, May, 1949.

Changes in the lens which were similar to those described in naphthalene poisoning in rats were produced by feeding B-tetralol. A large number of naphthalene derivatives were studied for their possible cataractogenic property. In addition to B-tetralol, 1,2,3,4-tetrahydro-2-naphthylpropionate and B-naphthylsalicylate were more potent as cataractogenic agents than was either naphthalene or B-naphthol; B-tetralol, parenterally administered, was more than twice as potent. Sulfhydryl compounds did not prevent the formation of cataract in rats fed B-tetralol.

Ralph W. Danielson.

Fontana, Giuseppe. **The action of emetine on the cornea.** Arch. di ottal. 52:113-132, May-June, 1948.

The effect of this drug on the cornea was first studied just before the first world war but the studies were rather incomplete. Corneal lesions ranging from a diffuse irregular nebular clouding to ulceration have been noted. Experiments were made with solutions varying from 1 to 5 percent. A reaction was evident in a few hours and may have been toxic, or anaphylactic. Corneal hyperesthesia, pain, and lesions of corneal nerve endings were noteworthy. The author studied the effects of 2-percent emetine injected under the conjunctiva of the bulb or the tarsus conjunctiva, and retrobulbarly. The corneal changes in most of these rabbits appeared after 48 hours and this tissue returned to normal in about 12 days. The hypothesis of anaphylaxis should receive some consideration. Francis M. Crage.

Fontana, Giuseppe. **Action of prostigmin on intraocular tension and on the diameter of the pupil.** Arch. di ottal. 52:165-181, July-Aug., 1948.

Research was carried out on three groups of rabbits and one group of patients with normal and glaucomatous eyes

among which were 22 cases of acute glaucoma, 12 of chronic glaucoma, and 2 of hydrophthalmus. There was marked reduction in tension in practically all acute and chronic glaucoma within 24 hours. In all the pupil came down to 2 mm. No effect was seen in the hydrophthalmic eyes. In the animals an iris prolapse was often partially or completely reduced within 48 hours after prostigmin especially when injected subconjunctivally. Pilocarpine and eserine were not as effective. The use of prostigmin alone, and in association with eserine, is recommended in prolapsed iris after limbal injuries.

Francis M. Crage.

Fontana, Giuseppe. **Farmocain in ophthalmology.** Arch. di ottal. 52:188-194, July-Aug., 1948.

This new anesthetic is p-butylaminobenzyl-diethylamine chloride. It is a white crystalline powder, odorless, bitter, and soluble in water and ethyl alcohol. Solutions of $\frac{1}{4}$, $\frac{1}{2}$, 1, 2, and 3-percent strength were instilled into the conjunctival sac of rabbits and patients. In the normal human eye a 1-percent solution produced a slight burning, hyperemia, and anesthesia in one minute. Anesthesia lasted for twenty minutes. When repeated twice within twenty minutes, engorgement of the conjunctival vessels took place but there was no corneal damage, change in the size of the pupil, or ocular tension. Where ulcers, keratitis, or foreign bodies were present, the burning and hyperemia were slightly increased.

Francis M. Crage.

Fralick, F. B., and Kiess, R. D. **Use of antihistaminic drugs in control of atropine dermatitis and conjunctivitis.** Arch. Ophth. 41:583-586, May, 1949.

Atropine sulfate may be continued after the development of atropine dermatitis and conjunctivitis, since the reaction is

controllable by concurrent antihistaminic therapy. Pronounced improvement with antihistaminic treatment was noted within forty-eight hours in 8 or 9 consecutive cases of atropine hypersensitivity. A combination of local and general antihistaminic therapy proved most effective. From this limited series, it would seem that the treatment of choice is a combination of oral administration of tripelennamine hydrochloride (pyribenzamine) and local use of diphenhydramine hydrochloride (benadryl). Ralph W. Danielson.

Heath, P., and Geiter, C. W. **Use of phenylephrine hydrochloride (neo-synephrine hydrochloride) in ophthalmology.** Arch. Ophth. 41:172-176, Feb., 1949.

Phenylephrine is a valuable member of the group of drugs possessing sympathomimetic activity. It may be used as a decongestive agent for the conjunctiva or globe. As a mydriatic it is used for fundus examination, in breaking adhesions of the iris to the lens, in refraction, and in some intraocular operations. Phenylephrine is of value in infiltration anesthesia as a decongestive and antispasmotic, and to prolong the action of the anesthesia. A number of less common uses are listed. The rapid absorption of substantial amounts of the drug causes marked and hazardous increase of the blood pressure. However, when applied to the anterior segment of the eye there is no significant change in either blood pressure or intraocular pressure. No harmful effects on the ocular tissues or the blood vessels have been observed nor has sensitivity or delayed healing been reported.

John C. Long.

Huggert, A. **A further support to the hypothesis that Ascher's aqueous veins contain aqueous humor.** Acta ophth. 27: 119-123, 1949.

The author dropped fluorescein into the conjunctival sac of patients with marked corneal erosions. When the aqueous was stained with the fluorescein previously localized aqueous veins were also filled with green fluid, and pressure on the eyeball was followed by an increased outflow of this fluid. The veins proximal to the point of entry of the aqueous veins remained unstained. In other eyes with a normal cornea the superficial conjunctival and episcleral vessels were stained, but pressure upon the eyeball was followed by an outflow of clear fluid.

Ray K. Daily.

Jahnke, W. **Does zinc sulfate act as an astringent?** Arch. f. Ophth. 148:775-779, 1948.

From several observations in men and rabbits the author concludes that instillation of zinc sulfate acts as an irritant or stimulant of the ocular tissues, not as an astringent. Ernst Schmerl.

Kiss, F. **The blood circulation of the eye.** Szemészet 1:1-20, 1949.

Branching and topography of the blood vessels of the eye were studied in completely injected human eyes and those of various animals. The vessel system of the ciliary body consists of two parts, the broad vessels of the ciliary processes and the narrow ones of the ciliary plexus in the region of the muscle. The first system serves the production of the aqueous humor, the latter its resorption. The ciliary plexus may be considered a second capillary region of the broad iris veins. The drainage system of the ciliary body and the canal of Schlemm have a right-angular bend with spiral course, so that drainage may be slightly retarded when the internal pressure is increased. Blood and aqueous circulation of the human eye are normally in labile balance, the latter is primarily regulated by the arterial afflux. In experiments the ciliary plexus proved

to be the most important region of re-sorption.   Gyula Lugossy.

Klang, Gunnar. **Measurements and studies of the fluorescence of the human lens in vivo.** Acta ophth. Supplement 31, 1948.

This monograph with an extensive bibliography is a report of a comprehensive investigation extending over a period of four years at the Ophthalmic Clinic in Lund, on a quantitative determination of the fluorescence of the normal human lens in vivo. This study is a preliminary to a planned investigation to determine whether changes in lens fluorescence can be established in pathological states. While fluorescence of the lens has been the subject of many investigations, the data of which are tabulated by the author, the only quantitative study of lens fluorescence preceding this report is that of Vannas and Wilska in 1935; their method of quantitative determination does not permit a study of the spectral composition of the fluorescent light, and is not applicable to cataractous lenses or work on experimental animals. In the author's investigation fluorescence was produced by ultraviolet rays of wave-length 365 μ isolated by filtration from the radiation of a mercury vapor lamp. The intensity of fluorescence was measured by comparing the light with that of a standard fluorescent screen and interposing filters until the two lights appeared of the same intensity. The instruments, experimental set-up, the technique, the sources of error, and their controls, are described in detail. The material for the investigation comprises 95 male and 163 female eyes of healthy persons, and 216 male and 102 female eyes of clinic patients treated for affections which could have no effect on the corneal or lens fluorescence. The lens fluorescence was measured in 576 eyes of 316 persons, and the corneal fluorescence on 446 eyes of 253 persons. The beam of

concentrated ultraviolet light in the lens in vivo or isolated is seen as a path of fluorescent light, which does not extend through the entire thickness of the lens but stops before it reaches the center. Since all parts of the lens fluoresce, the termination of the light path in the lens is due to the high absorption of ultraviolet by the lens; the visible path of fluorescence comes almost entirely from the anterior parts of the lens and from an anterior layer which becomes increasingly thinner with advancing age. The visible path of the fluorescent beam becomes shorter with age, because of the increased absorption of ultraviolet with age. The fluorescence of the lacrimal fluid is insignificant, and there is no fluorescence from the aqueous. Iris fluorescence was found to be greater in blue and less in brown than in green irises. The fluorescence of lens, cornea, and iris increases with age. The amount of blue in the fluorescent light from the lens increases relative to the amount of green with increasing age, and the amount of violet suffers a relative decrease. The fluorescent light contains an insignificant amount of red color. It was found that the fluorescence of lenses in the female is higher in summer and lower in winter. This seasonal variation also occurs in males but to a lower degree. There is probably a greater intensity of fluorescence of lenses in females than in males. No significant variation in fluorescence of the lens could be established relative to the refraction of the eye, refractive power of the cornea, color of the iris, or color of the hair. The author believes that the seasonal variations in fluorescence may be related to the amount of lactoflavin in the lens. While variations in fluorescence with different pathologic states of the lens will be reported in detail in a further study, it is reported here that a marked increase in fluorescence was observed in diabetic cataract at such an early stage of develop-

ment that no definite pathologic opacities could as yet be observed in the lens. However, in diabetics with incipient senile cataract no increase in fluorescence was found. (2 figures, 37 tables, 16 graphs.)

Louis Daily, Jr.

Monje, M. **The effect of helenien upon the dark adaptation.** Arch. f. Ophth. 148: 679-705, 1948.

Helenien is a lutein palmitinic acid ester obtained from Tagetes patula. After taking 375 mg. of helenien a day by mouth over a period of two weeks the sensitivity of seven subjects increased four to eight times for a period of two to three months. Ernst Schmerl.

Morone, G., and Andreani, F. **The behavior of the pupil under the action of some drugs after resection of the cervical sympathetic.** Riv. oto-neuro-oftal. 23:250-258, July-Aug., 1948.

A report is made on the pharmacodynamic behavior of the pupil in Bernard-Horner's syndrome in rabbits. The changes in the pupil were obtained by instillation of drops of atropine, cocaine and adrenalin solution. In one group of animals the pupil was dilated after a sympathectomy at the level of the second cervical neuron of Foerster and in a second group after the extirpation of the superior cervical ganglion or Foerster's third neuron. The writers are specially interested in the experiments with the adrenalin. The results in the second group agreed with Foerster's but the dilatation of the pupil in the first group did not. To explain the mydriasis the authors postulate an inhibitory system in the sympathetic pathways of which some of the fibers could originate below the superior cervical ganglion, or that some fibers independent of the main trunk bring residual mydriatic stimuli from the second neuron to the dilator of the pupil.

Melchiore Lombardo.

Pirie, A. **Ox vitreous humour. 2. Hyaluronic acid relationships.** Brit. J. Ophth. 33:271-283, May, 1949.

Studies of the physical state of hyaluronic acid in the ox vitreous and its chemical and structural relationships with the proteins of the vitreous are reported. This substance, a viscous polysaccharide, is probably concerned with the maintenance of the physical state of the vitreous body. It is found in the vitreous of all animals but perhaps in highest concentration in that of the ox. The author believes that the description of the vitreous as a tissue made up of a network of fibrils which are the prolongations of cells and permeated by a viscous fluid or jelly which easily flows out of it is justified. That there is no chemical union of the proteins with the acid is borne out by the fact that in washings with water the two are washed out at different rates and analysis of the compound which remains shows no union of the two. Hyaluronidase does not have the same destructive effect on hyaluronic in the intact vitreous as in the filtrate. It is assumed that the proteins in the vitreous help to maintain the aggregated hyaluronic acid and that the aggregated hyaluronic acid helps to maintain the vitreous structure.

Morris Kaplan.

Ross, E. J. **The formation of the intraocular fluids. Studies of the urea component of the aqueous humor.** Brit. J. Ophth. 33:310-323, May, 1949.

The concentration of urea in the aqueous and vitreous is appreciably less than in the blood plasma. This phenomenon could result from a selective secretion of urea across the barrier, utilization of urea within the eye, or the existence of a continuous outflow of aqueous from the eye, so that the rate of drainage of urea from the eye would exceed the rate of its entry. The first two of these possibilities are studied in this paper. In animals the rate

of penetration of urea into the aqueous is consistently higher than into the vitreous. That there is no deficit of urea in the aqueous and vitreous was determined by frozen section. Experiments with lenses both in vitro and in vivo and with normal and aphakic eyes showed that the utilization of urea is much too small to account for the difference. By Barany's method of ligating one carotid artery it was shown that ultrafiltration takes no part in the formation of the intraocular fluids. The difference in intraocular and in plasma urea has not been explained.

Morris Kaplan.

von Sallman, L., Evans, T. C., and Dillon, B. **Studies of the eye with radiosodium autographs.** Arch. Ophth. 41:611-626, May, 1949.

Radioautographic technics were applied to studies of the movement of Na²⁴ in the eye. A Gross method is used for frozen slices and the microscopic method of Evans for thin paraffin sections of the eye. Phases in the penetration of the tracer substance from the blood into the fluids of the eye were made visible. The regions of the ciliary body and of the optic nerve were shown as the main portals of entry. Diffusion of Na²⁴ in the vitreous and into the anterior chamber occurred at a rapid rate after intravitreal injection of the tracer. Its movement in the living eye exceeded that in the enucleated globe. The problem of absorption of electrolytes by the ciliary body was studied with Na²⁴; a conspicuous accumulation of the tracer was observed in the ciliary processes after intravitreal injection. The influence of an applied electric field on the movement of Na²⁴ in the eye was made visible by radioautography.

Ralph W. Danielson.

Sondermann, R. **The relationship between intraocular pressure, pressure in the retinal vessels and pressure of the** spinal fluid. Klin. Monatsbl. f. Augenh. 114:161-168, 1949.

The article is based on the author's theory that the intraocular pressure has its origin in increased pressure in the veins and capillaries in the uvea, which is the result of the impediment in the flow of blood through the narrow scleral channels of the vortex veins on the one hand and the small openings in the lamina cribrosa for the central retinal vein on the other hand. Progressive narrowing of these channels during the embryonic developments increases this intravenous pressure. The intraocular pressure itself compresses these channels and increases, thereby, the venous pressure. The pressure of the veins within the orbit is one of no significance for the pressure in the retinal veins. The pressure of the cerebrospinal fluid is normally negative in the skull and plays no part in originating the high venous pressure even though the vein passes through the subarachnoid spaces. The intraocular pressure prevents the signs of engorgement in the retinal veins, in spite of their high venous pressure. Intraocular and intracranial pressures are unrelated. An increase of the latter to a value greater than 4 mm., which is only possible under pathological conditions, will be a further impediment in the flow of venous blood and increase the intraocular venous pressure. One can deduce the intracranial pressure by measuring the intraocular venous pressure as well as the ocular tension under these abnormal conditions. (References.)

Max Hirschfelder.

Sorsby, Arnold. **Concentration in the aqueous of various sulphonamides after systemic administration.** Brit. J. Ophth. 33:347-358, June, 1949.

Sulphonamide concentrations in the aqueous were determined after oral administration in rats and intravenous ad-

ministration in rabbits. In the rat, the highest concentration in the aqueous was given by sulphanilamide with successively lower readings for sulphamerazine, sulphamezathine, sulphadiazine and sulphathiazole. Seven hours after administration sulphamerazine gave the highest aqueous value with successively decreasing values for sulphamezathine, sulphanilamide, sulphadiazine and sulphathiazole. Assessment of the highest aqueous level as a percentage of the highest plasma level showed the highest value for sulphanilamide with successively lower values for sulphamerazine, sulphadiazine, sulphamezathine and sulphathiazole. In the rabbit the highest concentration in the aqueous was given by sulphadiazine with successively lower values for sulphamezathine and sulphamerazine. Sulphadiazine also proved to be the most persistent as assessed by the aqueous concentration at three hours. The highest aqueous plasma ratio was shown by sulphamezathine.

Orwyn H. Ellis.

De Vincentiis, M., and Santamaria, L. **The lipidic metabolism of the retina.** Ann. di ottal. e clin. ocul. 74:523-530, Sept., 1948.

De Vincentiis and Santamaria report their study of the capacity of the rabbit's retina in vitro to oxidize butyric acid and its methylic and glyceric esters, and succinic acid and the corresponding monomethylic ester. They show that the retina has a lipidic metabolism corresponding to that of normal tissue, that is, it possesses the enzymatic systems of beta oxidation which are lacking in tumor tissue. It is suggested that the glycidic metabolism of the retina is normal in type and that the so-called neoplastic character which retinal tissue may show in vitro is due to alteration of the enzymes necessary for the aerobic desmolysis of glycides. (References.) Harry Messenger.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Balding, Grant. **Surgery for high degree of monocular astigmatism.** Eye, Ear, Nose and Throat Monthly 28:276-283, June, 1949.

A corneoscleral section was made perpendicular to the axis of the astigmatism. Although iris prolapse occurred on the third day, six months later the vision was 20/20, astigmatism was slight and the patient was able for the first time to wear glasses. He had binocular vision without discomfort. Orwyn H. Ellis.

Barnes, C. K. **Voluntary dissociation of the accommodation and the convergence faculty.** Arch. Ophth. 41:599-606, May, 1949.

Two very interesting case reports are given, and observations on the voluntary dissociation of the accommodation and convergence faculties are discussed. The first observation suggests that the psychic concept of the location of the horopter in space is primarily related to convergence, rather than to accommodation. It also suggests that the psychic magnification of near objects and minification of distant objects in excess of that based on the law of the square of the distance is predicated on convergence primarily, rather than on accommodation. The second observation involves an unusual case of fusion anomaly in which lifelong functional parallelism appeared to depend on alternation at or above the frequency of flicker. It is believed that this case may be evidence in favor of the theory of physiologic alternation as a basis of fusion. This may again revive the theory that strabismus occurs in persons who have defective synchronization of the paired oculoneural "stroboscopes." Ralph W. Danielson.

Gilbert, M., and Hopkinson, R. G. The illumination of the Snellen chart. Brit. J. Ophth., 33:305-310, May, 1949.

Studies were made on 15 adults to determine the effects of illumination on the reading of the Snellen chart. The subjects presented all types of ametropia and some emmetropia and were tested with and without their correction. The tests were conducted in illumination of 0.1, 3, and 100 foot candles. Each increase was in a ratio of 30 to 1. The results were not as startling as might be expected. An increase in illumination of the order of 10 to 1 improved the acuity by only one line on the chart, yet standard illumination for the Snellen chart seems necessary.

Morris Kaplan.

Granstrom, K. O. Transient myopia following the administration of sulfonamides. Acta ophth. 27:59-69, 1949.

A detailed description is given of seven cases of transient myopia, for a few days after the administration of sulfonamides. In one the drug was absorbed from a locally treated fistula. The changes in refraction were as high as six or seven diopters, and were identical in the two eyes. The refractive power of the cornea was unchanged. There was a decrease in the depth of the anterior chamber in two cases, and two had an aqueous flare which disappeared with the regression of the myopia. With objective stigmatoscopy it was possible to demonstrate that the refractive changes occurred axially.

Ray K. Daily.

Hartmann, E. Heterophoria and the decentering of lenses. Ann. d'ocul., 182:301-305, April, 1949.

A patient was uncomfortable with reading glasses fitted exactly to her pupillary distance, but was quite comfortable with the same lenses in a wider frame. The exophoria for near was therefore partially corrected by the prismatic action of decentered lenses. Chas. A. Bahn.

Heinsius, E. The examination of night vision with the nyctoscope. Arch. f. Ophth. 148:741-757, 1948.

In testing night vision, dark adaptation as well as visual acuity under diminished illumination should be examined. The author used phosphorescent Landolt rings or Snellen signs with definite optical qualities and measured the visual acuity in several thousand normal persons. With brightness per unit surface from about 10^{-6} to 10^{-8} stilb he finds the range of normal night vision to vary from 4 to 22 angular minutes. Ernst Schmerl.

Huggert, Arne. The form of the iso-indicial surfaces of the human crystalline lens. Acta ophth. Supplement 30, pp. 121, 1948.

This monograph, with an extensive bibliography, presents a detailed report of a four-year study carried out at the Ophthalmic Clinic in Stockholm, with the principal objectives of determining whether the surfaces of the lens or its iso-indicial surfaces have the wave-like course attributed to them theoretically by Gullstrand, and of explaining the genesis of the well-known phenomenon that a distant luminous point source of light is not perceived as a point only, but is surrounded by rays. Gullstrand, who made the most exhaustive study of this phenomenon, demonstrated that the refraction producing it is dependent upon a wave-like form of the lens surfaces or its iso-indicial surfaces. His opinion that this form could not be due to the anatomical structure, that is, the suture system of the lens, dates to a time when the complicated suture system of the adult lens nucleus was as yet unknown. Huggert, in this investigation tried 1. to ascertain radial ridges and valleys on the lens surfaces by slit-lamp examination and by examinations of the reflex images from the lens surfaces; 2. to determine the form of the iso-indicial surfaces by laboratory studies

of fixed and fresh human and cattle lenses; 3. to determine that the zones of optical discontinuity and iso-indicial surfaces in the lens are identical; and 4. to compare the shape of the star figure seen by subjective stigmatoscopy with the anatomical structure of the suture system of the anterior adult nucleus. Only the last investigation yielded definitely positive findings. Experimental errors and technical difficulties inherent in the methods employed in the first three problems tended to make their results inconclusive. No regular wave-like changes were found in the central parts of the anterior and posterior lens surfaces or their reflexes, and the findings in the peripheral portions were not certain. Direct laboratory examination of the form of the iso-indicial surfaces in fixed and fresh lenses justify the assumption that they are wave-like. A study of the correlation between the discontinuity zones of the lens and its iso-indicial surfaces indicates that within certain limits they are identical. However, slitlamp study of the surfaces and reflexes of the lens nucleus showed definitely that the adult nucleus surface has a fairly regular wavy form connected with the sutural system of the lens, and examination of fixed animal and human lenses demonstrated that the adult nucleus has 8 to 12 waves at the poles, and a larger although less distinct number near the equator. Comparative analyses of the correlation between the form of the star figures seen around small distant sources of light and the sutural figures of the lens nucleus prove the existence of such a correlation, and indicate that the form of star figures may be explained by the form of the nuclear surfaces. (27 figures, 20 tables.) Louis Daily, Jr.

Littmann, H. **The fundamentals of skiascopy.** Arch. f. Ophth. 148:658-678, 1948.

A theory of skiascopy based upon the principles of geometric optics is presented. The skiascopic shadow should

move freely over the whole pupillary area. Mirrors having a radius of from 15 to 20 mm. are preferred to the smaller ones used in electric skiascopes. The disturbances caused by the central hole can be avoided if a mirror without a hole in the glass is used. In order to determine the refraction of the foveal area, the patient should look into the direction of the examining eye. Ernst Schmerl.

Márquez, M. **The supposed torsions of the eye around the visual line in oblique directions of gaze.** An. Soc. mex. de oftal. 22:1-21 (including discussion), 1948.

This highly technical optical paper does not lend itself to abstract, but leads to the following conclusion. The fundamental error in the interpretation of consecutive images in oblique directions of gaze has been a double one. On the one hand their inclination has been attributed to turning of the eyeball upon the visual line instead of attributing it to a pseudoturning upon an oblique axis continued in Listing's plane, and on the other hand one has confused the axes of the eye, which pass through the center of rotation and which play no part in this case, with the vertical and horizontal meridians of the retina, which pass through the center of the fovea whose inclination in the same direction of gaze determines the obliquity of the consecutive image by a mechanism which is purely one of geometric optics. (10 figures, references.) W. H. Crisp.

Ribas Valero, Ramon. **The relation of the interfocal circle of the conoid of Sturm to the retinal surface.** Arch. Soc. oftal. hispano-am. 9:445-454, April, 1949.

This must be read completely.
Ray K. Daily.

Rivas Cherif, Manuel de. **High visual acuity with defective ocular refraction.** An. Soc. mex. de oftal. 22:37-54, 1948.

The author, who is a loyal admirer of Márquez's ophthalmometric method of

testing for biastigmatism, found combined astigmatism of cornea and crystalline lens in 63.3 percent of 327 cases of refraction. He urges that study of refractive errors in school children and others should not be limited to those manifesting visual defects. (9 figures, references.)

W. H. Crisp.

Sloane, A. E. **The management of early presbyopia and bilateral aphakia.** Tr. Am. Acad. Ophth. pp. 352-56, March-April, 1949.

The substitution of separate distance and near glasses for bifocals may greatly facilitate ocular comfort. In the double vision which occasionally follows bilateral cataract extraction, glasses fitting one eye for distance and the other for near may be of material service. An illustrative case of each is described. Chas. A. Bahn.

Tarle, E. **Rehabilitation of skiascopy.** Ann. d'ocul. 182:384-390, May, 1949.

The author advises the use of an electric retinoscope with flat parallel light at arm's length. A lens battery with half diopter intervals is also suggested.

Chas. A. Bahn.

5

DIAGNOSIS AND THERAPY

Ambrose, A. **A simplified perimeter of wall type.** Arch. Ophth. 41:633-636, May, 1949.

The author describes this instrument which is cheap and takes up but little room because suspended from the wall.

Ralph W. Danielson.

Arruga, H. **The utilization of binocularity for experimental investigations in therapy.** Arch. Soc. oftal. hispano-am. 9: 349-351, April, 1949.

To assess the value of new therapeutic agents Arruga uses them on one eye, while the other one serves as a control. In this manner he determined the ineffec-

tiveness of agents proposed for the arrest of cataracts, of various ointments for blepharitis, and of Filatov's tissue therapy in retinitis pigmentosa and myopic retinopathy. Ray K. Daily.

Basterra, J. **Tissue therapy in ophthalmology.** Arch. Soc. oftal. hispano-am. 9: 424-444, April, 1939.

Fifteen cases of retinal detachment, recurrent hemorrhage of the vitreous, retinitis pigmentosa, diabetic retinitis, senile macular degeneration, stubborn allergic conjunctivitis and tuberculous iridocyclitis, in which injections of cod liver oil, implantation of placenta, and injections of placental extract had no beneficial effect are briefly reported. Ray K. Daily.

Cogan, D. G., and Grant, W. M. **Treatment of pediculosis ciliaris with anticholinesterase agents.** Arch. Ophth. 41:627-628, May, 1949.

For the treatment of pediculosis ciliaris the time-honored ammoniated mercury has proved itself effective. Yet it is of considerable interest to know that the common physostigmine in the standard concentrations used for the treatment of glaucoma is just as effective. Tetraethylpyrophosphate, and presumably many other anticholinesterase compounds, are also effective. A case in which the authors had an opportunity to study the effect of physostigmine and tetraethylpyrophosphate is reported. Ralph W. Danielson.

Hallerman, W. **Operative risk and sudden increase in intraocular pressure.** Klin. Monastbl. f. Augenh. 114:144-148, 1949.

Sudden voluntary upward movements of the patient's eye lead to a considerable pull on the superior rectus muscle with subsequent rise in pressure. They should not be blindly counteracted by a superior rectus suture. A slight "give" in the pull is indicated. An injection of novocaine into the superior rectus muscle is recom-

mended for patients who are expected to be uncooperative or to press their lids together. (3 figures.)   Max Hirschfelder.

Krimsky, E. **A new hand slitlamp.** Tr. Am. Acad. Ophth. pp. 357-358, March-April, 1949.

An ordinary flashlight handle is used with two plano-convex lenses and a slit diaphragm properly adjusted. A supplementary magnifying lens is supported by a bracket.   Chas. A. Bahn.

Krimsky, E. **Concealed glare filters of supplementary lenses.** Tr. Am. Acad. Ophth. pp. 359-360, March-April, 1949.

Plastic glare filters are attached by a hinge to the temples of Zylonite frames. Each is approximately 1 cm. vertically and extends from the temple to the nose piece of each eye. Being hinged, the filters may be swung forward and nasally before the patient's vision, or backwards where they are concealed along the temples.   Chas. A. Bahn.

Krimsky, E. **Ferris-wheel attachment to Brewster type of stereoscope.** Tr. Am. Acad. Ophth. pp. 360-361, March-April, 1949.

A series of stereoscopic pictures are mounted on circular discs so that they may be rotated into the viewing position. By means of handles, these discs can be laterally regulated for ocular convergence or divergence.   Chas. A. Bahn.

Krimsky, E. **Clear-view lens frame for the Brewster stereoscope.** Tr. Am. Acad. Ophth. p. 361, March-April, 1949.

To facilitate ocular inspection especially in stereoscopic training in esotropia the author has constructed a lens frame in which the nasal sides of the frame are omitted.   Chas. A. Bahn.

Lepri, Giuseppe. **Rheumatic diseases of the eye.** Arch. di ottal. 52:133-163, May-June, 1948.

The author investigated the effect of salicylic acid injections (Mester diagnostic technique) on three groups of patients. His studies included a fourth or control group. From his studies he concluded that this diagnostic test was rather limited in its value with regard to ocular disease, but showed some cutaneous action of theoretical importance in rheumatic persons.   Francis M. Crage.

Losada Garcia, Jesus. **Details of photographic technic applied to retinography.** Arch. Soc. oftal. hispano-am. 9:459-474, April, 1949.

The author describes in detail the characteristics of the various emulsions, types of films and filters, and development techniques suitable for retinography in visible and infrared light. (5 tables, 3 formulas.)   Ray K. Daily.

Mata Lopez, Pedro. **Antibiotic therapy of ocular tuberculosis.** Arch. Soc. oftal. hispano-am. 9:415-423, April, 1949.

The literature on streptomycin is reviewed.   Ray K. Daily.

Miller, H. A. **The intraocular application of penicillin.** Ann. d'ocul. 182:378-383, May, 1949.

Recommended only in panophthalmitis, 5,000 to 10,000 units of penicillin in 0.1 to 0.2 cc. of solution is injected into the vitreous. Prolonged, severe pain follows. For infected ulcers injection into the aqueous is preferred and 0.2 to 0.3 cc. of aqueous is removed and an equal amount of penicillin solution is substituted. The injection of penicillin into Tenon's capsule with scarification of the sclera is less drastic than injection into the vitreous and apparently more effective than injections into the anterior chamber. The intraocular injection of penicillin is of uncertain value in uveitis of unknown origin and is definitely contraindicated if a tuberculin reaction is positive.
    Chas. A. Bahn.

Moore, J. I. An evaluation of the use of beta rays in ophthalmology. South. M. J. 41:1092-1094, Dec., 1948.

This paper summarizes the results of the Radium Clinic of the Wilmer Institute of the Johns Hopkins Hospital. In the past nine years beta rays have been used in the treatment of a variety of ophthalmological conditions. Almost all beta rays are absorbed by the first 3 mm. of tissue. Obviously this form of therapy is suitable only for superficial lesions of the skin of the lids, conjunctiva, cornea and sclera. The beta ray applicator used consists of a glass bulb, 5 mm. in diameter, containing radon, enclosed by brass except for the open end through which the unfiltered beta rays emerge. This active portion of the applicator is attached to a handle 35 cm. long. The side walls and end toward the operator contain sufficient brass to exclude all the beta rays, but not the gamma rays. The beta and gamma rays unfiltered pass through the open end.

Beta ray therapy is the treatment of choice in vernal conjunctivitis, vascularization of the cornea following ulcers, chemical burns, trauma or keratitis and tuberculous keratitis, and epitheliomas of the cornea and limbus. Pterygia, papillomata of the skin, warts, granulation tissue of lids and globe, keloids of lids, and heavy scarring of conjunctival flaps following glaucoma surgery are successfully treated with beta rays, but may also be treated with other types of therapy. Dense old corneal scares without vascularization, dark pigmented moles of the lids, sebaceous cysts, chalazion and xanthelasma are not helped by beta ray therapy.   Theodore M. Shapira.

Neerdam, H., and Lawoetz, B. Chemotherapy in perforating injuries of the eye. Acta ophth. 27:69-73, 1949.

On the basis of a shortened stay in the hospital and delayed and less frequent indications for enucleation in 147 perforat-

ing ocular injuries, the authors conclude that prophylactic sulfonamide therapy is effective in inhibiting intraocular infection.   Ray K. Daily.

Scholtyssek, H. Sanatorium treatment for tuberculosis of the eye in the flat country? Klin. Monatsbl. f. Augenh. 114:97-105, 1949.

The author reviews the results of sanatorium treatment in ocular tuberculosis and points out favorable results obtained in the German institution Walsrode, which is situated in a relatively low altitude. Climatic therapy of not too great an intensity is apparently desirable and the results equal those obtained in higher altitudes. (References.)
          Max Hirschfelder.

Shoemaker, R. E. Intravitreal use of streptomycin. Arch. Ophth. 41:629-632, May, 1949.

Intravitreal injection of streptomycin was used clinically in a case of bacterial endophthalmitis and appears to be a safe procedure when indicated. Unfavorable effects on the vitreous were practically nil. Retinal degeneration occurred, as in experimental animals, but one could minimize this by not exceeding the recommended dosage (800 micrograms per injection).   Ralph W. Danielson.

Stevenson, W. An applicator for beta radium D. Tr. Am. Acad. Ophth. p. 366, March-April, 1949.

The radium container is attached to two movable arms. The more distal is attached to any speculum. Thus the radium can be placed and held in any desired position without manual support.
          Chas. A. Bahn.

Stevenson, W. A new eye needle holder. Tr. Am. Acad. Ophth. p. 367, March-April, 1949.

The author uses a spring forceps simi-

lar to the Beaupre lash forceps as a needle holder. Chas. A. Bahn.

Thorpe, H. E. **Lens for deep vitreous examination.** Tr. Am. Acad. Ophth. pp. 362-363, March-April, 1949.

To facilitate more detailed examination in some types of retinal detachment and posterior vitreous abnormalities, the author modified the −55 D lens of Hruby. A hard rubber mounting which fits into an ordinary trial frame is used to prevent lashes touching the lens and also to avoid lens scratching. Reflections are minimized by lens coating. Chas. A. Bahn.

Thorpe, H. E. **Electrified suction tip.** Tr. Am. Acad. Ophth. p. 363, March-April, 1949.

To prevent annoying oozing of blood in scleral surgery the author has placed an electric screw tip connection on a suction tube. By turning on the diathermic current with the foot switch a bleeding point is at once dried and electrically coagulated. Rubber gloves are worn to insulate the operator from the diathermic current. Chas. A. Bahn.

Thorpe, H. E. **Aperture slide for binocular ophthalmoscope.** Tr. Am. Acad. Ophth. p. 363, March-April, 1949.

To avoid dazzling light reflexes with the binocular ophthalmoscope, on opaque semi-circular stop is substituted for the filters. This covers the lower half of one eye and the upper half of the other. Chas. A. Bahn.

Thorpe, H. D. **Modified Kalt electrified needle holder for inserting micropins in retinal detachment surgery.** Tr. Am. Acad. Ophth. p. 364, March-April, 1949.

The lock catch and spring were removed from the ordinary stainless steel Kalt needle holder and an electric connection was placed on the back end of the handle. Thus the needle holder may be used in retinal detachment surgery for different types of micropins. Rubber gloves are worn by the operator. Chas A. Bahn.

6
OCULAR MOTILITY

Abraham, S. V. **Etiology of nonparalytic strabismus.** Ann. West. Med. and Surg. 3:115-125, April, 1949.

The author reviews the literature on the etiology. The comparative anatomy is well presented with illustrations. The convergence mechanism is late in evolution and is still comparatively immature in the individual. The accommodation-convergence mechanism is also studied. The causal factor in nonparalytic strabismus is an interference with convergence and this functional unit determines the anatomic position of rest of the eyes. The fusion faculty is normally weak in the formative years. Orwyn H. Ellis.

Carreras Duran, B. **Internuclear paralysis.** Arch. Soc. oftal. hispano-am. 9:359-366, April, 1949.

A woman, 56 years old, is described, who had a paralysis of the right internus when looking toward the left, but not in convergence. The differential diagnosis of the various central lesions to be considered is discussed in detail. Ray K. Daily.

Drucker, A. P. **Cyclic or rhythmic oculomotor paralysis.** Eye, Ear, Nose and Throat Monthly 28:274-276, June, 1949.

A child with cyclic or rhythmic oculomotor paralysis is described and the literature reviewed. Exotropia and unilateral ptosis were also present. Orwyn H. Ellis.

Johnson, W. F. **A surgical approach to the inferior oblique muscle.** Arch. Ophth. 41:607-610, May, 1949.

After the eye is pulled far nasally, an

incision is made parallel to the external rectus muscle and extended along its lower border to the lateral fornix.

Ralph W. Danielson.

Lloyd, I. **Recession of the inferior oblique.** Brit. J. Ophth. 33:291-296, May, 1949.

In both vertical and horizontal imbalance of the eyes the action of the inferior obliques must be studied adequately. As many as 53 percent of convergent squints in children were associated with a vertical defect and 30 percent were characterized by overaction of the inferior oblique. The vertical defect must also be corrected to achieve the desired cosmetic and functional result. The indications for reducing overaction of the inferior oblique are presented. Measured recession of the muscle is always done. Partial and complete tenotomy are dismissed as unreliable. The transconjunctival route is used and the external rectus either moved aside with a hook or severed if it is to be operated upon also. The oblique is recessed 6 to 9 mm. and reattached horizontally just below the lower border of the external rectus. Twelve cases in which results were uniformly good are reported.

Morris Kaplan.

Oaks, L. W. **Divergence insufficiency as a practical problem.** Arch. Ophth. 41:562-569, May, 1949.

Divergence insufficiency is a definite clinical entity characterized by esophoria which is greater for distance than for near. It occurs, in some degree, in more than 10 percent of all patients with binocular vision who are refracted. The cause is unknown, but there seems no reason why the condition should not occur from the same causes that produce other imbalances of the horizontally acting muscles. Symptoms include headache (not relieved by correction of refractive errors), ocular fatigue and occasional diplopia,

nausea, dizziness, blurring of distant vision and panoramic headache. Diagnosis is made by use of screen-prism tests, prism duction measurements and lateral vergence tests at the near point. The relation of convergence and divergence at the near point are found not to conform to statements in some textbooks. Treatment is best accomplished by 1. proper refraction, 2. increase in the plus sphere correction, 3. use of base-out prisms, when accepted, 4. orthoptic training, and 5. surgical intervention.

Ralph W. Danielson.

Piper, H. F. **Concomitant strabismus.** Arch. f. Ophth. 148:555-616, 1948.

The author studied the phorias, fusion, depth perception and retinal correspondence in a small number of patients. Concomitant strabismus is a pathologic entity. The controlling cortical areas are weakened. Subcortical centers regulate the motor functions of the binocular unit. In horizontal strabismus the subcortical stimuli are associated with impulses for the accommodation of the single eye. In vertical strabismus the impulses are linked to stimuli for the upward and outward rotation of each eye during sleep.

Ernst Schmerl.

Remky, H. **Changes of the sensory apparatus in strabismus.** Arch. f. Ophth. 148:725-740, 1948.

The author studied a number of patients with stereoscope and perimeter. Usually a more or less pronounced central scotoma of the squinting eye could be demonstrated even in cases with bilateral amblyopia. A nervous disturbance, probably in the area of the vestibular nucleus, is suggested as the primary cause of strabismus.   Ernst Schmerl.

Urrets Zavalia, Alberto, Jr. **Disturbances of the vertical ocular muscles.** An. Soc. mex. de oftal. 22:237-262, 1948.

The author recognizes four groups of these disturbances: 1. pure concomitant vertical deviations; 2. acquired paralysis of the vertical muscles; 3. congenital unilateral or bilateral insufficiencies of the vertical muscles; and 4. dissociated vertical deviations. The first class is extremely rare or non-existent. Bielschowsky's explanation of dissociated vertical deviations is the only logically adequate one. (20 figures, chiefly clinical; references.)

W. H. Crisp.

7

CONJUNCTIVA, CORNEA, SCLERA

Arques Girones, Emilio. **Superficial punctate kerato-conjunctivitis.** Arch. Soc. oftal. hispano-am. 9:287-292, March, 1949.

The author believes that punctate keratoconjunctivitis is a neuritis of the terminal subepithelial corneal nerves, which spreads through Bowman's membrane. Since the corneal epithelium and Bowman's membrane are related embryologically to the conjunctiva they could be involved with it in a process which originates in the respiratory passages and ascends on the nasal and lacrimal mucous membrane. The characteristic piercing pain is due to the involvement of the corneal nerves and the opacities develop in Bowman's membrane at the points where it is perforated by the nerves. Occasionally the opacities extend deeper into the corneal parenchyma. Ray K. Daily.

Cameron, E. H. **The treatment of hypopyon ulcer of the cornea.** Brit. J. Ophth. 33:368-371, June, 1949.

Since the introduction of sodium sulphacetamide for the treatment of corneal abrasions in miners in Scotland the incidence of hypopyon ulcer has been greatly reduced, and the number of severe ulcerations has likewise decreased. No eye has been lost in the last seven years. In a series reviewed in 1931 there was a 10-percent loss. Improved prophylaxis and earlier treatment of minor injuries undoubtedly played a part.

Orwyn H. Ellis.

Chavarria, F. A. **Simplification of pterygium surgery.** Arch. Soc. oftal. hispano-am. 9:454-458, April, 1949.

Chavarria describes his procedure as simple and efficacious. He thoroughly dissects the head of the pterygium from the cornea, continues for four millimeters over the sclera, and then cuts the pterygium off with straight scissors, perpendicular to its fibers. The eye is bandaged, without sutures. Ray K. Daily.

Cogan, D. G. **Principles of corneal pathology: hydration properties of the cornea.** An. Soc. mex. de oftal. 22:87-98, 1948.

This is a statement, in Spanish, of material already published in English by the author. It is part of a continuing series in the Anales. W. H. Crisp.

Cogan, D. G. **Principles of corneal pathology: III. Epithelial edema and related conditions: A, epithelial edema.** An. Soc. mex. de oftal. 22:167-174, 1948.

See preceding title. W. H. Crisp.

Fierro del Rio, Leonel. **Endocrinologic studies of spring conjunctivitis.** An. Soc. mex. de oftal. 22:54-71, 1948.

Of 33 patients with vernal conjunctivitis studied, 22 showed endocrine disorders by simple physical exploration. The other patients were normal except as to the ocular disturbance. All with endocrine disturbance had gonadal insufficiency. The author believes that disturbed interaction between the sex gland and the pituitary produces a condition similar to allergy. W. H. Crisp.

Friede, R. **Megalocornea congenita, a phylogenetic anomaly.** Arch. f. Ophth. 148:761-774, 1948.

A case of congenital megalocornea and

theoretical considerations concerning its genesis are presented. The differentiation between megalocornea and hydrophthalmus is emphasized.   Ernst Schmerl.

Gasteiger, H. **Rodent ulcer of the cornea and corneal changes in scleroperikeratitis (Szilly).** Klin. Monatsbl. f. Augenh. 114:112-126, 1949.

The author observed rodent ulcer in six patients 42 to 75 years of age. Three eyes were examined histologically. Some of the patients were well-nourished and otherwise healthy; one had advanced necrosis of the sclera. Various forms of scleritis and episcleritis with involvement of the cornea are described for comparison. There is no doubt of the inflammatory character of the lesion; it is not a carcinoma-like epithelial process or trophoneurotic change. The etiology is varied; marginal ulcers, acne of the cornea, small corneal injuries, scleritis and episcleritis as well as beginning degenerative processes may be the beginning from which a rodent ulcer finally develops, if certain constitutional characteristics are favorable to its formation. (1 color plate, 8 figures, references.) Max Hirschfelder.

Harbater, M. **Scleromalacia perforans: report of a case.** Arch. Ophth. 41:183-187, Feb., 1949.

A case of scleromalacia perforans and the pathologic findings in one enucleated eye are described. The clinical appearance of the lesion and the pathologic features conformed closely to the description by Verhoeff and King. The disease accompanied chronic rheumatoid arthritis of long standing and, in the course of about twenty months, slowly progressed to involve most of the anterior portion of the sclera in a necrotizing process. The eyes have become blind as a result of an accompanying uveitis. An unusual feature of this case was an associated marginal necrosis of the cornea.   John C. Long.

Huggert, H. **Is the embryotoxon corneae posterior Axenfeld an error in development of Schlemm's canal?** Arch. f. Ophth. 148:780-786, 1948.

Two cases of embryotoxon corneae are reported. Whereas some authors ascribe the embryotoxon to the persistence of mesodermal tissue between iris and cornea, the author regards this condition as a displaced Schlemm's canal.
                    Ernst Schmerl.

Klein, M. **The lacrimal strip and the precorneal film in cases of Sjøgren's syndrome.** Brit. J. Ophth. 33:380-388, June, 1949.

The precorneal film consists of a deep mucoid layer, an intermediate lacrimal watery layer, and a thin oily layer. This is for the protection of the eye and is responsible for the brightness of the corneal surface. In kerato-conjunctivitis sicca there was a decrease in lacrimal secretion although the marginal strips of lacrimal fluid and precorneal film were present. The precorneal film seemed to be composed of the usual three elements, but the mucoid component predominated.
                    Orwyn H. Ellis.

Llorca Perez. **Two cases of bilateral crystalline dystrophy of the cornea.** Arch. Soc. oftal. hispano-am. 9:280-286, March, 1949.

Two paracentral annular opacities of the cornea, consisting almost entirely of small iridescent needle-like crystals, are reported. One patient, 12 years old, developed the opacities at the age of six. The other, a sailor, noticed them while in the service. In both the center and an area adjacent to the limbus were entirely transparent. There were no inflammatory phenomena, and no blood vessels. The arrangement of the crystals was parallel in the first case, and irregular in the other; they were in the anterior parenchymal layers. General examinations were nega-

tive, except for a slight hypercholesterolemia. The literature on fatty corneal dystrophy, and the lipoid metabolism of the cornea is reviewed. (4 figures.)

Ray K. Daily.

Meyer, F. W. **Critical report on eighteen corneal transplantations.** Klin. Monatsbl. f. Augenh. 114:131-140, 1949.

Both homoplastic and autoplastic corneal tissue may be used. The use of the latter gives no assurance of a clear transplant and is not superior to the former. Discs which were obtained as late as 42 hours post mortem from the donor eye remained clear. The status of the cornea into which the transplant material is implanted is the most important factor in the subsequent course. Clear and healthy corneal islands are a prerequisite for successful transplantation. When the first implant becomes opaque, a repetition of a transplant with a second disc is recommended. When there is a difference in the level of the endothelium between the cornea of the host and the implant, scar tissue is apt to develop. On the epithelial side the differences in level disappear.

Max Hirschfelder.

Ravn Sorensen, C. H. **A case of primary conjunctival tuberculosis.** Acta ophth. 27:113-118, 1949.

In a woman with Parinaud's conjunctivitis biopsy suggested Boeck's sarcoid and culture from the tissue revealed tubercle bacilli of the human type. Since no other tuberculous focus was revealed, the tuberculosis of the conjunctiva was assumed to be primary. The diagnostic difficulties of ocular tuberculosis are discussed. (3 figures.) Ray K. Daily.

del Rio, L. F., and Aupart, D. A. **Endocrinologic studies in spring conjunctivitis: III. Determination of urinary 17-ketosteroids.** An. Soc. mex. de oftal. 22:107-111, 1948.

Determination of the elimination in the urine of these hormonal substances was made in a group of patients with spring conjunctivitis. The figures were normal in children of less than twelve years, but below normal in patients of greater age. In this latter group the findings were regarded as significant of a gonadal lesion. In six men examination of spermatic fluid and of testicular biopsies indicated a manifest lesion of the testicle. (References.) W. H. Crisp.

Sédan-Bauby, S., Sédan, J., and Payan, H. **Corneas conserved in ice.** Ann. d'ocul. 182:364-377, May, 1949.

To determine the best method of preserving corneal transplants, the authors study four series of enucleated eyes of dogs. Those preserved in ice with humid air 24 hours after death developed massive desquamation of the epithelium with bullae on the fifth day. In those similarly preserved immediately after death the same changes took place in nine days. When the eyes were preserved in citrated autoblood, necrosis of the basal membrane was noted on the ninth day. In the fourth series paraffin oil was used as a preservative; bullae were visible on the seventh day. The anterior epithelium was least destroyed when the enucleated eyes were immediately placed in paraffin oil.

Chas. A. Bahn.

Silva, D. **Epidemic keratoconjunctivitis in Mexico.** An. Soc. mex. de oftal. 22:131-140, 1948.

Numerous outbreaks of this disorder occurred in the Mexican capital between February and April, 1947, after return of the Mexican laborers who worked in the United States during the war. The number of cases was apparently at its height in August, 1947. Sixty-eight cases are discussed from the author's experience. The article includes five excellent photomicrographs showing epithelial cell inclusions.

It is recommended that the disease be included in the list of those whose notification is required by law.   W. H. Crisp.

Sommer, G. **Total transplantation of the cornea.** Klin. Monatsbl. f. Augenh. 114:126-131, 1949.

The author reports operative procedure and course in a case of total transplantation of the cornea in a patient with an extensive total staphyloma of the cornea. A sudden opacification of the donor cornea occurred on the nineteenth day, possibly as a result of an anaphylactic tissue reaction. The eye finally had light perception and perception of handmovements.   Max Hirschfelder.

Starke, H. **Primary tuberculosis of the conjunctiva.** Klin. Monatsbl. f. Augenh. 114:107-112, 1949.

The author reviews the differential diagnosis of Parinaud's syndrome. The importance of bacteriological investigation and animal inoculation is stressed. Biopsy in a nine-year-old boy revealed tuberculous infiltration of the conjunctiva. The preauricular gland became necrotic and tubercle bacilli were found in material obtained by aspiration. Two similar cases of primary conjunctival tuberculosis are also reported. (References.)
     Max Hirschfelder.

Tavolara, L. **The gonioscopic picture of embryotoxon corneae posterius.** Boll. d'ocul. 28:91-100, Feb., 1949.

This congenital anomaly, described and named by Axenfeld in 1920, has been studied gonioscopically only by Busacca in 1948. Two of Tavolara's patients were siblings. All eyes had gonioscopically visible strands originating from different levels of the iris periphery and inserted into the opaque area of the limbus or in the brilliant streak which marked the internal border of the embryotoxon. The strands, "goniosynechiae," are ascribed

by Tavolara to a prolonged contact between the posterior corneoscleral surface and the iris which, in all cases, was hypoplastic and had but few crypts in the areas near the limbal opacities. Although embryotoxon may be a developmental anomaly the author also considers the possibility of intrauterine inflammatory disease a possible cause. (9 figures, references.)   K. W. Ascher.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Arjona, L. **Observations on dyschromias of the iris.** Arch. Soc. oftal. hispano-am. 9:397-404, April, 1949.

The biochemistry of the pigment elements of the eyeball, and a description of the changes which they undergo in glaucoma, diabetes, diseases of the liver, and senility are reviewed. The increase of iris pigment in association with malignant tumors of the eyeball, and melanosis of the globe in Sturge-Weber's disease are examples of hyperpigmentation. A case of choroidal sarcoma in which a pigmented focus in the iris, which had always been there, became denser and darker with the development of the intraocular tumor, is reported to demonstrate the effect of an adjacent pigmented malignant process on the metabolism of pigment cells. The increased activity of the pigment cells can be attributed either to an increase of dopa oxidase which extended beyond its source or to a cellular disturbance, which expressed itself in an increased production of dioxyphenylalanin. (2 figures.)   Ray K. Daily.

Bocci, G. **Recurrent iritis with hypopyon.** Boll. d'ocul. 28:32-40, Jan., 1949.

This disease was termed ophthalmia lenta or septic iridocyclitis by Gilbert, and recurrent uveitis due to staphylococcus allergy by Weve. The author's pa-

tient was a three-year-old boy with corneal perforation and traumatic cataract due to an explosion which also caused multiple skin lesions with secondary pyogenic infection. One week after the injury hypopyon developed and disappeared in five days with sulfonamide therapy. During the following weeks there were three recurrences. (References.)

K. W. Ascher.

Cavara, V., and Di Ferdinando, R. **Sympathetic ophthalmia and herpetic infection.** Boll. d'ocul. 28:1-16, Jan., 1949.

Two men, aged 40 years had recurrent herpetic keratouveitis of one eye only. After 16 years in one patient and five months in the other, a severe deep uveitis with keratitis developed in the previously normal fellow eye. In both cases, the first eye was enucleated and one of them was examined histologically; it showed typical sympathetic ophthalmia. Similar observations have been reported of "sympathetic" involvement after herpes zoster in the other eye. These patients, however, present the first cases of sympathetic ophthalmia after herpes febrilis of one eye. (10 photomicrographs, references).

K. W. Ascher.

Magitot, A. **Trichloracetic acid and iris prolapse.** Ann. d'ocul. 182:216-218, March, 1949.

Local application of trichloracetic acid in saturated solution is advised in old and recent iris prolapse with or without conjunctival covering and in some corneal injuries in which vitreous prolapse interferes with wound healing. It is preferred to galvanocautery which requires greater anesthesia. The cauterization may be repeated at two or three-day intervals for two or three weeks. Penicillin ointment is subsequently used. Chas. A. Bahn.

Rossi, Giuseppi. **A case of bilateral exudative choroiditis with retinal detachment and meningeal symptoms. (Harada's disease).** Arch. di ottal. 52:218-230, July-Aug., 1948.

The author reports a case of this disease, first described by Harada of Japan and so rare in Caucasians, that occurred in a young white woman in generally excellent health. The extension of the process to the anterior uveal tract was the only change which bore a relationship between this and the Vogt-Kojanagj syndrome. Another case under observation began like Coats's disease but later took on the aspects of both the Harada and Vogt-Kojanagj syndromes. The author assumes that these syndromes are different expressions of one disease which is probably infectious. Francis M. Crage.

Vergara, L., Ramírez, A., and Bolaños, F. A. **Penetrating wounds of the eyeball. Intraocular foreign bodies. Sympathetic ophthalmia.** An. Soc. mex. de oftal. 22:21-37, 1948.

Upon a review of 25 patients with penetrating wounds of the eyeball, in two of which the eyeball was enucleated after unsuccessful attempt at removal of an intraocular foreign body, and a consideration of the various theories put forward by different authors with regard to the etiology of sympathetic ophthalmia, the author speculates as to whether a nonspecific iritis prepares the field for a virosis or whether the dominant factor is sensitization to uveal pigment. (15 figures, 5 pp. references.) W. H. Crisp.

BRAZIL

SOCIEDADE DE OFTALMOLOGIA DE MINAS GERAES

The following officers were elected to serve during 1949-1950: President, Prof. Hilton Rocha; vice-president, Dr. Geraldo Queiroga; secretary, Dr. Oswaldo de Cervalho; treasurer, Dr. José Tarcísio de Castro; librarian, Dr. Ary Alvares Pires.

SOCIEDADE DE OFTALMOLOGIA DE SÃO PAULO

The following officers were chosen to serve during 1949-1950: President, Dr. Plinio Toledo Piza; vice-president, Dr. Manoel A. da Silva; general secretary, Dr. Avelino Gomes da Silva; 1st secretary, Dr. Artur Amaral Filho; treasurer, Dr. Aureliano Fonseca; files, Dr. João Carneiro.

CHILE

SOCIEDAD CHILENA DE OFTALMOLOGÍA

At its first meeting for 1949, this society reëlected the officers who had served during the past year, as follows: President, Prof. Italo Martini; vice-president, Prof. Cristobal Espildora Luque; secretary, Dr. Adrian Araya Costa; pro-secretary, Dr. Hernán Brinck; treasurer, Dr. Rene Contardo.

MEXICO

The post-graduate department of the University of Mexico announces the second series of lectures on ophthalmology. The course will last three weeks and will include lectures, demonstration of patients, and practical training in ophthalmoscopy, perimetry, campimetry, angioscotometry, tonometry, and gini-oscopy.

The course will deal especially with internal diseases of the eye, including the optic nerve and vitreous. In addition, there will be lectures and demonstrations in surgery of the eye—detachment of the retina, surgery of intraocular cysticercus, surgery of the eyeball, exenteration of the globe, Mules's operation, and so forth, as well as surgery of intraocular tumors. The course will end with practical lectures on the pathology of the eye (the technique of pathologic anatomy was studied in the first series of the course). In this second series, the student will learn by projections of microscopic sections the pathology of the internal diseases.

In addition to the General Hospital, the following institutions will coöperate: Hospital of La Luz, Hospital of the Association for the Prevention of Blindness, and the services of ophthalmology of the Juarez military and children's hospitals. The course is under the direction of Dr. M. Puig Solanes, professor of ophthalmology, University of Mexico, with the coöperation of a group of physicians of the other institutions. Enrollment price is 350 pesos.

SOCIETIES

JOINT MEETING OF PAN-AMERICAN ASSOCIATION AND N.S.P.B.

At a meeting of the executive committee of the Pan-American Association of Ophthalmology, held in New York City on May 7, 1949, it was decided to hold an interim meeting at the same time and place as the 1950 annual meeting of the National Society for the Prevention of Blindness. The dates set were March 26th to 30th and the place Miami Beach, Florida, with headquarters at the Floridian Hotel.

The following tentative program was drawn up:

Sunday, March 26th. Registration and cocktail party.

Monday, March 27th. A joint meeting of the two organizations, with the opening session at approximately 10 o'clock. The first scientific paper will be a résumé of the accomplishments of the committee on the prevention of blindness of the Pan-American Association of Ophthalmology. Dr. A. Vazquez Barriere (Montevideo, U.) is chairman. The second scientific paper, by Dr. Anderson will be on the rice diet and hypertension. This is to be discussed by Dr. Kempner. At noon there is to be an informal buffet luncheon. In the afternoon there will be a fuller discussion of the committee on the prevention of blindness, with representatives of the different countries represented on the committee speaking in the alphabetical order of those countries.

Tuesday, March 28th. Tuesday morning will be devoted to a program of the Pan-American Association of Ophthalmology: Dr. Albert D. Ruedemann (United States), "The prevention of blindness in industry from the medical standpoint"; Dr. Jorge Valdeavellano (Peru) "Observation of the effect of sunlight on the eyes"; Dr. Robison Harley and Dr. Robert Peckham (United States), "The effect of sunlight on retinal sensitivity." The fourth paper is to be a report of the committee on teaching of ophthalmology on the prevention of blindness, by Dr. Cecil O'Brien (United States) and Dr. Alberto Urrets Zavalia (Cordoba, Argentina). Tuesday afternoon will be devoted entirely to a program of the National Society for the Prevention of Blindness.

Wednesday, March 29th. In the morning the program will be arranged by the National Society for the Prevention of Blindness. In the afternoon the program, under the auspices of the Pan-American Association of Ophthalmology, will include: "Military ophthalmology in the prevention of blindness," Dr. Victor Burns, Admiral Swanson, and Colonel Stone; "Trachoma clinics," Dr. Magin A. Diez (Brazil) and Dr. Cosgrove.

Thursday, March 30th. In the morning there will be a "Glaucoma symposium" under the auspices of

the Pan-American Association of Ophthalmology. It was decided to limit this symposium to secondary glaucoma. The following division of the subject was tentatively agreed upon: Secondary to cataract; secondary to uveitis; secondary to trauma; and congenital glaucoma. The moderator is to be Dr. Conrad Berens.

Dr. Lijó Pavía of Buenos Aires has been invited to give a course this month in Mexico City on photography of the retina in black and white and color. Dr. Pavía will also speak on and demonstrate the ophthalmoscopy of the fundus with red-free light, yellow light, and other lights.

NEWS ITEMS

Edited by Donald J. Lyle, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

DEATHS

Dr. Eugene Orr, Nashville, Tennessee, died May 18, 1949, aged 60 years.

Dr. Homer Jonas Rhode, Reading, Pennsylvania, died June 3, 1949, aged 71 years.

Dr. William D. Rowland, Boston, Massachusetts, died July 1, 1949.

MISCELLANEOUS

CLEARING HOUSE FOR PUBLICATIONS

Later this year, the UNESCO Clearing House for Publications plans to publish a manual on the international exchange of publications and, as a supplement to this manual, a classified list of libraries, universities, scientific institutions, learned societies, and so forth throughout the world which are willing to exchange either their own publications or other publications regularly at their disposal.

All institutions which have not, as yet, sent to UNESCO details of their exchange material are urged to communicate the following information to the UNESCO Clearing House for Publications, 19 Avenue Klebrt, Paris 16°: (1) Name and full address of institution, (2) exact titles of publications offered, (3) conditions under which exchange will be made.

This information must reach UNESCO by October 1, 1949.

SOCIETIES

AOS OFFICERS

Officers of the American Ophthalmological Society elected at the recent meeting are: President, Dr. Parker Heath, Boston; vice-president Dr. John H. Dunnington, New York; secretary-treasurer, Dr. Maynard C. Wheeler, New York.

NEW YORK SOCIETY OFFICERS

The New York Society for Clinical Ophthalmology has elected the following officers for the coming year: President, Dr. Sidney A. Fox; vice-president, Dr. Samuel Gartner; recording secretary, Dr. Bernard Kronenberg; corresponding secretary, Dr. Leon H. Ehrlich; treasurer, Dr. Edward Saskin; librarian, Dr. Howard Agatston. The retiring president, Dr. Benjamin Esterman, was elected to the advisory council.

CINCINNATI OPHTHALMOLOGIC CLUB

During the school year 1948-49, the Cincinnati Ophthalmologic Club held nine meetings at which the following subjects were discussed: "Principles of extraocular muscle surgery," Dr. Hermann Burian, Boston; "Demyelinating diseases of the central nervous system with associated ophthalmic findings," Dr. McIntyre, Cincinnati.

"Industrial responsibility of the ophthalmologist," Dr. Hedwig S. Kuhn, Hammond, Indiana; "The differential diagnosis of the acute glaucomas," Dr. Peter C. Kronfeld, Chicago; "Reparative surgery," Dr. Alston Callahan, Birmingham; "Surgical anatomy of glaucoma operations," Dr. F. Bruce Fralick, Ann Arbor, Michigan; "Surgical treatment of hypermature cataract," Dr. Derrick Vail, Chicago; "Medical treatment of glaucoma and its pharmacologic basis" Dr. Harold G. Scheie, Philadelphia; "Medical treatment of ocular tuberculosis," Dr. G. B. Bietti, Pavia, Italy.

At the final meeting of the year, the following officers were elected: President, Dr. Donald J. Lyle; vice-president, Dr. K. W. Ascher; vice-president and secretary, Dr. D. J. Weintraub.

READING MEETING

On June 22nd, at the 94th meeting of the Reading Eye, Ear, Nose, and Throat Society, Dr. Frank D. Costenbader, Washington, D.C., was guest of honor. He spoke on "Pediatric ophthalmology." Other speakers were Dr. Maurice Saltzman and Dr. Matthew S. Ersner of Philadelphia, and Dr. Frederick Vastine and Dr. Harold L. Strause of Reading.

PERSONALS

TO GIVE GIFFORD LECTURE

Dr. John Dunnington, New York, will deliver the sixth annual Sanford R. Gifford Lecture on January 16, 1950, at Chicago.

TORONTO APPOINTMENTS

The University of Toronto faculty of medicine has appointed Dr. H. L. Ormsby clinical teacher in charge of eye bacteriology, and Dr. O. B. Richardson clinical teacher in charge of eye pathology.

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EXPERIMENTAL OCULAR HISTOPLASMOSIS*

ROBERT DAY, M.D.
Baltimore, Maryland

Human infection with Histoplasma capsulatum was first described by Darling in 1906,[1] but only during the past 10 years has this disease become of general interest and of possible significance in ophthalmology.

Darling's original case was a 27-year-old Negro of the Canal Zone who, on clinical examination, was thought to have miliary tuberculosis. At autopsy, however, there was found a widespread infection of lungs, liver, spleen, blood, and lymph nodes with a small oviform organism about three microns in diameter. Darling believed it to be a parasite related to the Leishmania of kala azar. It was free in the tissues and was also widely phagocytosed by the reticulo-endothelial cells of the affected organs.

In 1934, the nature of this parasite was established.[2] De Monbreun cultivated a fungus from a fatal infection of a 6-month-old Tennessee infant. This occurred in both a yeast and a mycelial form and produced in monkeys a disease similar to the human infection from which it was recovered.

Conant,[3] in 1941,, made a careful study of the fungus which he classified among the moniliaceae of the Fungi imperfecti. The mycelial form has aerial branching septate hyphae containing large and small, round, pyriform, or tuberculate chlamydospores (figs. 1 and 2). On synthetic media the fungus ordinarily assumes the mycelial form, but in infected animals it appears as a thin-walled, oval, yeastlike cell about 2 by 3μ which reproduces by a single bud

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from the end of its long axis (figs. 1 and 3).

Prior to De Monbreun's work in 1934, only 11 cases of histoplasmosis had been reported. All ended fatally. Since then, more than 80 additional fatal cases have been described. Parsons and Zarafonetis[4] summarized these up to 1945 and described lesions of skin, mucous membrane, nasopharynx, lymph nodes, lungs, liver, spleen, gastrointestinal tract, and blood. Ocular lesions were mentioned only once, as "small white irregular areas, surrounded by hemorrhage, in the ocular fundi, not unlike tubercles." The eyes from this case, reported by Reid and others in 1942, were unfortunately not obtained at autopsy.[5]

Simultaneous with the increased recognition of the fatal form of the disease, there developed a growing suspicion that nonfatal cases existed, perhaps on a large scale. Pulmonary calcifications, resembling those of tuberculosis, in negative reactors to tuberculin have long been known.[6-11] Various hypotheses have been offered to explain them, such as pneumonoconiosis, skin anergy in tuberculosis, and mycotic infection.

In 1938[6] the study of this problem received impetus from the observation that routine X-ray examination showed an unusually high number of such pulmonary calcifications in persons from Tennessee and neighboring states. In 1943, Dr. C. E. Smith of Stanford University suggested to Dr. Amos Christie of Vanderbilt University that mild histoplasma infections might explain this peculiar abundance of pulmonary lesions in persons insensitive to tuberculin.
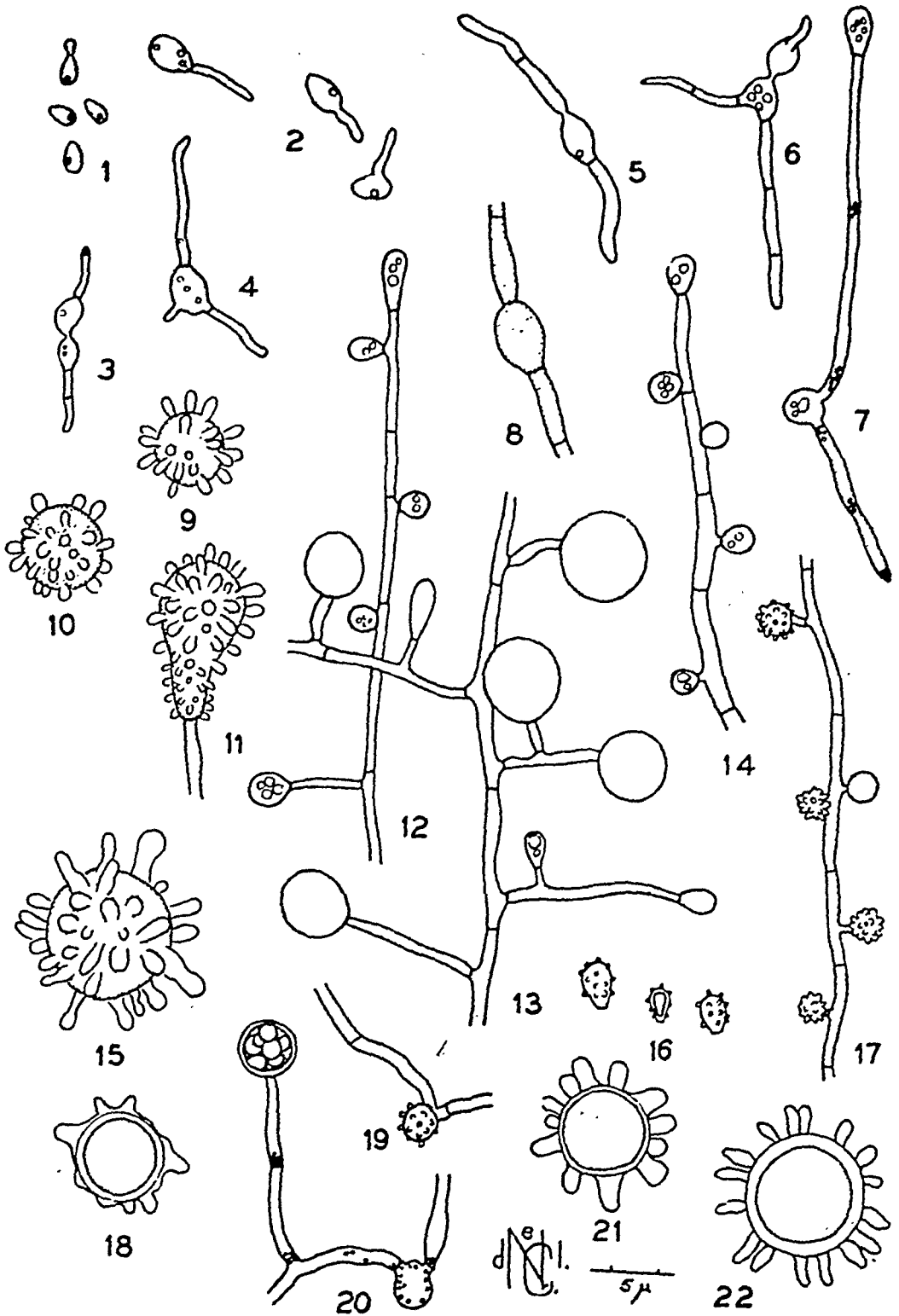
Fig. 1 (Day). Histoplasma capsulatum. (1) represents the yeast form of the fungus.
(2 to 22) represent the hyphae and chlamydospores of the mycelial form of the fungus
in various stages of development. (N. F. Conant, 1941.)

In 1945, Christie[12] reported the results of a study of Tennessee school children tested with tuberculin and with histoplasmin, an antigen obtained from a broth culture of the mycelial form of the fungus. Seventy-nine of 181 children had pulmonary lesions demonstrable by X ray, resembling those of tuberculosis. Of these 79 only 3 were sensitive to tuberculin alone; 48 were sensitive to histoplasmin alone. Comparable results were

thereafter obtained in other similar studies of both adults and children.[13-18] In spite of the uncertain specificity of the histoplasmin skin test,[19-20] these reports strengthened the possibility that there exists, particularly in all cases. All had positive histoplasma complement fixation reactions;[22] 4 gave positive skin reactions to histoplasmin and negative reactions to tuberculin (the 5th case reacted to both antigens). Four of these patients
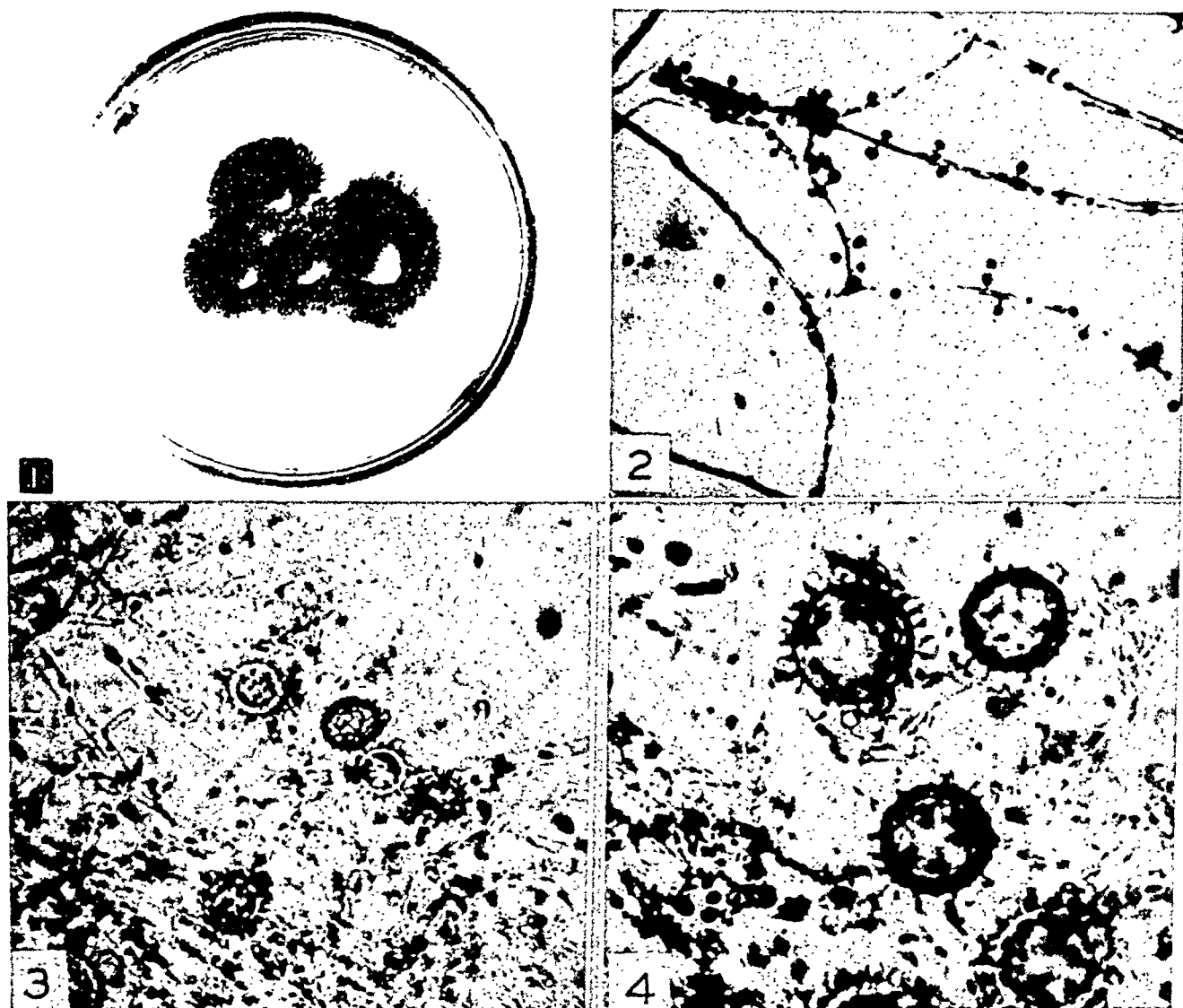
Fig. 2 (Day). Histoplasma capsulatum, mycelial form. (N. F. Conant, 1941.) (1) Gross appearance on Saboraud's agar. (2 to 4) Microscopic appearance of spores and aerial hyphae.

the central and east-central United States, a subclinical form of fungus disease which produces lesions not unlike those of tuberculosis.

The concept of a nonfatal form of histoplasmosis is further supported by the report in March, 1948, of Bunnell and Furcolow[21] from Kansas City. These observers reported nonfatal infections with Histoplasma capsulatum, 2 in adults and 3 in children. The organism was recovered from also had pulmonary calcifications demonstrable by X ray.

A fatal fungus disease, histoplasmosis, is now definitely recognized. This disease produces in many organs granulomatous lesions resembling those of tuberculosis. A milder form of the disease is also recognized, and widespread subclinical or arrested infections are suspected. It seems possible that some cases of granulomatous uveitis may be due to ocular infection with Histoplasma cap-
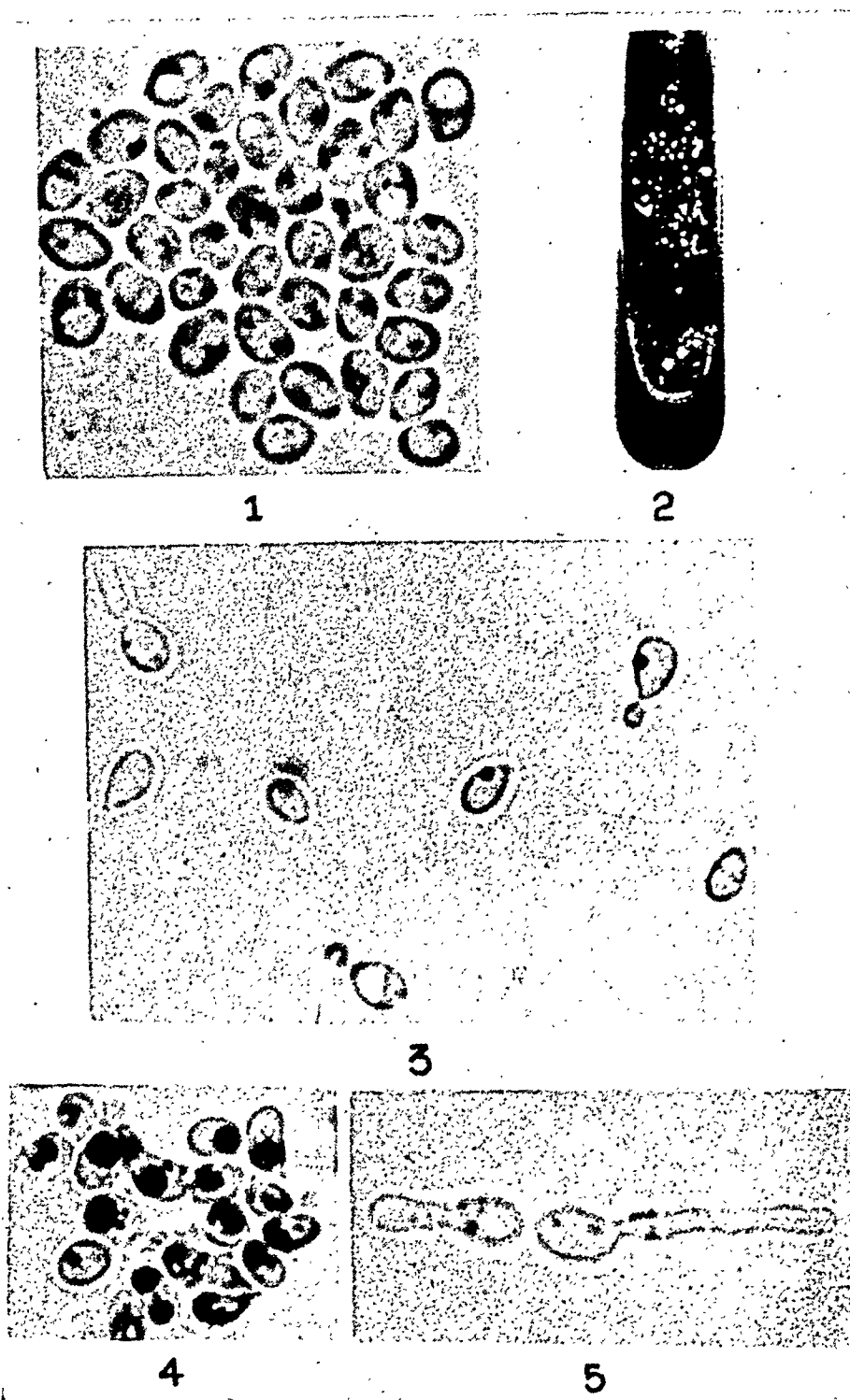
Fig. 3 (Day). Histoplasma capsulatum, yeast form. (2) Gross appearance. (1, 3, and 4) Yeast cells, (5) Transitional form. (W. A. De Monbreun, 1934.)

sulatum. To test this hypothesis preliminary clinical and experimental studies have been made.

A. CLINICAL STUDIES

One hundred eighteen unselected cases on the public wards of the Wilmer Institute were tested with histoplasmin by intra-cutaneous injection with 0.1 cc. of histoplasmin (H-15 or H-3), diluted 1:100 and 1:1000. Positive reactions were those in which induration and erythema measured more than 5 mm. in diameter 48 hours after injection. No selection was made either by

race, age, or sex. (The H-15 was obtained through the courtesy of Dr. Arden Howell, and the H-3, through the courtesy of Dr. Chester Emmons, both of the United States Public Health Service.)

Twenty-one of the 118 cases had either active or inactive uveitis. Of the 97 patients without uveitis 29, or 30 percent, gave cutaneous reactions to histoplasmin. This figure compares closely with the 31.9 percent found

these 4, 2 had a single attack of choroiditis, 1 had recurrent choroiditis, and 1 had a single attack of acute granulomatous anterior uveitis. The remaining 10 patients had other positive clinical findings which indicated other possible causes of uveitis.

B. Experimental studies

In order to study histoplasma infections of the eye, both uninfected and previously
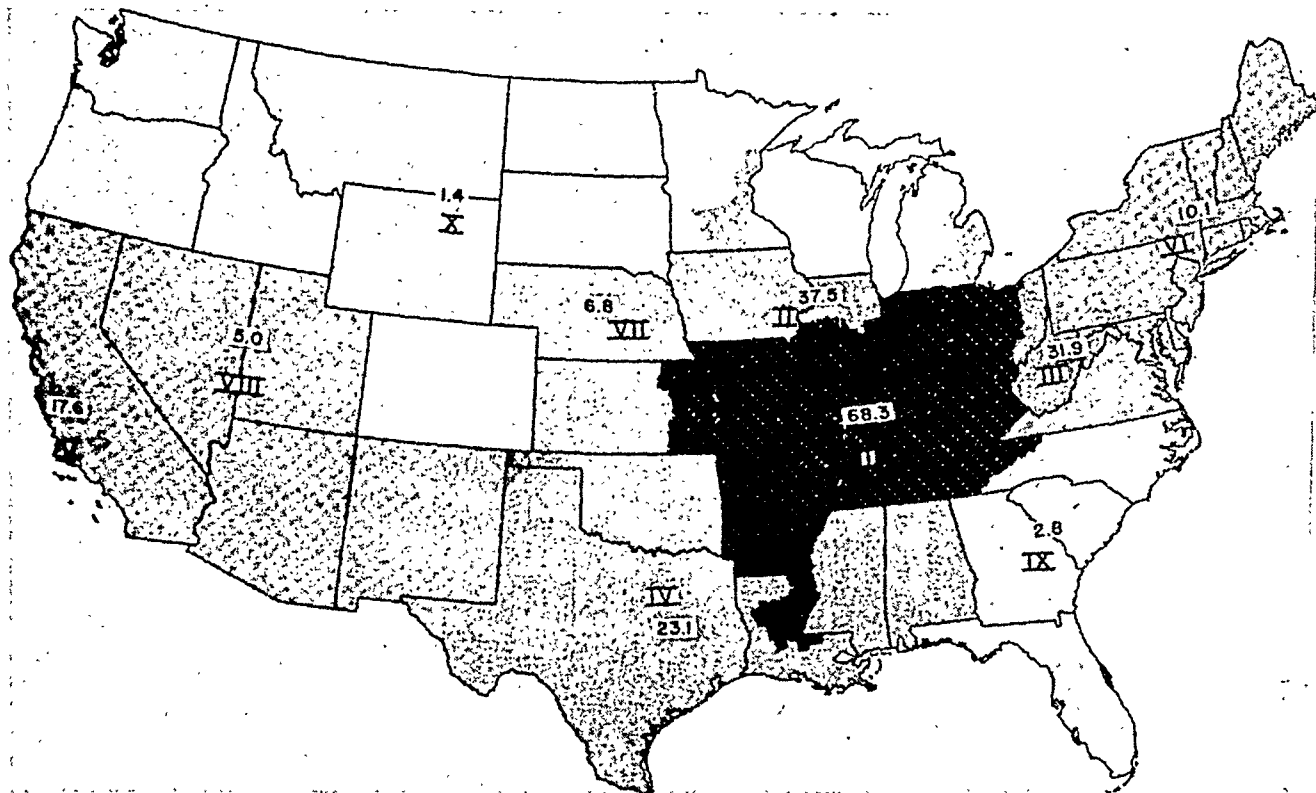
Fig. 4 (Day). Histoplasmin sensitivity among student nurses classified by state of lifetime residence. (C. E. Palmer, 1946.)

by Palmer, in 1946, for student nurses of the Maryland area[23] (fig. 4). Fourteen, or 67 percent, of the 21 cases of uveitis had positive skin reactions as compared with 30 percent for the group without uveitis. This difference is unlikely to occur by chance. Four of these 14 histoplasmin reactors did not react to intracutaneous injection with 1 mg. of old tuberculin or with 0.1 cc. brucellergin; they had negative serologic tests for syphilis, were apparently free of foci of infection, and had normal serum albumin/globulin ratios. They did have pulmonary calcifications and were sensitive to histoplasmin. Of

infected rabbits were inoculated with the mycelial form of the fungus. The clinical course and histologic picture were then studied.

1. The ocular reaction in normal rabbits

Seventeen eyes in 15 previously uninfected young adult albino rabbits were injected with living spores via the anterior chamber. The technique of the injection was as follows:

The fungus was scraped from a two weeks' growth on Saboraud's agar at room

temperature, was then suspended in saline, and ground to a smooth suspension with a sterile mortar and pestle. A spore count was then made with a blood-counting chamber. The suspensions contained from 125,000 to 3,000,000 spores per cc. Using a sterile syringe and hypodermic needle, 0.05 to 0.2 cc. of aqueous was removed from the anterior chamber. An equivalent amount of the suspension was then injected by the same needle without removing it from the

reflected light, could often be seen on trans-illumination as minute opacities seeded throughout the iris. These scattered nodules grew larger, the iris vessels became more dilated, and, within a week or two, a diffuse exudative nodular iritis occurred (figs. 5, 6, and 7). Within another 1 to 2 weeks, the angle in most cases became blocked and secondary glaucoma developed with vascularization and edema of the cornea (fig. 8). After 2 to 4 weeks of severe inflammation

Fig. 5 (Day). Rabbit D-10, L.E. Two weeks after infection with H. capsulatum.

Fig. 6 (Day). Rabbit D-22, L.E. Three weeks after infection with H. capsulatum.

anterior chamber. From 10,000 to 300,000 spores were thus introduced.

Ten eyes in 10 rabbits developed nodular iritis. An inflammatory reaction followed within 24 hours after infection. The iris and pericorneal vessels became dilated and an exudate appeared in the pupillary space, over the anterior iris, and frequently on the posterior cornea. This immediate reaction either subsided within a week, leaving the eye quiescent for 2 or 3 weeks, or, in most cases, persisted without appreciable change for 1 or 2 weeks.

In those eyes in which the initial reaction subsided, iris nodules appeared 1 to 4 weeks after infection. These were single or multiple, but, even when apparently solitary by

and progressive buphthalmos, the signs of inflammation began to subside (fig. 9). The total period of acute inflammation was thus 4 to 6 weeks. At this interval after infection, the skin test became positive. Two to 3 months after infection, the eyes were quiescent with nodular scars in the irides and leukomatous corneas.

The eyes in which the initial inflammation failed to subside developed a severe nodular iritis 1 to 2 weeks after infection (fig. 10). This led to a buphthalmos and corneal scarring indistinguishable from that of the less fulminating form of iritis described in the last paragraph.

Five eyes in 5 normal rabbits developed buphthalmos within the first week after in-

Fig. 7 (Day). Rabbit D-6, L.E., Six weeks after infection with H. capsulatum.
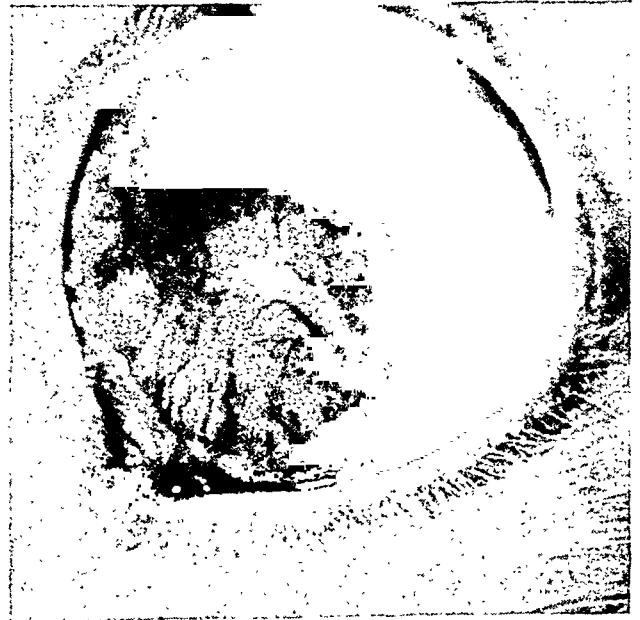
Fig. 8 (Day). Rabbit D-14, L.E. Six weeks after infection with H. capsulatum.

fection, thus making it impossible to follow the course of the disease. However, in these rabbits the skin test to histoplasmin became positive, and yeast cells were found in 3 eyes on microscopic examination. The corneal scarring and buphthalmos were indistinquishable from that already described.

Two of the above rabbits were infected simultaneously in both eyes; one eye was removed from each rabbit a week after in-

fection, before the development of a nodular iritis.

2. Development of cutaneous sensitivity

All rabbits were initially insensitive to 0.1 cc. of a 1:10 dilution of H-3 histoplasmin given intradermally. The animals were then given periodic intracutaneous injections with 0.1 cc. H-3 histoplasmin (1:10 and 1:100).

Fig. 9 (Day). Rabbit D-10, L.E. Ten weeks after infection with H. capsulatum.
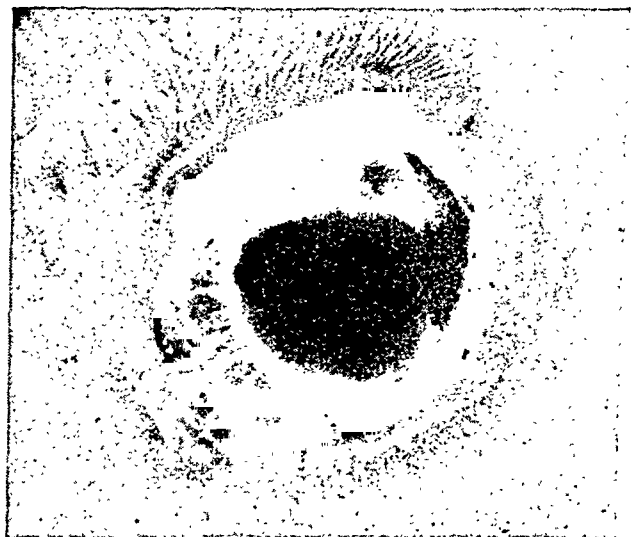
Fig. 10 (Day). Rabbit D-11, L.E., Two and one-half weeks after infection with H. Capsulatum.

A few rabbits were skin sensitive to H-3 (1:10) 2 to 4 weeks after infection. The majority became skin sensitive in 4 to 6 weeks. By the end of the 6th week after infection all rabbits but one, regardless of the route of infection, were skin sensitive to 0.1 cc. of 1:10 and 1:100 H-3. The organism was recovered by culture, however, from the insensitive rabbit 6 months after infection.

3. THE OCULAR REACTION IN PREVIOUSLY INFECTED RABBITS

In order to determine whether previous infection altered the clinical course of subsequent reinfection, 8 of the 15 rabbits used in the initial experiment were reinfected in the anterior chamber of the other eye from 2 to 14 weeks after the original infection and after enucleation of the previously infected eye. None of the previously uninfected eyes showed clinical signs of disease at the time of reinfection.

Five eyes were inoculated in 3 rabbits given previous extraocular infection. One of these received an intravenous injection of 1,000,000 spores 1 month before the ocular injection. The other 2 rabbits received 500,000 spores each by retrobulbar inoculation 1 month and 2 months respectively before the ocular injection. None of the eyes of these rabbits showed signs of clinical infection at the time of reinfection.

Altogether 13 eyes were inoculated in 11 previously infected rabbits. Seven of the 13 eyes were in 5 rabbits which had been inoculated 2 to 4 weeks previously, either systemically or in the anterior chamber. Three of these eyes developed nodular iritis, 2 developed buphthalmos and simultaneous iritis, 1 had a bacterial panophthalmitis, and 1 eye was enucleated a few days after infection so that its clinical course was not followed. The disease process in these eyes closely resembled that in the primary infections already described.

The remaining 6 eyes, in 6 rabbits, originally infected 6 to 14 weeks previously,

had an initial inflammatory reaction after reinfection but failed to develop iritis.

Under the conditions of this experiment it appears that some immunity is conferred by ocular or systemic infection and that this immunity develops its effect in 4 to 6 weeks.

4. THE OCULAR REACTION AFTER INTRAVENOUS INJECTION

Five rabbits were given intravenous injections of the fungus. One case of spontaneous ocular infection occurred. This rabbit received an initial injection via an ear vein of 1,000,000 spores. Two weeks later he received 1,500,000 spores intravenously. Four weeks after the original injection he was skin sensitive to 0.1 cc. 1:100 H-3. Three months after the original injection, a third intravenous injection of 1,125,000 spores was given, and 3 weeks later, a fourth injection of 1,500,000 spores.

One week after the last injection, the pupil of the left eye was peaked from the 1- to 5-o'clock positions. There was a bloody exudate in the lower anterior chamber. The aqueous was clouded with a fibrinous exudate. A good red reflex was obtained but no fundus details could be made out. During the next 2 weeks the eye whitened, but the pupil remained peaked at the 3-o'clock position and there appeared to be a mass behind the iris at that point. There were many coarse intravitreous opacities.

The eye was enucleated. On histologic examination the positive findings were a small collection of round cells in the ciliary body, a few round cells in the vitreous, and one giant cell in the ciliary body which contained no yeast cells.

5. THE OCULAR REACTION AFTER INTRAVITREOUS AND RETROBULBAR INJECTION

Localized vitreous abscesses developed in 4 eyes of 2 rabbits following intravitreous inoculation. These progressed for 1 to 2 weeks and then slowly regressed, leaving heavy localized opacities.

No clinical change was observed in the
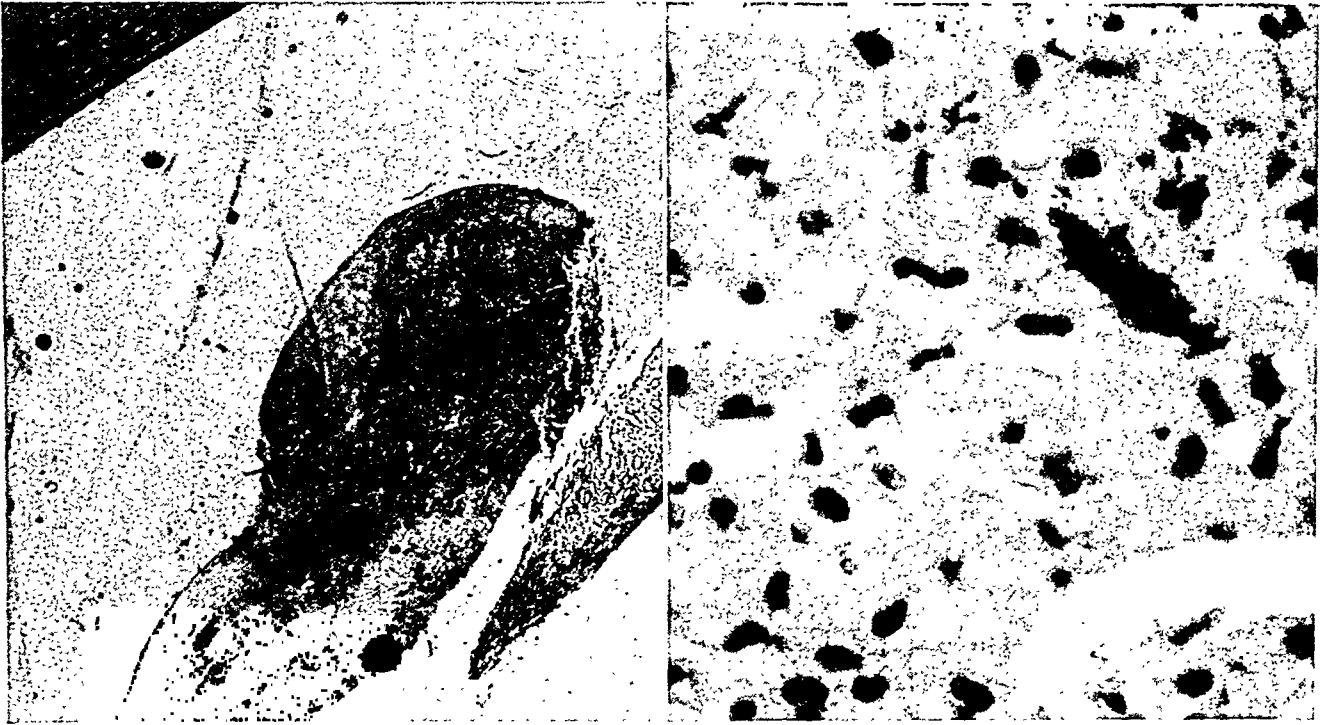
Fig. 11 (Day). Rabbit D-1, L.E. One week after infection with H. capsulatum. Exudate in anterior chamber, round cells, a few polys, and mycelial debris. (Left ×35; right ×600.)

eyes of 2 rabbits following retrobulbar injection.

6. THE OCULAR REACTION AFTER INOCULATION WITH HEAT-KILLED SPORES

Three eyes in 3 rabbits were inoculated in the anterior chamber with heat-killed spores. These eyes, except for an initial inflammatory reaction which subsided within a week, did not develop iritis.

7. SUMMARY OF OCULAR REACTIONS

To recapitulate, normal rabbits when injected via the anterior chamber with a saline suspension of the mycelial form of Histoplasma capsulatum developed a nodular iritis which led to secondary glaucoma, buphthalmos, and the loss of the eye.

The interval between infection and the appearance of the nodular iritis varied with the size of the infecting dose. Animals in-
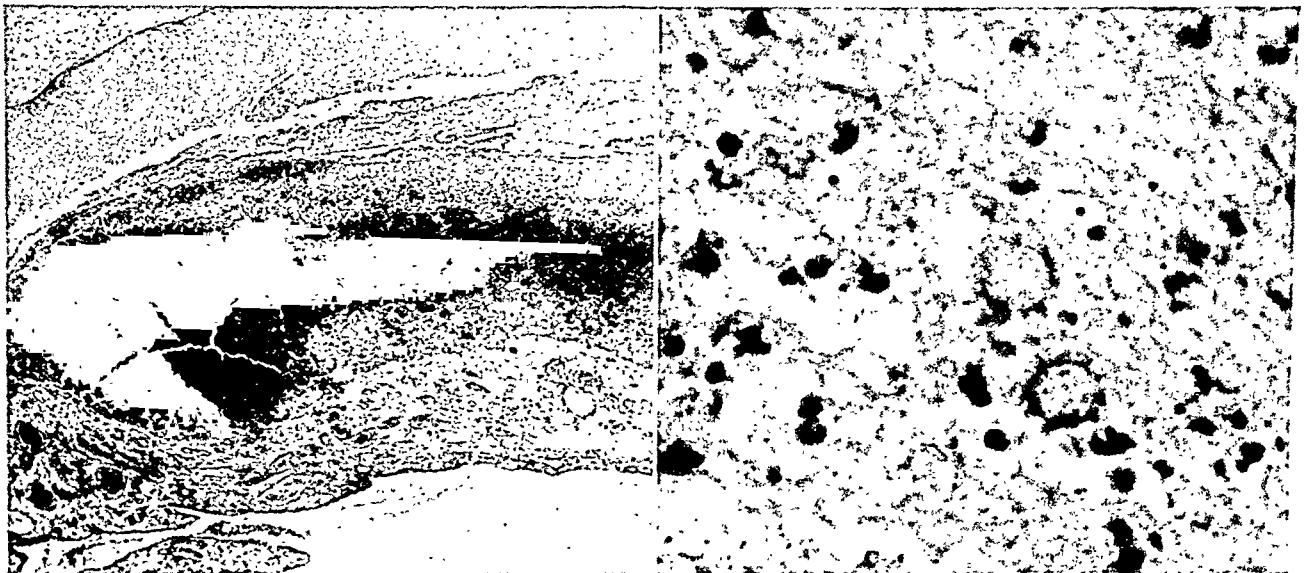
Fig. 12 (Day). Rabbit D-1, R.E. One week. Massive exudate in anterior chamber, polys, round cells, fibrin. Note two spores near center of high-power photomicrograph (right ×600). (Left ×35.)
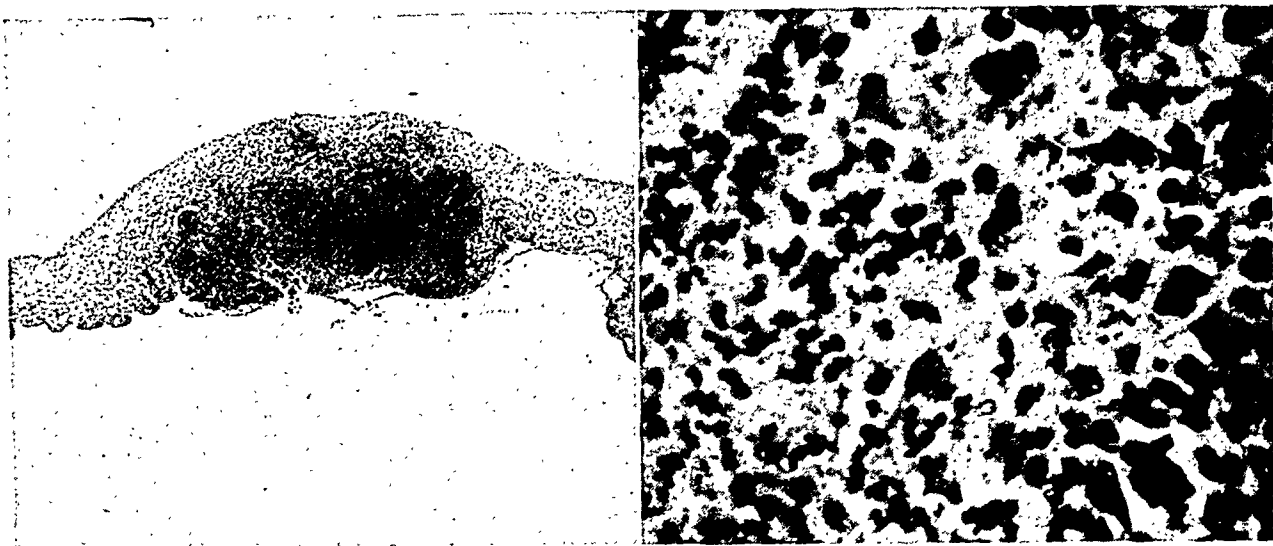
Fig. 13 (Day). Rabbit D-5. One month. Iris, left eye. A few intracellular yeast cells.
(Left ×35; right ×600.)

fected 1 to 3 months previously appeared to have considerable resistance to reinfection via the anterior chamber and this resistance seemed to be coincident with the appearance of skin sensitivity to histoplasmin.

The ocular reaction was thus analogous to that of immune-allergic animals upon reinfection with the tubercle bacillus. Ocular histoplasmosis, in fact, resembles ocular tuberculosis, not only in this apparent immunity but also in the granulomatous nature of the lesion and in its destructiveness. The organism is also believed to cause benign pulmonary calcifications almost identical by X-ray examination with those of tuberculosis.

C. HISTOLOGIC STUDY

Two routine histologic sections were made of each eye, the first stained with hematoxylin and eosin, and the second either by the Bauer technique[24] or by the periodic-acid method developed by Hotchkiss, McManus,[25-26] and others. The two latter methods are used to stain polysaccharides and will stain the yeast form of Histoplasma capsulatum.

Miscroscopic study of the eyes removed during the first week after infection gives a
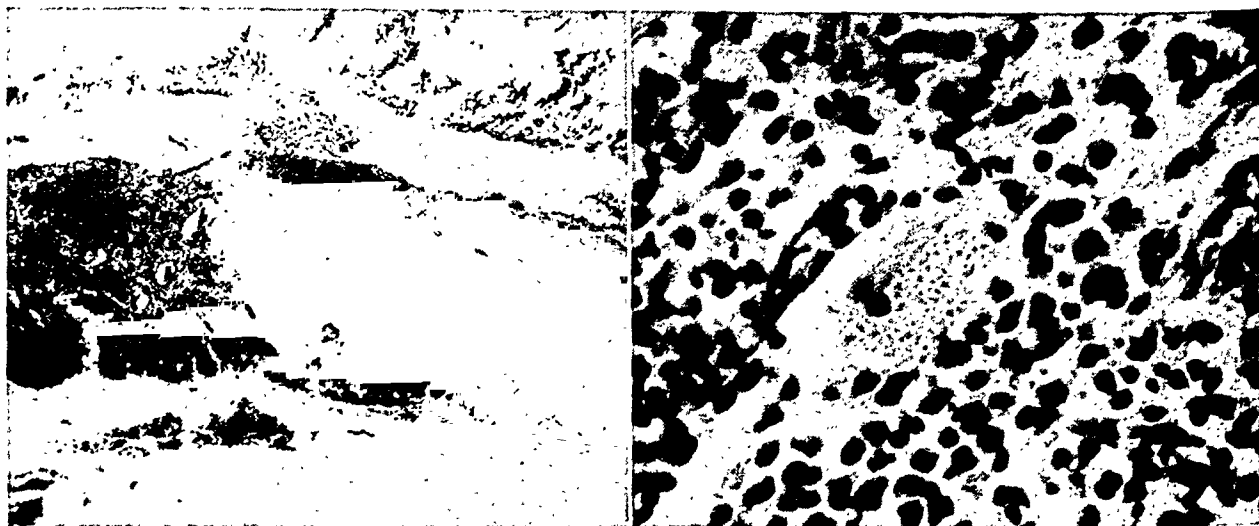
Fig. 14 (Day). Rabbit D-6. Two months. Iris, left eye. Note intracellular yeast cells in high-power photomicrograph (right ×600). (Left ×35.)
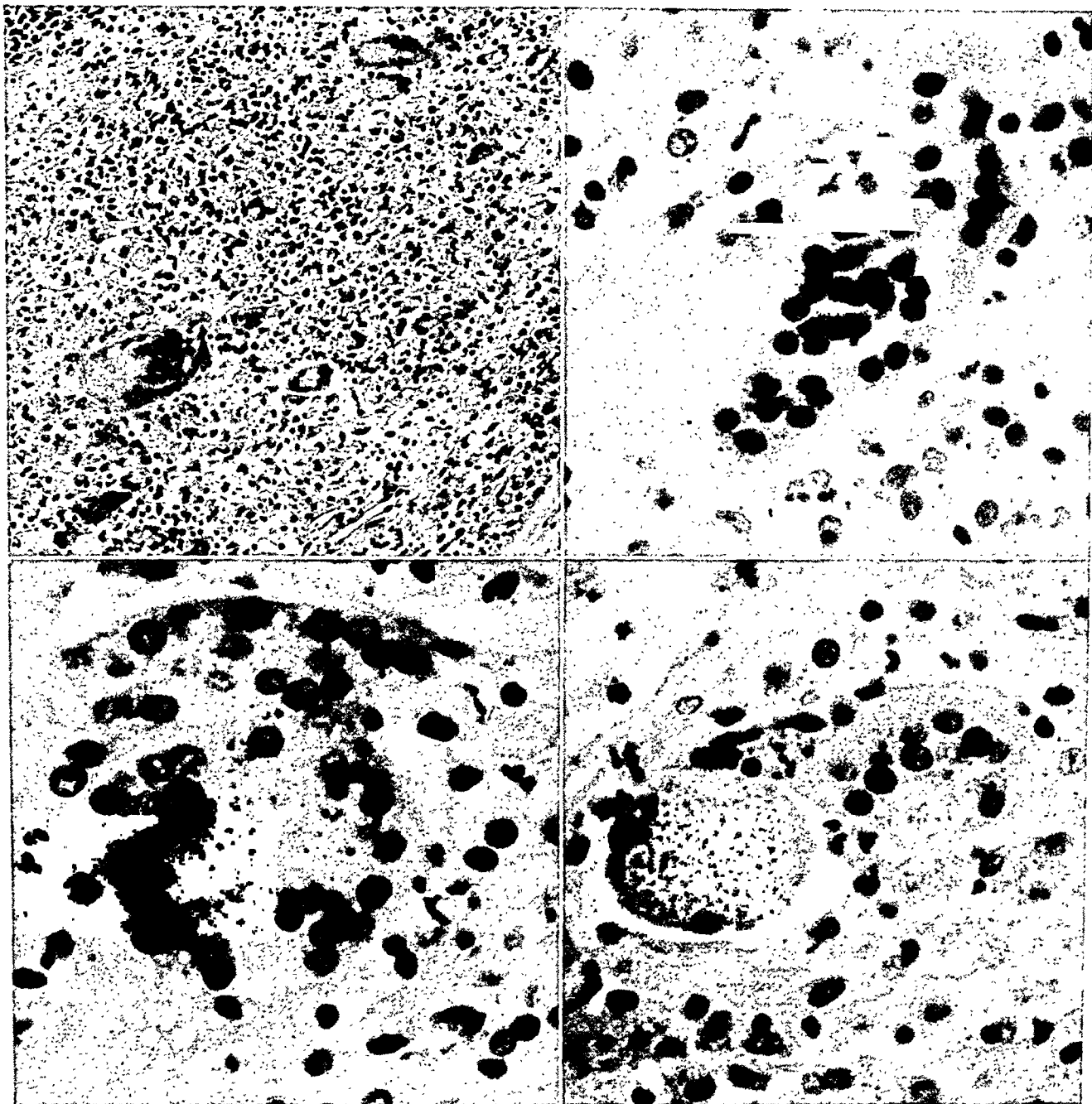
Fig. 15 (Day). Rabbit D-9. One month. Iris, right eye. In figure at lower right (×600) there are numerous intracellular yeast cells; at lower left (×600) there are fewer. The giant cell in figure at upper right (×600) contains possibly 1 or 2 organisms. (Upper left ×140.)

variable picture, dependent upon the degree of immunity and the size of the infecting dose. The less violently inflamed eyes show a few spores and a small amount of mycelial debris in the anterior chamber; a few polymorphonuclear and mononuclear white blood cells on the posterior cornea, on the anterior iris, and in the iris stroma; and an occasional intracellular phagocytosed yeast cell (fig. 11). The more violently inflamed eyes show marked exudate, debris, polys, spores,

and yeast-containing macrophages in the anterior chamber, and marked edema of the iris with a variable infiltration of the iris stroma and ciliary body with macrophages, other round cells, occasional epithelioid cells, and rare giant cells (fig. 12).

With the appearance of the iris nodules, a granulomatous picture predominates (figs. 13 and 14). In some eyes there is a nodular infiltration of the iris with round cells, epithelioid cells, and a few polymorphonu-
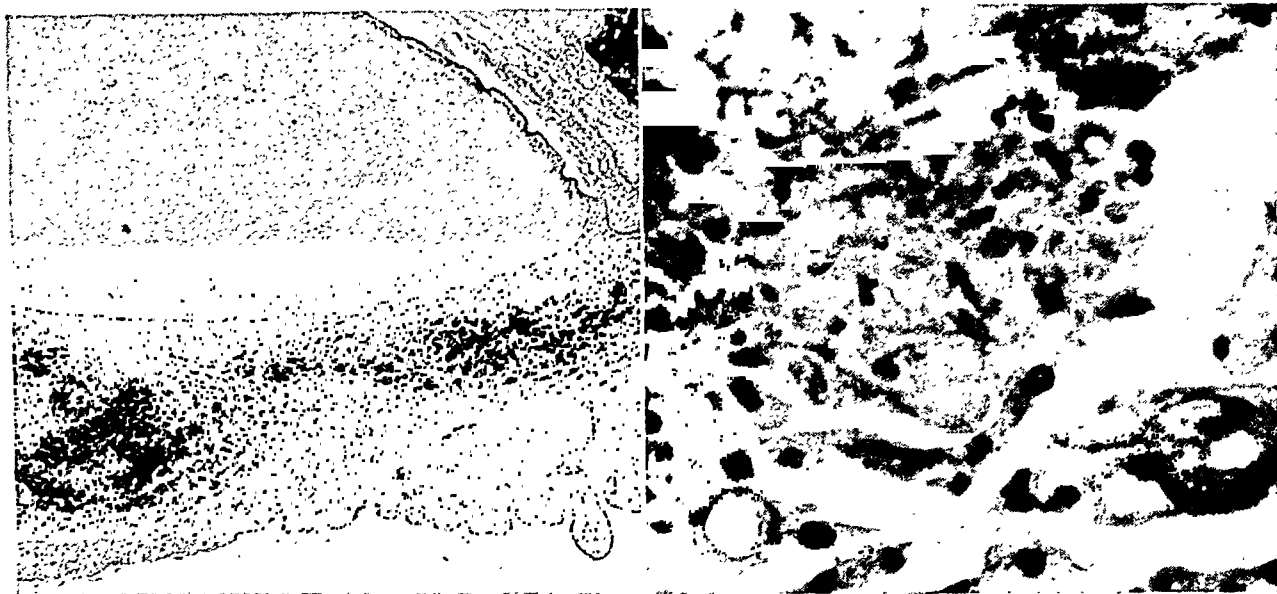
Fig. 16 (Day). Rabbit D-11, L.E., Two and one-half weeks. Note the spore in the lower left corner of the high-power photomicrograph. These are not often seen at this stage of infection. (Left ×35, right ×600.)

clear leukocytes. Yeast cells can be seen within mononuclear wandering cells (figs. 13 and 14). In other eyes there are, in addition, many giant cells in some of which large numbers of yeast cells can be seen, apparently in various stages of digestion (fig. 15). There is considerable tissue destruction, usually beginning 4 to 6 weeks after infection, and, in many eyes, there are abscesses of cornea, iris, or ciliary body (fig. 16).

Two to 3 months after infection while the clinical signs of inflammation are subsiding, in addition to glaucomatous or phthisical changes, the eyes still show extensive round-cell infiltration of the anterior uveal tract and a few polymorphonuclear leukocytes. Some eyes have localized abscess of the iris or ciliary body, characterized by central necrosis and peripheral collections of round cells, epithelioid cells, giant cells, and yeast-containing macrophages, with a
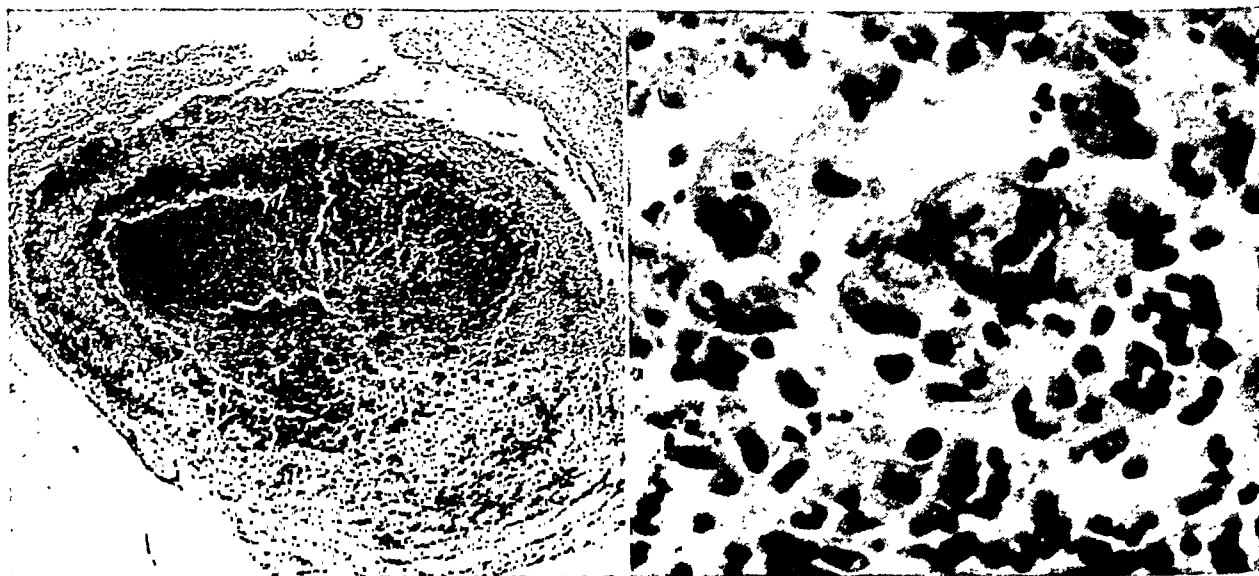
Fig. 17 (Day). Rabbit D-17. Iris, left eye. Three months. Abscess with necrotic center and peripheral granuloma.

few polymorphonuclear cells scattered among them, not unlike the lesions of experimental ocular brucellosis (fig. 17). Most of the eyes examined at 3 months or later have extensive round-cell infiltration of the uvea without visible giant cells, and with few epithelioid cells. They present the picture of a nonspecific subsiding granulomatous inflammation (fig. 18). Phagocytosed

The injection of Histoplasma capsulatum into the anterior chamber of rabbit eyes produces a destructive granulomatous anterior uveitis closely resembling tuberculosis in its clinical appearance, but apparently self-limited in course. Systemic infection in rabbits may result in ocular involvement. Infected animals, as in tuberculosis, tend to develop resistance to reinfection and become
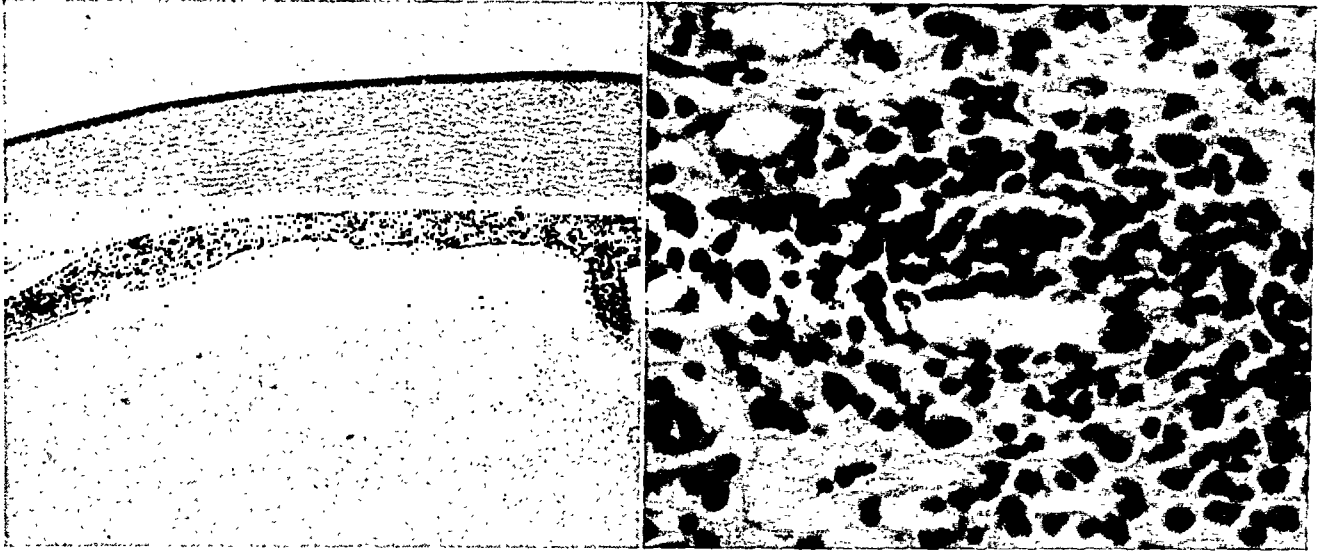
Fig. 18 (Day). Rabbit D-18. Iris and cornea, left eye. Three months. Subsiding granuloma.

yeast cells are seldom seen in the late stages, yet from one eye in which no organisms were visible by microscopy, they were recovered by culture six months after infection.

COMMENT

What bearing do the foregoing fragmentary data have upon the possibility of human ocular histoplasmosis?

It is credible from the work of Furcolow, Bunnell, Christie[21,12] and others that a non-fatal form of systemic histoplasmosis exists in human beings. Four patients with acute uveitis have now been observed, all of whom had skin sensitivity to histoplasmin and benign pulmonary calcification, yet had negative results from other routine clinical studies. In these patients the existing evidence points to the possibility that histoplasmosis was the cause of their ocular infection.

skin allergic to an extract derived from the infecting organism. The infection tends to subside and the organism to disappear from the eye following the development of skin sensitivity to histoplasmin. These facts are circumstantial evidence in support of histoplasma uveitis.

On the other hand, there is as yet no direct proof that the organism can produce subclinical or recurrent human infection anywhere in the body. There is no direct proof that the disease causes uveitis in human beings. The final proof must be the isolation of the fungus from the suspected case. There are to date insufficient data as to the duration of viability of the organism within the rabbit eye, but the evidence indicates a steadily decreasing viability which parallels the clinical course of the experimental disease. It is noteworthy, however, that the fungus was recovered from a clinically quiescent eye 6 months after infec-

tion. If the human disease exists and is analogous to the rabbit infection, the organisms and typical lesions are likely to be found only during the acute phase. Further clinical and histologic study of Histoplasma capsulatum as a possible cause of ocular disease is necessary in order to distinguish it from other causes of granulomatous uveitis.

SUMMARY

1. A brief review of the history of systemic infection with Histoplasma capsulatum has been made.

2. A significantly higher percentage of patients with uveitis reacted positively to skin testing with histoplasmin than of patients without uveitis. Four of these patients had a positive skin test to histoplasmin, pulmonary calcification, and uveitis as the only positive clinical findings.

3. Rabbits can be infected via the anterior chamber with Histoplasma capsulatum and develop a granulomatous anterior uveitis which is apparently self-limited in course.

The Johns Hopkins Hospital (5).

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HISTAMINE AND UVEAL INFILTRATION*

T. F. SCHLAEGEL, JR., M.D.

Indianapolis, Indiana

Because of the importance of allergy in the etiology of uveitis it was considered desirable to determine what histologic effect the ocular injection of histamine has upon the attraction of leukocytes.

A review of the literature indicates that histamine is not chemotactic for leukocytes although not all experiments along this line are in agreement.

In 1921, Wolf[1] published the results of her study on the influence of chemicals upon the chemotaxis of leukocytes in vitro. She found that histamine was strongly and positively chemotactic in molecular concentrations of over 0.000,025 percent. In 1922, Bloom[2] reported on the reaction of the cat to histamine dihydrochloride. He found practically no difference between the effects produced by injections of histamine in physiologic saline and of physiologic saline alone. Also glass tubes containing the histamine did not attract leukocytes either in vivo or in vitro. In 1923, Wolf[3] continued her studies on chemical inflammation, this time in vivo, and concluded that histamine produces a marked inflammatory reaction in frogs and mice.

In 1928, Grant and Wood[4] said that, since it seemed impossible to reconcile these conflicting results, they repeated Wolf's observations on the frog and made others on the rabbit and on human skin. Throughout their experiments they used 0.5-percent histamine acid phosphate dissolved in physiologic saline with the addition of sodium hydrate immediately before use to give a pH of 7.3. As a control a phosphate buffer solution of the same pH was employed.

They found that in frogs the mesenteric circulation remained active, no diapedesis of red cells took place, and no emigration of leukocytes could be detected until after 80 to 227 minutes, at which time emigration was found in mesenteries irrigated with phosphate solution alone or in those allowed to become dry.

In experiments on human beings, histamine was pricked into the skin and, when the vascular reaction was at its height, 20 minutes later, sections showed no leukocytic migration. In another subject the local reddening and whealing was maintained for 9 hours by pricking histamine into the same spot every 40 minutes. No increase in leukocytes was found except along the needle tract. The experiment was repeated and maintained for 25 hours with a control of phosphate solution. Microscopic examination failed to differentiate the two, there being leukocytes along the needle tract in both cases.

In 1928, Findlay[5] inoculated rabbits intravenously with staphylococci, streptococci, or pneumococci, 24 hours after several intradermal injections of histamine. Polymorphonuclear leukocytes were found diffused throughout the area injected with histamine, while in the area injected with a control of phosphate solution they were few and far between. Findlay's experiments thus indicate that histamine may act by favoring the localization of bacteria.

In 1934, Morgan[6] used histamine acid phosphate in a physiologic solution of sodium chloride on guinea pigs, rabbits, dogs, and human beings. An attempt was made to produce an inflammatory reaction in the rabbit by applying histamine by various methods. The conclusion was reached that histamine, when repeatedly instilled into the conjunctival sac, applied to the intact, burned, scratched, or cut skin for as long as 72 hours, or repeatedly injected into the muscle of the rabbit, does not produce an inflammatory reaction.

Another experiment consisted of producing a wheal with histamine and one of equivalent size by the injection of a physiologic solution of saline. Microscopic examination failed to demonstrate any difference between the areas into which the saline solution was injected and the areas in which wheals were produced by histamine.

Both tissues showed a diffuse infiltration of leukocytes with a slight concentration of white cells around the point of injection. Since there was a rapid increase of fluid in both cases, Morgan felt that the tearing and distortion of the cellular structures liberated products of tissue disintegration.

In 1935, Moon[7] reported experiments following the technique of Wolf and with modifications of it in vitro and did not note increased migrations of leukocytes toward inert substances containing various concentrations of histamine.

Moon then performed experiments to obtain further evidence on this point in vivo. Cylindric bits of elder pith of uniform size were cleared of soluble substances and then saturated with a physiologic solution of sodium chloride containing histamine phosphate in a 1:10,000 solution and were implanted in animal tissues through a canula. Some were introduced into the peritoneal cavity and others into the loose subcutaneous areolar tissue. In every instance a bit of elder pith saturated with physiologic solution of sodium chloride was similarly implanted as a control. Plugs saturated with histamine were implanted in 9 monkeys, 8 cats, and 4 guinea pigs. After from 6 to 24 hours the animals were killed and the reaction about the histamine pith was compared to that of the control.

In every instance, there was a marked zone of congestion about 2 cm. in diameter surrounding the pith saturated with histamine, but none about the controls. Microscopic examination revealed numerous leukocytes about both test and control piths. There was no evidence of active invasion of the pith by cells, and leukocytes were apparently as numerous about the control piths as about the ones containing histamine.

Moon also concluded that the evidence indicated that some product of cellular injury, other than histamine, is responsible for the local attraction of leukocytes.

Soon afterwards Menkin[8] demonstrated a factor in inflammatory exudates. This factor was later found to be a crystalline nitrogenous substance and was called leukotaxine.[9] It is capable of increasing capillary permeability and of attracting leukocytes. Within 15 to 30 minutes following its intracutaneous inoculation, polymorphonuclear leukocytes accumulate in abundance in the lumen of small vessels and then soon migrate actively into the extracapillary spaces.[10] Menkin gave repeated evidence that leukotaxine was not histamine and in no way related to it.[11-13]

In 1942, Rigdon[14] reopened the question of the chemotactic property of histamine. Using histamine phosphate diluted in saline to 1:1,000 to 1:8,000, he found that polymorphonuclear leukocytes were present in the extravascular tissues of the rabbit usually within an hour following the injection. The number of these cells appeared to increase during the following 4 to 5 hours and then to decrease. Control experiments apparently were not done, so Rigdon's conclusion that histamine phosphate was the chemotactic agent is to be questioned.

EXPERIMENTS

Although a review of the literature indicates that histamine has no unique chemotactic properties, it was decided to extend such experimentation to rabbit eyes. The problems of allergic uveitis focused attention on the reaction in the uvea. The uvea is prone to develop a cellular infiltration. For example, an injection of horse serum into the vitreous of normal rabbits results in cellular infiltration that is confined almost entirely to the uvea.[15]

PRELIMINARY TESTS

PART 1

The effect of two readily available strengths of histamine acid phosphate were compared (ampule form, 0.275 percent and vial form, 0.055 percent). Eight rabbits, divided into two groups, received injection of 0.1 cc. of the ampule or vial strength into the vitreous. After killing the animals by air embolism, the eyes were enucleated at 6 hours and at 1 week.

Clinical observations. One and one-half hours after the injection of either strength of histamine, a moderately severe chemosis was present. The pupils were contracted to a diameter as small as 2 mm. (The average apparent diameter of the pupils of 64 normal rabbit eyes under the same conditions of illumination was 7 mm.) After 4 hours the chemosis and miosis were unchanged, but at 6 hours there was beginning abatement.

Ophthalmoscopy at this time revealed haziness of the vitreous and slight dilatation of the retinal vessels. After 24 hours, the pupils were normal in size and the chemosis almost gone. The fundi showed no definite changes. Four days later the eyes were normal and remained so until the enucleation at 1 week.

Microscopic study. No significant histopathologic features were noted in any of the eyes.

PART 2

In this second experiment the vial strength (0.055 percent) was used and repeated injections were employed to determine whether it was possible to attract leukocytes by means of repeated injections of histamine. Six rabbits each received 0.1 cc. in the vitreous of the right eyes 7 mm. behind the limbus in the 12-o'clock meridian. The left eyes served as untreated controls. Such injections were given regularly on Monday, Tuesday, and Wednesday. Two rabbits were killed on Thursday for each of 3 weeks.

Clinical observations. In general the reactions in the anterior ocular segment of the right eyes were similar to those recorded in Part 1. Some signs of iritis, such as blurring of the iris pattern, were observed early. It was soon impossible to see the fundi because of clouding of the media.

Repeated injections caused changes in the lens producing posterior opacities while the vitreous was made very hazy. An increase of mucoid conjunctival discharge was common. In general the reaction to each injection of histamine became less as the experiment progressed, although definite evidence of endophthalmitis developed in some of the eyes.

Microscopic study. No significant differences were found between the 1, 2, and 3-week periods. A moderate infiltration of polymorphonuclear leukocytes was seen external to the sclera and in the region of the injection site, but the main finding was of endophthalmitis. A moderately heavy collection of polymorphonuclears was seen in the vitreous, lying especially behind the lens, over the ciliary body, and internal to the retina. A minimal accumulation of mononuclear cells in the choroid of some of the eyes was considered to be of no significance because: (1) such an infiltration is seen occasionally in the eyes of apparently normal rabbits, (2) such an infiltration in the presence of a severe endophthalmitis is to be expected.

MAIN EXPERIMENT

To subject the question of whether the uvea will react to histamine by a cellular infiltration to a more refined test, an attempt was made to place the fluid in the suprachoroidal space in direct contact with the choriod, and to study the histologic response at frequent intervals from 15 minutes to 3 days.

This time a control solution was made by adding 0.066 M. phosphate buffer of pH 7 to distilled water to make a solution that had a pH of 6.81 after autoclaving. The 0.275-

percent histamine acid phosphate was diluted with the phosphate buffer and distilled water to a strength of 0.055 percent and its pH brought up to the same level by the addition of a few drops of 10 percent NaOH. These two solutions were cultured before use and found to be sterile.

Under pentothal anesthesia an anteroposterior incision was made through the sclera over the pars plana. A beveled 23-gauge needle with blunted tip was introduced with the bevel hugging the inside of the sclera and was passed posteriorly for 5 to 8 mm. Where the injection of the 0.1 cc. was made.

Eighteen rabbits were used. Histamine was injected into the right eyes and the phosphate control into the left eyes. Two at a time the rabbits were killed by air embolism and their eyes enucleated at 15 and 30 minutes, at 1, 2, 4, and 6 hours, and at 1, 2, and 3 days.

Clinical observations. Clinically chemosis and miosis were observed in both eyes, but they were usually more pronounced in the right eyes injected with histamine.

Microscopic study. There is no significant histopathologic differences between the right eyes injected with histamine and the left eyes injected with the control solution except for more edema in the ciliary region of the histamine injected eyes. The following chronological survey of the more important histologic features, therefore, will consider both groups together and point out only the changes with time. The irides of most of the eyes of all stages present a bulge suggestive of iris bombé, although no evidence of posterior synechias is noted.

15 and 30 minutes

Suprachoroidal hemorrhage and detachment of the choroid are found at this period and in most of the eyes of the following stages.

1 hour

There is added a definite edema of the ciliary body, especially the processes. Chemosis of the conjunctiva is prominent and is accompanied by an infiltration of polymorphonuclear leukocytes.

4 and 6 hours

There are large cysts on the ciliary processes filled with edema fluid. Polymorphonuclear leukocytes are found outside the sclera and in its superficial lamellas. There are also a few polymorphonuclears in the suprachoroidal space, but those in the chemotic conjunctiva are beginning to be replaced by large mononuclear cells and fibroblasts.

1 day

At 1 day there is added definite round-cell infiltration of the pars plana and most of the choroid has small flat areas of mild lymphocytic infiltration.

2 and 3 days

The reaction appears to be waning. There are a few round cells in the ciliary body and choroid and a severe congestion of the ciliary processes.

No difference in cellular infiltration between the histamine and control eyes is noted at any stage.

COMMENT

A number of investigators have studied the effects of histamine upon the pupil and upon the intraocular pressure,[16-19] but as far as I know Alajma and Friedenwald are the only ones who have reported microscopic findings.

After the injection of histamine into the vitreous, Alajma[20] found an intense plastic uveitis which, on sectioning, showed an area of infiltration containing large numbers of eosinophils.

Friedwenwald[21] injected histamine into the eyes of dogs, cats, rabbits, and monkeys in an experimental study of acute congestive glaucoma. He found a marked edema of the ciliary body with extravasations of serum and fibrin about the capillaries just beneath

the epithelium. The ciliary processes were much swollen, especially at their tips, which were sometimes distended so as to form great bags filled with serum. The irides showed varying degrees of edema, usually less intense than that found in the ciliary body. Coagulated serum was found in the anterior, posterior, and vitreous chambers. In some instances there was slight bullous keratitis, and often marked conjunctival edema. Friedenwald did not mention the presence of wandering cells and the sections photographed do not indicate their presence.

Although our experimental methods differed, many of the features described by Friedenwald were observed.

The use of rabbits as experimental animals might be criticized. Darsie and others[22] found that, after the intradermal injection of various strengths of histamine diphosphate, no wheals developed in guinea pigs, rabbits, and cats, but they did develop in dogs, goats, and man. In the first group, not developing wheals, histamine results in vasoconstriction, while in the second it produces vasodilatation.

It is probable that a vascular reaction is the fundamental response to sensitization. This vascular reaction, however, is one of arteriolar constriction with stoppage of circulation and the migration of leukocytes, while histamine, in man, produces an active hyperemia by arteriolar and capillary dilatation.

From our review of the literature there was no evidence that the various animals, including man, showed any differences in the leukocytic response to injections of histamine. The consensus appears to be that histamine in itself does not attract leukocytes in any of those animals.

Histamine is commonly incriminated as the cause of allergic reactions. Although histamine undoubtedly plays a role in some allergic responses, it must be remembered that many other factors are involved. In fact, to explain the many different manifestations of allergy it can be assumed either that some

toxic agent is liberated, different for the various types of allergic response, each to produce its own special effect, or that the specific antibody permits the antigen to exert its own effect upon the sensitized cell.[23] This conception postulates unknown allergotoxins in addition to histamine.

The question of why wandering cells were attracted, although in small numbers, by both the histamine and the buffer control, seems to be answerable by one or both of two mechanisms. It is possible that the distention by fluid liberated a product of cellular injury, such as leukotaxine, which then attracted leukocytes; or it is likely that bacteria were introduced either at the time of the operation or subsequent to it. The fact that wandering cells were much more common in the main experiment, in which an incision was made with a knife, than in the first experiment, where the injection was made by a small needle, seems to indicate that the larger opening may have predisposed to infection.

SUMMARY

Because of the importance of allergy in the etiology of uveitis it was considered desirable to determine what histologic effect the ocular injection of histamine has upon the attraction of leukocytes. A review of the literature indicated that histamine is not chemotactic for leukocytes and this conclusion was confirmed for rabbit eyes.

Histamine acid phosphate was injected into the suprachoroidal space of the right eyes of 18 rabbits and a phosphate buffer control of the same pH into the suprachoroidal space of their left eyes. Microscopic study after periods ranging from 15 minutes to 3 days indicated no difference in the degree of cellular infiltration found.

It may be concluded that 0.055-percent histamine acid phosphate is not positively chemotactic for leukocytes and does not produce a uveal infiltration in rabbit eyes.

1040 West Michigan Street (7).

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RETINITIS PIGMENTOSA ASSOCIATED WITH GLAUCOMA*

Samuel Gartner, M.D., and Abraham Schlossman, M.D.

New York

The association of retinitis pigmentosa with glaucoma was observed by us in several clinical cases and pathologic specimens. This raised the question whether the two diseases were coincidental or whether they bore a relationship to each other. The literature on the subject was found to be meager, but indicated that others have also felt that glaucoma was in some way related to retinitis pigmentosa. The migration of pigment is an outstanding characteristic of retinitis pigmentosa. Since the presence of pigment in the angle of the anterior chamber has been stressed as a possible etiologic factor in glaucoma, it was hoped that a careful study of these cases would shed some light upon this problem.

Retinitis pigmentosa is an important disease for it causes blindness sooner or later to all who suffer from it. When combined with glaucoma, this blindness occurs sooner. Our knowledge of retinitis pigmentosa is very limited, and our therapeutic results are very close to zero despite many attempts, including the recent suggestions of the Russians for the use of tissue extracts.

Retinitis pigmentosa has many peculiarities. It usually appears as an hereditary and familial disease with several different forms of heredity which will be discussed later in this article. It may be the only disease in otherwise healthy people. It may be associated with other ocular disorders, such as myopia or macular hole.[1]

Retinitis pigmentosa is frequently associated with other systemic disorders, particularly deaf-mutism, and occasionally with defects of the central nervous system, mental retardation, and idiocy. The Laurence-Moon-Biedl syndrome is an atypical retinitis pigmentosa with mental retardation, polydactyly, and pituitary disorders, such as obesity, and hypogenitalism.

LITERATURE

In 1862, Galezowski[2] described the first case of retinitis pigmentosa associated with glaucoma. Schnabel,[3] in 1878, published a case of acute glaucoma in a patient with retinitis pigmentosa and described the pathologic findings in the enucleated eye. The literature on the subject and 38 cases of glaucoma associated with retinitis pigmentosa were studied, and are outlined in Table 1. A large number of the cases were reported by the Russians who seem to have been particularly interested in retinitis pigmentosa. Among the papers which give a good review of the subject are those by Schmidhauser,[16] Mueller,[20] and Kotliarevsky.[27] Leber[29] and Peters[30] have written short reviews. Julia Bell[31] in her monograph on inheritance in retinitis pigmentosa has collected from the literature seven pedigrees showing an association with glaucoma.

Of the cases reported, 15 were apparently chronic simple, 7 inflammatory, 5 acute, and 3 absolute glaucoma. Two more cases were probably chronic simple glaucoma, and in 6 instances it was not possible to determine the type. Some of the cases of retinitis pigmentosa were atypical. Since many of the cases were described before the advent of the Schiøtz tonometer, it is difficult to know whether some of those reported really suffered from glaucoma. Optic atrophy in eyes with deep cupping may resemble glaucomatous excavation.

On the other hand, it is well known that the ophthalmoscopic picture of retinitis pigmentosa may be simulated by other conditions, such as, syphilitic and other forms of chorioretinitis, and trauma. The increased

TABLE 1
CASES REPORTED IN LITERATURE AS SHOWING RETINITIS
PIGMENTOSA WITH GLAUCOMA

No.	Author	Year	Apparent Type of Glaucoma	Apparent Age at Onset	Sex	Hereditary
1.	Galezowski[2]	1862	R. & L., acute	60	M	
2.	Schnabel[3]	1878	L., acute	54	M	
3.	Mandelstamm[4]	1891	R. & L., simple	56	M	
4.	Mandelstamm	1891	?	?	?	
5.	Bellarminoff[5]	1893	R. & L., chronic	40	M	55-year-old sister blind, cousin blind
6.	Heinersdorff[6]	1897	Simple	22	M	Sister ret. pig.
7.	Goldzieher[7]	1897	Simple	30	F	4 sibs nyctalopia. 1 brother ret. pig.
8.	Natanson[8]		Simple	35	M	
9.	Natanson		L., simple	55	F	
10.	Strachow[9]	1901				
11.	Strachow	1901				
12.	Filatov[10]	1902	Simple	40	M	
13.	Komarowitsch[11]	1903	L., acute	46	M	
14.	Masllenikoff[12]	1903	Chronic	17	F	
15.	Weiss[13]	1903	L., simple	48	F	Brother ret. pig.
16.	Wider[14]	1885	R. & L., simple	25	F	
17.	Wider	1885	R. & L., chronic inflammatory	48	F	All sibs except brother ret. pig.
18.	Herrlinger[15]	1904	R., chronic inflammatory, L., absolute	42	M	Consanguinity
19.	Schmidhauser[16]	1904	R. & L., inflammatory	57	M	Brother is Case 17
20.	Schmidhauser	1904	L., inflammatory	63	M	
21.	Carbone[17]	1904	R. & L., chronic inflammatory	54	M	Father probably syphilitic
22.	Isupow[18]	1910	R. & L., chronic inflammatory	38	M	
23.	Weinstein[19]	1911	L., simple	35	M	Brother nyctalopia
24.	Mueller[20]	1916	L., simple	53	M	
25.	Mueller	1916	R. & L., simple	48	F	Grandmother blind at age of 40 yrs.
26.	Henderson[21]	1903	R., absolute	72	F	
27.	Henderson	1903	L., absolute	21	M	
28.	Baumgarten[22]	1916	R., simple	34	M	
29.	Bradbourne[23]	1916	?	51	F	5 out of 6 sisters had ret. pig. Cases 29, 30, and 31 had ret. pig. and glau. Mother blind
30.	Bradbourne	1916	L., acute	50	F	
31.	Bradbourne	1916	L., simple	49	F	
32.	Ayres[24]	1886	Acute		M	Grandmother blind 2 sisters ret. pig.
33.	Ayres	1886			F	1 brother ret. pig., 1 brother ret. pig. and glaucoma
34.	Vegodsky[25]	?	?			
35.	Tobalovsky[26]	?	?			
36.	Kotliarevsky[27]	1931	R. ? L., simple	38		
37.	Kotliarevsky	1931	R., inflammatory	48	M	
38.	Attiah[28]	1941	Simple	28	M	

tension in some cases in the literature may have been secondary to other ocular diseases. Since most of the reports were made before tonometry was in general use, the individual cases in the literature are not discussed, but are only outlined in Table 1. Conclusions will be drawn from the more recent cases and those described in this paper.

CASE REPORTS

Eight cases were collected and three of them were examined histologically.

CASE 1

History. J. C., a man, aged 30 years, was a patient in Dr. Boyes's service at the New York Eye & Ear Infirmary and is reported

through his kind permission. Retinitis pigmentosa was diagnosed at the age of 14 years. He developed glaucoma at 20 years of age, and surgery was performed at another hospital for this condition.

Eye examination. Vision was light perception in both eyes with fair projection. The right pupil was large, the lens opaque, and the iris tremulous indicating a dislocated lens. The left pupil was small and distorted. There was some lens opacity. The fundi were not visualized at this time. The tension in the right eye was 50 mm. Hg (Schiøtz) and in the left, 20 mm. Hg. The dislocated lens was removed from the right eye, but the tension remained elevated. Prostigmin and mecholyl controlled the tension and, since that time, it has been maintained with pilocarpine.

Family history. The patient's parents were first cousins. Two brothers have retinitis pigmentosa but no glaucoma. Three other brothers are normal. The patient posed the question whether he should have any children. We do not have sufficient data to know whether the inheritance is autosomal recessive or sex-linked recessive. If his maternal grandfather had suffered from retinitis pigmentosa, the disease probably would be sex-linked. Since his father and mother were first cousins, it is possible that the condition is an autosomal recessive. At all events, the only safe course was to advise him against having children.

Case 2

History. N. K., a man, aged 41 years, a patient at Montefiore Hospital, had suffered from night blindness since childhood. A diagnosis of retinitis pigmentosa was made in 1941 when he was 33 years old. He developed tuberculosis in 1944. In 1945, while at Montefiore, bilateral glaucoma was diagnosed.

Eye condition. At that time, the intraocular tension was 48 mm. Hg (Schiøtz) in the right eye, and 45 mm. Hg in the left. Vision was : R.E., 15/20; L.E., 15/25. The visual fields were constricted. The retina in

both eyes showed typical bone corpuscle pigment accumulations, narrow blood vessels, and atrophy of the optic nerve.

Since miotics did not control the tension, bilateral iridencleises were performed. Following surgery, the anterior chambers remained very shallow. Both irides were vascularized and patches of iris atrophy were visible. The pupils were drawn up and a small filtering bleb was present in each eye. The tension was 25 mm. Hg in both eyes. Corrected vision was : R.E., 15/100; L.E., 15/70. He uses pilocarpine (2 percent) three times a day.

Case 3

This case is presented through the courtesy of Dr. Charles A. Perera.* The patient was originally one of Dr. Charles H. May's and was subsequently treated by Dr. Perera.

History. F. T., a woman, aged 36 years, gave a history of night blindness and poor vision for many years. Since early childhood, she suffered from a marked strabismus, which was corrected in 1933 with an excellent cosmetic result.

Eye examination in May, 1936, showed normal intraocular pressure and shallow anterior chambers. The fundi revealed marked narrowing of the vessels, pallor and blurring of the discs. The peripheral retina contained small irregular pigment deposits and small pigmented areas were scattered throughout the fundi. The visual fields of each eye were contracted concentrically to 15 degrees from fixation. Vision in the right eye was corrected to 15/30 with +3.OD. sph. ◡ +1.25D. cyl. ax. 105°, and the left eye to 15/25 with +3.0D. sph. ◡ +0.75D. cyl. ax. 85°

The patient returned one month later, in June, and stated that five days previously she had experienced blurring of vision lasting five hours. There was no evidence, how-

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*This case was presented at the meeting of the Section of Ophthalmology, New York Academy of Medicine, May 16, 1943, by Dr. Perera.

ever, of recent ocular disturbance. Four months later, in October, 1936, she returned with an acute iridocyclitis in the left eye which became quiescent after four weeks of atropine and salicylate therapy. Her intraocular pressure was normal at this time.

In November, 1937, the patient suffered an acute attack of glaucoma in the left eye which became stony hard. Tension was reduced to nearly normal by repeated instillations of eserine and pilocarpine. Two days later, the tension in both eyes rose to over 85 mm. Hg. Miotics did not help, and a bilateral Lagrange operation reduced her tension to normal.

The patient was last seen in February, 1948, at which time the intraocular pressure was 18 mm. Hg in the right eye, and 25 mm. Hg in the left. Her visual fields have not contracted further during the last 10 years. Her corrected vision is: R. E., 20/40; L.E., 20/30. The reduction in visual acuity was probably due to some increase in the posterior central lenticular opacities.

CASE 4

This case and Case 5 were briefly included in a previous report[32] and are from the practice of Dr. Adolph Posner.

History. The patient, W. F., a man, aged 53 years, gave a history of night blindness and retinitis pigmentosa was diagnosed in 1936. At that time, his intraocular pressure was normal.

Following a head injury in January, 1940, he was unconscious for 5 or 10 minutes. After that, he began to see halos around lights and experienced foggy vision after reading. He was seen by Dr. Posner in January, 1940. The tension was 42 mm. Hg (Schiøtz) in the right eye, and 49 mm. Hg in the left eye.

Eye examination. Vision of the right eye was 20/20 with a −0.75D. sph. ⊃ +1.5D. cyl. ax. 180°, and 20/20 in the left eye with +0.25D. sph. ⊃ +0.5D. cyl. ax. 90°.

There was shallow cupping of both optic discs, which showed a yellowish tinge. The

blood vessels were approximately normal in caliber and, in the periphery of the fundus, there were pigment deposits of the bone corpuscle type. The fields showed ring scotomas.

The tension responded temporarily to pilocarpine, but two weeks after the institution of medication, an acute attack of glaucoma occurred in the right eye. Iridencleisis was performed on one eye in January, 1940, and on the other in February, 1940, and the tension became normal. In 1946, when the patient was last seen, the tension in the right eye was 15 mm. Hg and in the left eye 20 mm. Hg. The visual fields were further contracted.

CASE 5

History. N. F., a white woman, aged 38 years, was seen in 1940 with a history of retinitis pigmentosa of 20 years' duration. She had married in 1940 and two months after marriage she had a sense of heaviness over the right eye and blurring of both eyes. Within a week, she lost all vision in the right eye.

Eye examination. When she was seen in August, 1940, vision of the right eye was nil and with the left eye she counted fingers at 12 inches. The right eye showed conjunctival congestion, edema of the cornea, and a tension of 90 mm. Hg (Schiøtz). The left eye had a tension of 50 mm. Hg and was somewhat congested. There was bilateral horizontal nystagmus. The discs were yellow and the vessels narrow. There were some irregular pigmented areas in the periphery of the fundus.

Family history. Two of her sisters suffer from retinitis pigmentosa and one of them, three years older than the patient, also has glaucoma in the left eye. One brother and sister are normal. Her parents are normal.

We are indebted to Brig. Gen. R. O. Dart and Mrs. H. C. Wilder of the Army Medical Museum for Cases 6, 7, and 8, and these cases are presented with the kind permission of the donors of these specimens.

CASE 6

History. The patient (Accession 81319—contributed by Dr. E. C. Ellett) was a 26-year-old white woman. Both she and her sister had retinitis pigmentosa. Hyperopia was found at the age of six years. Since then, her vision had become progressively worse until now, at her 26th year, she had developed severe pain in her left eye following dilatation of her pupils. The tension in the eye was 50 mm. Hg (Schiøtz), and an iridectomy was performed. Three years later, the anterior chamber filled with blood following a bout of sneezing. Elevated tension returned with severe pain, and it was necessary to enucleate the eye.

Pathologic Examination

Gross. The specimen consists of a small eye measuring 20 by 20 by 19 mm. The cornea is cloudy. There is irregular pigmentation of the fundus. The lens is opaque, the optic disc is cupped, and the anterior chamber is filled with blood-stained exudate.

Microscopic (figs. 1 and 2). The scar of iridectomy does not appear in the sections examined. There is little edema of the basal layer of the corneal epithelium. The anterior and posterior chambers contain blood. There are peripheral anterior synechias. The iris is atrophic and there are hyalinization and vascularization of the pupillary zone. The ciliary body is also atrophic.

There is considerable irregularity of the pigment epithelium which is depigmented in some areas, while in other regions it is deeply pigmented. Large clumps of pigment appear in the retina. Retinal vessels show obliterating changes and perivascular deposits of pigment. The rods and cones have almost completely disappeared. There is a loss of the normal architecture with replacement by glial tissue. The hole in the nervehead apparently was the site of calcified drusen which were lost during the technical procedures. One section shows small basophilic-staining drusen at the edge of the hole. The lamina cribrosa is depressed.

Diagnosis. Retinitis pigmentosa, glaucoma, drusen in nervehead, and recent hemorrhage in anterior chamber.

CASE 7

History. G. I. (Accession 72718—contributed by Dr. William M. Scales), a woman, aged 57 years, was seen in 1934 and a diagnosis of bilateral retinitis pigmentosa was made. The patient was not seen again until two weeks prior to enucleation when she complained of suffering for the past 6 months with pain which was apparently due to glaucoma in her left eye.

Eye examination. There was moderate pericorneal injection and the cornea showed degeneration with the formation of bullae. Transillumination was unsatisfactory. There was a brown cataract through which no reflex was obtained. Tension in the left eye was 70 mm. Hg (Schiøtz) while that in the right eye was 24 mm. Hg. The anterior segment of the right eye was normal except for a generalized opacity of the lens. Since the left eye was painful and did not have any light perception, it was enucleated.

In June, 1946, after a right cataract extraction, the vision corrected to 20/40 and there was ophthalmoscopic evidence of retinitis pigmentosa. There was no family history of night blindness or poor vision.

Pathologic Examination

Gross. Firm eye measuring 24 by 23 by 22 mm. The clouded cornea has a peripheral zone of opacity. The anterior chamber is shallow and the lens cataractous. Posterior to the equator, the fundus is deeply pigmented. The optic disc is cupped.

Microscopic (fig. 3). There are peripheral anterior synechias. The iris and ciliary body are atrophic and the ciliary processes are flattened and hyalinized. The entire uveal tract is rather deeply pigmented. There are multiple chorioretinal adhesions where Bruch's membrane has disappeared. The retina is atrophied and gliosed, with loss of rods and cones.

Fig. 1 (Gartner and Schlossman). *Case 6.* This shows peripheral anterior synechias and the absence of pigment in the angle.

Fig. 2 (Gartner and Schlossman). *Case 6.* This figure also shows peripheral anterior synechias and the absence of pigment in the angle.

Fig. 3 (Gartner and Schlossman). *Case 7.* There are peripheral anterior synechias but no pigment in the angle.

There is hyalinization, occlusion, and perivascular pigmentation of retinal vessels. Masses of pigment are present in the retina, and there are numerous areas in which the pigment epithelium is flattened and depigmented, or has disappeared entirely.

It is only in the macular region that any of the normal architecture is retained and here there is marked loss of ganglion cells. The optic disc is deeply excavated and the lamina cribrosa is correspondingly depressed. There

dilated. There was absolute glaucoma. Tension in the right eye was 95 mm. Hg (Schiøtz), and in the left eye it was 17.5 mm. Hg. The left eye showed marked retinitis pigmentosa. Her father is alive and also suffers from retinitis pigmentosa.

Pathologic Examination

Gross. Firm eye measuring 24 by 23 by 23 mm. There is some peeling of the corneal epithelium. The pupil is dilated and eccentric.
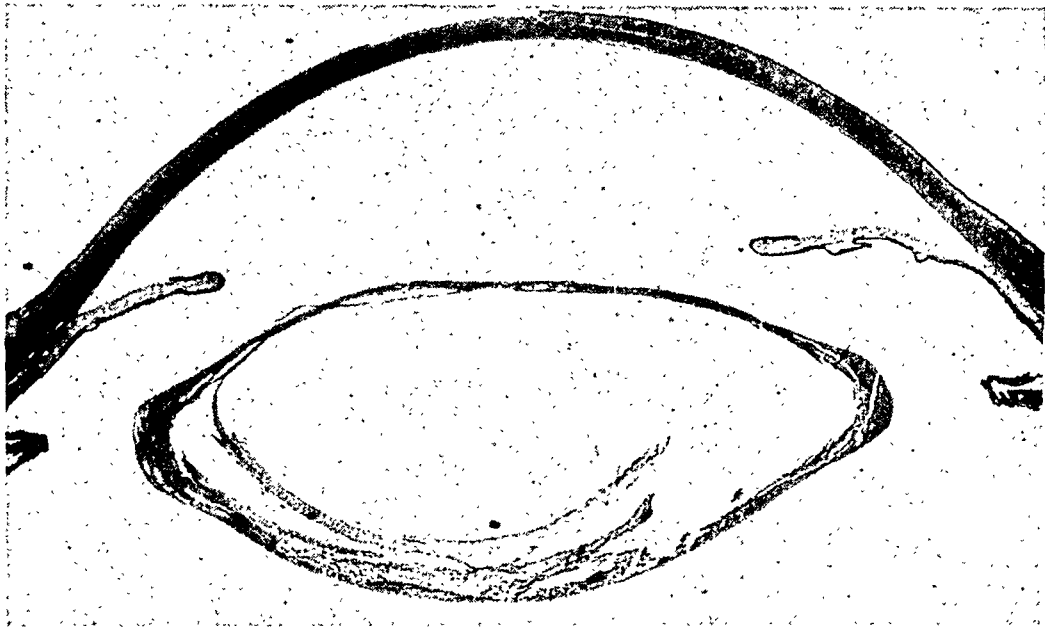
Fig. 4 (Gartner and Schlossman). *Case 8.* This demonstrates the presence of anterior synechias, ectropion uveae, and iris cysts.

is an atrophy of the optic nerve and lymphocytic infiltration around the central vein. Embedded in paraffin and cut separately, the lens shows cataractous changes.

Diagnosis. Retinitis pigmentosa, glaucoma, cataract, and optic atrophy.

CASE 8

M. B. (Accession 78871—contributed by Dr. C. A. Veasey, Sr.), a woman, aged 41 years, was known to have retinitis pigmentosa since her early twenties. In December, 1941, she was blind in the right eye and the left eye had a field which contracted to within 10 degrees of fixation. The right eye had previously had iritis with a large synechia at the 4-o'clock position. The pupil was irregularly

There are numerous minute pigmented spots in the retina. The lens is opaque and the vitreous cloudy.

Microscopic. There are peripheral anterior synechias, vascularization of the anterior surface of the iris, and ectropion uveae (figs. 4, 5, and 6). The pigment epithelium is separated and serous exudate fills the resultant cystlike spaces. There are degenerative changes in the cortical fibers of the lens. The ciliary body is atrophic. The iris and ciliary body are sparsely infiltered by chronic inflammatory cells. Lymphocytes more densely infiltrate the choroid. Occasional drusen are seen on Bruch's membrane.

The retinal pigment epithelium is markedly flattened and in many areas it is depigmented.
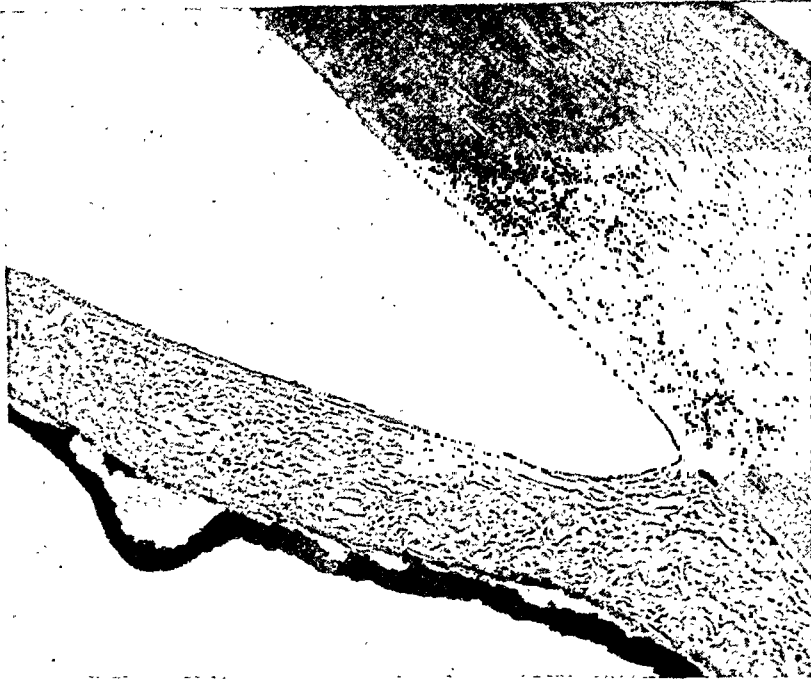
Fig. 5 (Gartner and Schlossman). *Case 8.* High-power view of the section in Figure 4, showing the angle with peripheral anterior synechias and a small amount of pigment in the angle. The pigment epithelium of the iris shows cyst formation.

architecture, microcystic degeneration, and gliosis. Particularly in the peripheral portion of the retina, there are obliterative changes in the blood vessels with perivascular pigmentation.

The optic disc and lamina cribrosa are depressed. There is a little organizing inflammatory and hemorrhagic exudate in the vitreous chamber at the ora serrata.

Diagnosis. Retinitis pigmentosa, chronic uveitis, glaucoma, and cataract.

Between the choroid and the retina, foreign-body giant cells surround cholesterin slits which remain as evidence of old hemorrhage. The retina is partially detached by serous exudate and pigment-laden phagocytes beneath it.

Retinal rods and cones and their nuclei in the outer nuclear layer have disappeared and are replaced by gliosis. The inner retinal layers show considerable loss of normal

DISCUSSION

INCIDENCE AND TYPE

It is difficult to obtain data on the incidence of glaucoma in patients with retinitis pigmentosa. Many cases of symptom-free
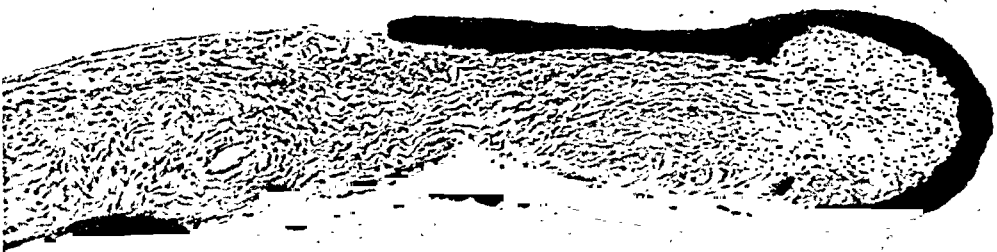
Fig. 6 (Gartner and Schlossman). *Case. 8.* High-power view of the section in Figure 4, showing ectropion uveae. There is a delicate, newly formed membrane on the anterior surface of the iris.

chronic glaucoma are probably missed, particularly when the eye is blind. Seven out of the 8 patients reported in this paper suffered from congestive glaucoma and the eighth probably had congestive glaucoma.

Weiss[13] reported 1 case of glaucoma among 55 patients with retinitis pigmentosa. Schmidhauser[16] reported 5 cases of glaucoma among 180 patients with retinitis pigmentosa at the Tuebingen clinic, a percentage of 2.78 as compared with 0.73 percent for all glaucoma in the clinic. In the private practices of Dr. Mark J. Schoenberg and Dr. Adolph Posner, glaucoma was diagnosed in 3 percent of all cases. Two patients out of 20 with retinitis pigmentosa, or 10 percent, suffered with glaucoma. However, with such small numbers, it is better to avoid conclusions. Suffice it to say that it is the opinion of most authors, including Leber[29] and Verhoeff,[33] that the occurrence of the two diseases together is more frequent than one would expect if it were based on coincidence alone.

It is generally believed that the glaucoma is secondary to the retinitis pigmentosa. Still, glaucoma occurs in relatively few cases. The ocular hypertension occurs in cases which clinically appear no different from other cases of retinitis pigmentosa. The glaucoma is similar to the usual case of primary glaucoma. In Case 1, the increased tension may have been due to the dislocated lens but, 10 years previously, the patient had suffered from glaucoma which required surgery. It is interesting to note that, in Cases 3 and 8, there was an attack of iridocyclitis before the glaucoma was evident.

The action on the eye of toxic substances which accumulate from the degeneration of the retina and the pigment epithelium may be a factor in the development of the glaucoma. A toxic action on the meshwork of the angle may impair its function.

We really do not know how much of the drainage of the intraocular fluids takes place through the retinal and choroidal vessels. Sclerosis of these vessels is commonly found in glaucoma of all types. It is difficult to determine whether this is a cause or effect; or whether it compounds the damage.

PATHOLOGY

In the literature, we have been able to find only three reports of pathologic studies of eyes with retinitis pigmentosa and glaucoma. These are by Schnabel, Komarowitsch, and Henderson.[3, 11, 21] Komarowitsch reported that the posterior lens surface was covered by a glass membrane thicker than the lens capsule. It was grown to the iris as in "glaucoma and iridochoroiditis."

The pathologic findings in the three cases presented here are similar to those found in glaucoma and in retinitis pigmentosa. There was atrophy of the iris and ciliary body. Peripheral anterior synechias were always present. The lamina cribrosa had receded and and the optic discs were excavated.

In addition, there were areas of depigmentation and degeneration of pigment epithelium and in many areas of the retina, especially around the vessels, there were large pigment deposits (figs. 7 and 8).

There was a loss of the normal retinal architecture; the rods and cones had largely disappeared and were replaced by glial tissue. The other retinal layers were diminished in their cellular content, irregular in their arrangement, with glial proliferation throughout the retina. The macular retina was best preserved, and formed a striking contrast to the remainder. Pigment deposits were found in the retina in characteristic bone corpuscle shapes and surrounding the blood vessels.

Von Hippel[34] described two enucleated eyes with glaucoma and retinal findings similar to retinitis pigmentosa. However, many pathologic conditions of the retina and choroid simulate retinitis pigmentosa. Chorioretinitis, particularly the luetic type, and trauma, particularly with an intraocular foreign body, are among the more common offenders. Careful perusal of the histories in Von Hippel's cases makes one rather dubious
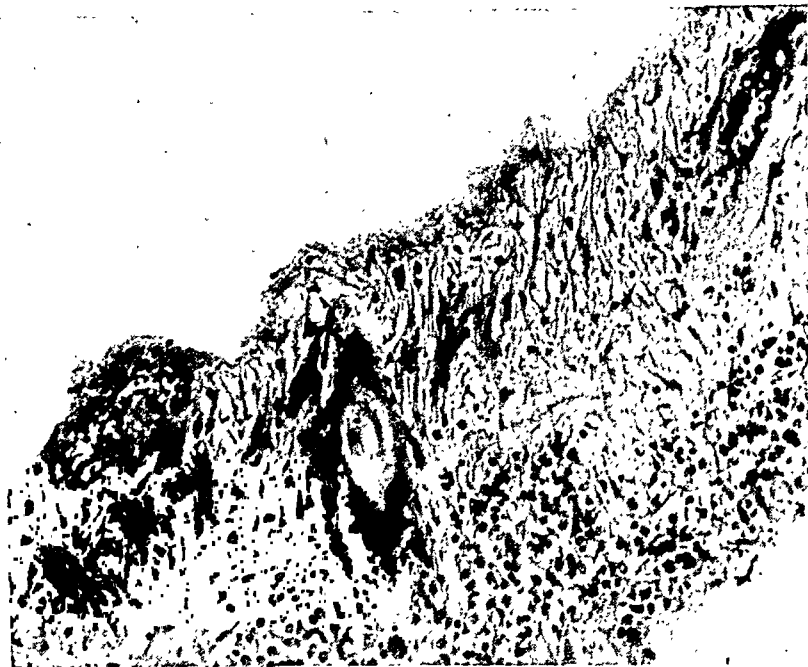
Fig. 7 (Gartner and Schlossman). Oblique section of the retina in a case of retinitis pigmentosa, showing the pigment deposits mainly above the vessels and a few irregular clumps of pigment.

whether they are true cases of retinitis pigmentosa.

He proposed the hypothesis that pigment accumulation in the angle was the cause of the glaucoma. As proof, he showed a picture of the chamber angle in one case with a considerable amount of pigment. Consequently, the belief has taken hold that the ocular hypertension in retinitis pigmentosa is caused by an accumulation of pigment in the trabeculum, mechanically blocking filtration.

The angles of the anterior chamber in the cases presented in this study were carefully examined (figs. 1, 2, 3, and 5). While pigment was present, the amount was not excessive nor even considerable. In one case, there was hardly any pigment at all in the trabecular spaces.

A survey was made of the anterior-chamber angles in a large number of slides from a variety of other cases. Pigment in the angle was found to increase with age and was present in larger amounts at the lower part of the angle. The normal Negro eye has considerable pigment in the trabeculum. Small amounts of pigment are common in glaucoma.

Malignant melanoma of the choroid with secondary glaucoma shows little or no pigment in the angle in most cases. We found only one case of glaucoma secondary to melanoma of the iris with a very heavy deposit of pigment in the trabecular spaces. The angle of the anterior chamber is open and there are no posterior synechias (fig 9).

Only in this particular case does it seem possible that pigment in the trabeculum may have been a factor in producing glaucoma. Even in this instance, we cannot be certain

Fig. 8 (Gartner and Schlossman). Flat section of the retina in a case of retinitis pigmentosa, showing the pigment deposits mainly above the blood vessels with some irregular clumps of pigment.

Fig. 9 (Gartner and Schlossman). Case of melanoma of the iris with glaucoma, showing an extensive deposit of pigment in the trabeculum without peripheral anterior synechias.
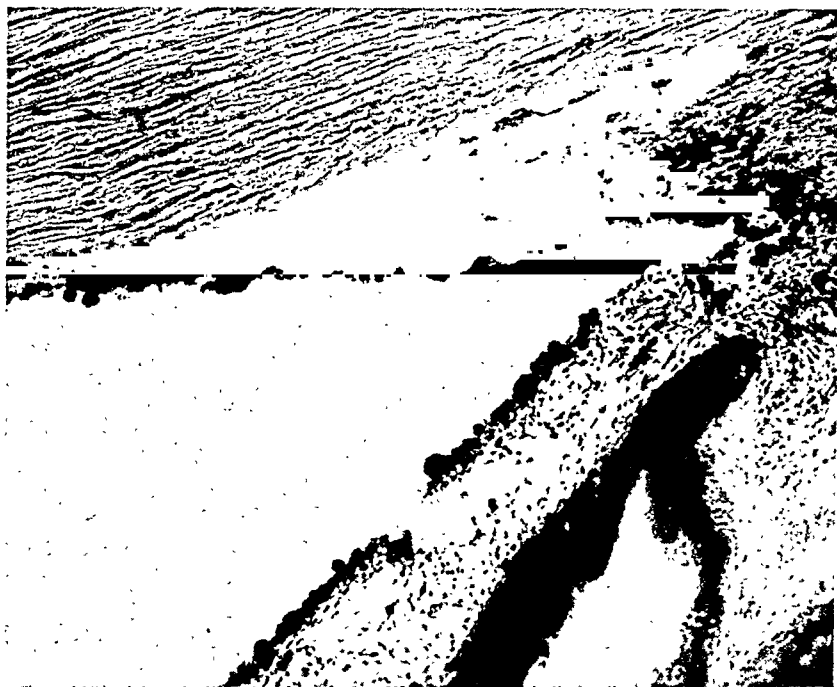
that some other mechanism, which produces glaucoma in the usual case of melanoma, was not operative in this one.

Gonioscopic studies in several of our cases of retinitis pigmentosa did not show any abnormal amount of pigment in the trabecular spaces. We believe that in the cases of retinitis pigmentosa and glaucoma, it is not a simple mechanical block of the angle by pigment which produces the glaucoma. It is possible that the dispersed pigment and the products from retinal degeneration are toxic to the trabeculum, alter its permeability, and thus produce glaucoma.

One finding is common to both retinitis pigmentosa and glaucoma; namely, sclerosis of the retinal vessels. While this condition may not exist in early cases of glaucoma, it is usually prominent by the time the eyes become pathologic specimens. Its influence on the course and development of both diseases is not clear.

The narrowing of the retinal vessels in retinitis pigmentosa was noted long ago and it was assumed by some that the retina became degenerated due to a spasm of the vessels causing a poor blood supply. Attempts have been made to widen these vessels by sympathectomy. That this type of approach was doomed to failure can be readily understood when these eyes are examined histologically. The vessels are narrow due to extensive sclerosis with endothelial proliferation and dense connective-tissue formation which usually has undergone hyalin degeneration. In these vessel walls, no muscle can be identified. Such a wall cannot conceivably be affected by sympathectomy. Only if there

were a muscular spasm narrowing the vessels could sympathectomy possibly widen them.

The impaired circulation in retinitis pigmentosa is apparently a result of the disease affecting the vessels. The perivascular accumulation of pigment may be a factor in causing the sclerosis. Early stages of retinitis pigmentosa are frequently seen in young people who have a rich retinal circulation. Among the aged, we see large numbers who develop narrow retinal vessels due to extensive arteriosclerosis without ever developing the picture of retinitis pigmentosa. Therefore, it does not appear likely that the arteriosclerotic process causes the retinitis pigmentosa. The reverse seems more probable.

A study of a disease in rats which resembles retinitis pigmentosa was reported by Bourne, Campbell, and Tansley.[35] They found that it was inherited as a recessive Mendelian character. Retinal degeneration began in the rods, then proceeded to the outer nuclear layer. Later, the pigment epithelium became degenerated apparently as a secondary effect. The subsequent wandering of the pigment into the retina gave the characteristic picture. These authors agree with Treacher Collins[36] that there is an abiotrophy of the retinal epithelium, and also with Ver-

hoeff[33] that it is not the choroidal changes which produce this disease.

HEREDITY

The pedigrees which have been collected from the literature by Bell[31] demonstrate that retinitis pigmentosa may be inherited in a number of different ways. Retinitis pigmentosa may be inherited as a dominant, partially dominant, recessive, or sex-linked recessive character. It is also possible that a gene for retinitis pigmentosa may be present in the y-chromosome and even cross over to the x-chromosome.[37]

In addition, it is possible that there are several recessive forms of the disease, each with separate genes. Thus, even from an heredity point of view, retinitis pigmentosa seems to represent several diseases. Primary glaucoma is hereditary in approximately 13 percent of the cases. Posner and Schlossman[38] recently reported a series of pedigrees of glaucoma families showing that, although the disease is dominant, there is a certain amount of lack of penetrance; also the possibility of recessive inheritance was not excluded.

Similar to its combination with deafness and myopia, the cases of retinitis pigmentosa and glaucoma may be inherited together as coincidental or associated defects. It is possible that the genes for these separate diseases are linked on the same chromosome. Glaucoma and retinitis pigmentosa may be a single hereditary syndrome similar to the Laurence-Moon-Biedl syndrome.

Of the seven reported pedigrees of retinitis pigmentosa and glaucoma, only two show glaucoma in more than one sibling. Blessig,[39] on the other hand, reported an interesting family tree which suggests that the occurrence of the combinations of both diseases is more than mere coincidence. Among 9 children, 2 sisters suffered from glaucoma and did not have retinitis pigmentosa, while 2 brothers and 1 sister suffered from retinitis pigmentosa without glaucoma. One of the siblings with glaucoma and all of those with

retinitis pigmentosa suffered from deafness. Bradbourne's[23] pedigree shows 5 sisters out of 9 siblings with retinitis pigmentosa. Three of them also had glaucoma.

Among the cases presented in this paper, Case 1 has 2 brothers with retinitis pigmentosa; Case 5 has 2 sisters with retinitis pigmentosa and 1 of them also suffered with glaucoma. Case 6 has a sister with retinitis pigmentosa, and the father of Case 8 had retinitis pigmentosa.

Unfortunately, we were not able to obtain enough data on any of our cases to determine the exact nature of the inheritance. The occurrence of only one disease in one member of the family and two diseases in other members is an interesting phenomenon. This is similar to the occurrence of arachnodactyly in some members of a family, dislocated lenses in other members, and a complete Marfan's syndrome in still other siblings.

Case 1 was concerned about having children. From the meager pedigree that is available on this patient, it is difficult to know whether the heredity is sex-linked recessive or autosomal recessive with the development of the disease as the result of the consanguineous marriage of his parents. We need to know whether his maternal grandfather had suffered with retinitis pigmentosa to decide whether the inheritance was sex-linked. Unfortunately, this information was not available. We advised him against having any children because of the possibility that the condition was sex-linked. It is important to know the mechanisms of heredity because patients are well aware of the hereditary nature of disease and the physician has the responsibility of giving eugenic information and advice.

ENDOCRINE

The pituitary gland has been implicated in retinitis pigmentosa, especially in the Laurence-Moon-Biedl syndrome. Some cases have pigmentary changes elsewhere in the body. Zondek and Wolfsohn[40] have stressed symptoms of pituitary involvement in some

cases of glaucoma. It is well known that the autonomic nervous system plays a role in the pathogenesis of glaucoma. Some think there is a relation between the vegetative nervous system and retinitis pigmentosa. These considerations, however, are so speculative that they are mentioned without discussion.

Undoubtedly, many cases of glaucoma remain undiagnosed in patients who are blind from retinitis pigmentosa. All cases of retinitis pigmentosa should be studied for early signs of glaucoma.

The appearance of retinitis pigmentosa is probably produced by a number of disease processes. The heredity and the course of the disease varies a great deal in different families. It is possible that the retinitis pigmentosa associated with glaucoma is different from the other forms of retinitis pigmentosa.

SUMMARY

Eight cases of retinitis pigmentosa associated with glaucoma are presented and the pathologic findings in three of these cases are described. Accumulation of pigment in the trabecular spaces with blockage of the filtration channels was not a factor in the development of glaucoma in these cases.

The possible etiologic connections between the two diseases are discussed. The role of toxic substances from the degeneration of the retina and pigment epithelium and sclerosis of the vessels is considered.

From an hereditary point of view, it is possible that the two diseases are linked together on the same chromosome and form a single hereditary syndrome.

521 Park Avenue (21)
667 Madison Avenue (21).

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UNILATERAL RETINITIS PIGMENTOSA*

REPORT OF A CASE

DAN M. GORDON, M.D.
New York

The occurrence of unilateral retinitis pigmentosa is one of the rarer events in ophthalmology. Beigelman,[1] in his review of the literature, in 1931, was able to collect only 10 cases, besides his own, which he felt fitted into this category.

He makes note of the fact that many writers have voiced doubt as "to the very existence" of this condition, and states, "Two objections are raised against cases reported as unilateral pigmentary retinitis; (1) The ophthalmoscopically and functionally normal eye might be affected in the future, particularly when the diagnosis is made on the basis of a single examination, or (2) the condition is not a true pigmentary retinitis but an acquired chorioretinal atrophy with pigmentation. Syphilis is often blamed."

Beigelman's own case was followed by him for over five years with no change in the "normal" eye and with increase in the severity of the affected eye.

REVIEW OF THE LITERATURE

Four other cases of unilateral retinitis pigmentosa have been reported since Beigelman brought the subject up to date in 1931. The complete list, including those noted by him is as follows:

1. Pedraglia (1865) a man, aged 36 years, with affected right eye.
2. de Wecker (1868) a girl, aged 15 years, with affected left eye.
3. Baumeister (1873), a man, aged 44 years, with affected left eye.
4. Dehrig (1882), a woman, aged 46 years, with affected right eye.
5. Gunsburg (1890) a man, aged 42 years, with affected left eye.
6. Gonin (1902) a man, aged 25 years, with affected left eye.
7. Nettleship (1907) a woman, aged 30 years, with affected right eye.

8. Hine (1924) a man, aged 34 years, with affected right eye.
9. Rossi (1926) a woman, with affected right eye.
10. Shoji (1926) a girl, aged 10 years, with affected left eye.
11. Beigelman (1931) a woman, aged 36 years, with affected left eye.
12. Agatston (1939) a man, aged 53 years, with affected right eye.
13. Agatston (1939) a woman, aged 45 years, with affected left eye.
14. Schupfer[2] (1937) a woman, aged 55 years, with affected right eye.
15. Schupfer[3] (1937) a man, aged 24 years, with affected left eye.
16. Gordon (1948) a man, aged 26 years, with affected right eye.
17. Bentzen[4] (1917) a woman, aged 30 years, with affected right eye.
18. Lowegren[4] (1948) a woman, aged 63 years, with affected left eye.
19. Dreissler[4] (1948) a woman, aged 53 years, with affected left eye.

It is noteworthy that Beigelman's case was the first of such a condition to be reported from this country and that but three others, including mine, have since been reported from the United States.

REPORT OF CASE

History. R. R., a 26-year-old white man, was first seen on June 11, 1946, when he stated that his eyes began tiring and tearing in 1944. He did not note any difficulty in darkness. He was in the Navy at that time and was examined by their medical officers on several occasions; finally, he was discharged in November, 1944, with a diagnosis of retinitis pigmentosa. He was seen at another eye clinic prior to his visit to the New York Hospital and was told that he had retinitis pigmentosa, which was more pronounced in his right eye than in his left.

Navy records. The patient has furnished photostatic copies of his Navy records, the pertinent data of which is, "Disability is not the result of his own misconduct and was incurred in line of duty. Vision 20/20 each eye on induction in the navy, October 23, 1940.

"This patient was admitted to the sick list September 4, 1944, from the staff of the hospital, complaining of difficulty in reading.
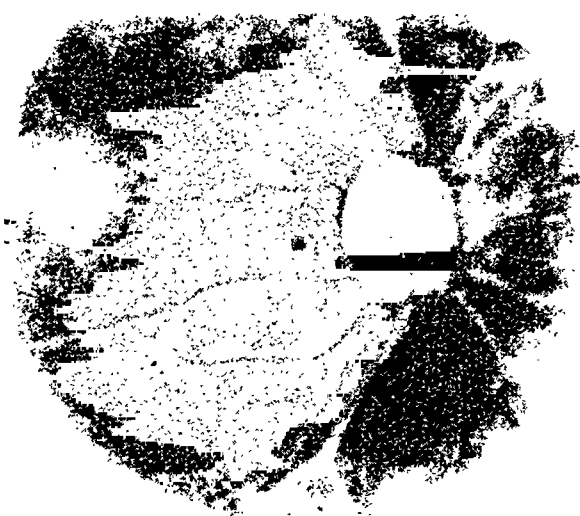
Fig. 1 (Gordon). The unaffected left eye.

Physical examination was essentially negative except for the eyes. Vision was: O.D., 10/20; O.S., 20/15. Pupils round, react to light and accommodation. Ophthalmoscopic examination of the right eye shows a small posterior polar opacity of the lens. The vitreous is clear. Examination of the fundus shows some attenuation of the arterioles. The disc is slightly pallid. In the entire periphery of the fundus there is a degeneration, proliferation and migration of pigment which over-lies the retinal vessels.

"Ophthalmoscopic examination of the left eye is essentially negative. Field studies of the right eye show a concentric contraction

Fig. 2 (Gordon). The affected right eye. Note the blurring of the disc and the marked attenuation of the vessels. The arteries are barely visible.
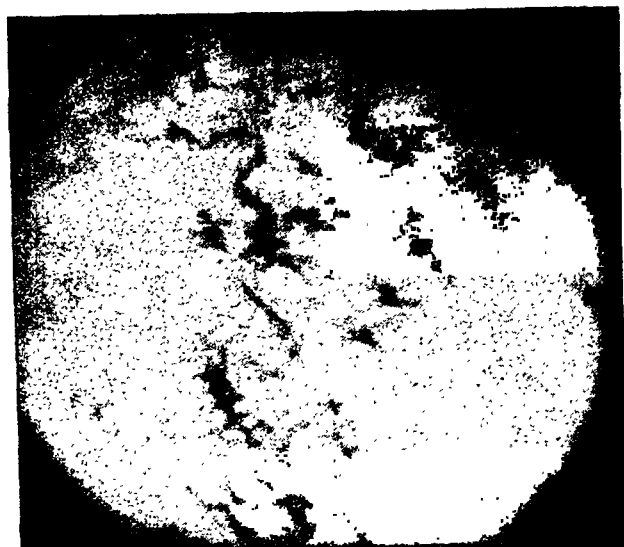
Fig. 3 (Gordon). Superior periphery of the right eye, showing the typical pigmentation.

mentation with one small particle of pigment on the disc, nasally.

L.E., media are clear, the disc is normal in color and outline, the vessels are normal, no tapetoretinal reflexes. There is one small patch of pigment superotemporally, which is not spidery in shape.

Slitlamp examination reveals an early central posterior subcapsular lens opacity on the right. No lens opacities on the left.

Field studies. R.E., constricted to from 5 to 10 degrees; L.E., full and normal. Careful search with small white and with colored targets, failed to reveal the scotomas described by the Navy.

DISCUSSION

The occurrence of the unilateral retinitis

to eight degrees. Field studies of the left eye show two small scotomas about 10 degrees in diameter in the extreme lower temporal quadrant and moderate concentric contraction. Routine laboratory examinations were negative and the spinal fluid Kolmer test was negative.

"The diagnosis of retinitis has been established."

Family history. This patient has gone into his family history very thoroughly and can find no evidence of the existence of any night-blinding disease in his ancestry. His parents were unrelated prior to marriage. He has two brothers and two sisters who have no visual complaints.

On physical examination here on June 11, 1946, his vision was: R.E. 20/70; L.E., 20/15 with J2 and J1, respectively. R.E., with a −0.5D. sph. ⊃ −0.25D. cyl. ax. 45°, he reads 20/30 on the Snellen chart. The external examination reveals no pathologic condition of note.

Fundus examination. R.E., there are some linear vitreous floaters. The disc is pale and somewhat blurred. The arteries are very attenuated. There is the typical golden metallic glinting reflex of the tapetoretinal diseases seen in the mascular area. There is dense midperipheral corpuscular shaped pig-

Fig. 4 (Gordon). A series of visual field charts, showing the progressive loss of visual field in the right eye, with essentially no change in the field of the left eye. (A) August 5, 1946, for 1/330 white. (B) August 14, 1947, for 1/330 white. (C) July 6, 1948, for 1/330 white.

pigmentosa (or a condition in every way similar to it) is chiefly of interest for two reasons. (1) Until recently the primary pigmentary degenerations of the retina have been considered as fairly well worked out and understood diseases, and (2) its occurrence runs counter to every etiologic theory that has been advanced thus far.

Atypical cases of primary pigmentary degeneration do occur and, with the exception of the condition now being discussed, are always bilateral. Hence, their existence has not conflicted with the various theories advanced to account for their etiology. All of these theories take into account a systemic etiology, whether it be diencephalic or abiotrophic. That either of these mechanisms can permanently affect only one eye is not conceivable. There would remain but one other explanation; trauma or disease of the afflicted one eye. Yet, neither of these conditions have been recorded as important factors in the histories of the cases reported. It is obvious that we have no satisfactory explanation for unilateral retinitis pigmentosa, and probably none for the bilateral form, either.

Agatston[2] states that "the suggestion of traumatic origin of the disease promoted by Wagenmann's experiments is not consistent with the statistics which show that retinitis pigmentosa following trauma is practically unknown."

Beigelman, in 1931, wrote in a similar vein and quoted A. L. Whitehead and M. H. Horning as "observing not a single case of bone corpuscle arrangement of pigment in the vast material of direct and indirect ocular injuries during the World War." He also stated that the literature does not contain a single convincing case of retinitis pigmentosa which was caused by or precipitated by trauma.

Beigelman went on to point out that Wagenmann, himself, described the changes produced, in his classical experiment of section of the ciliary arteries in rabbits, as resembling a healed chorioretinitis. This is a point which has been apparently overlooked by many who have concluded that Wagenmann produced a retinitis-pigmentosalike picture by his arterial sections.

The author has no further suggestion at present to add to the number of theories now confusing the literature as to the etiology of retinitis pigmentosa.

SUMMARY

A case of retinitis pigmentosa occurring in but one eye, with the other eye apparently normal, is reported, and the literature brought up to date.

525 East 68th Street (21).

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OCULAR MANIFESTATIONS OF PRIMARY NASOPHARYNGEAL TUMORS*

DAVID C. BOYCE, M.D., AND NORMAN BOLKER, M.D.

Iowa City, Iowa

Ocular signs and symptoms are common in patients with primary nasopharyngeal tumors, but, as far as is known, there are only two reports on this subject in the American ophthalmic literature.[1, 2] Therefore, it seems worth while to report the results of a survey of the 44 cases of this type which have been seen in the University Hospitals during the past 15 years.

TYPES OF TUMORS

Tumors of the nasopharynx may be either benign or malignant. Among the benign types are fibroma, hemangioma, neurofibroma, lipoma, xanthoma, dermoid, teratoma, chondroma, and mixed tumors.

By far the most common of these is the fibroma; this tumor arises from the periosteum covering the bony walls of the nasopharnyx and usually occurs in young adults, developing in the years of puberty and spontaneously regressing during the twenties. It has a smooth, vascular structure which histologically resembles fibrosarcoma, but it never infiltrates or metastasizes. Its most common symptoms are nasal bleeding and obstruction.

Malignant neoplasms of the nasopharynx are relatively more common than non-malignant tumors. They are more often seen in males and occur more frequently in younger individuals than other malignant growths of the upper respiratory and alimentary tracts.[3] Godtfredsen[4] has pointed out that the most common site of origin of a primary malignant tumor of the nasopharynx is in the lateral wall, and it was his impression that about half of the malignant tumors arose from this portion. The second most frequent site was the roof and the least was the posterior wall of the nasopharynx.

Hayes Martin, however, claimed the tumors arise more often from the posterior wall in the region of the nasopharyngeal tonsil with the lateral wall less often involved.[3]

The most common form of malignant growth noted in the nasopharynx is the epidermoid carcinoma. Lympho-epithelioma, neuroblastoma, sarcoma, fibrocytoma, and adenocarcinoma are encountered in fewer numbers.

AGE AND SEX DISTRIBUTION

In this series of cases, the age and tumor type incidences agree in general with those reported by others (tables 1 and 2). The

TABLE 1

AGE DISTRIBUTION OF MALIGNANT NASOPHARYNGEAL TUMORS

Years	Number
0– 9	1
10–19	6
20–29	2
30–39	2
40–49	5
50–59	8
60–69	7
70–79	1

TABLE 2

DISTRIBUTION OF TUMOR TYPES IN 44 PATIENTS WITH NASOPHARYNGEAL TUMORS

Malignant:

Epidermoid carcinoma	18
Undifferentiated epidermoid carcinoma	7
Lympho epithelioma	4
Neuroblastoma	1
Sarcoma	1
Fibrosarcoma	1
Adenocarcinoma	1
Lymphosarcoma	1

Nonmalignant:

Juvenile fibroma of Ewing	7
Sclerosing angioma	2

Unknown: 1

distribution by sexes conforms to that usually reported, there being 25 males and only 9 females in this group.

SYMPTOMS

Characteristically, primary malignant tumors of the nasopharynx do not cause symptoms during the early stages of development. The patient comes for examination usually because of enlarged cervical lymph nodes, occasionally because of manifestations of intracranial involvement, and less often because of symptoms localized to the nasopharynx.[5] It is not uncommon to find that patients have received treatment for a variety of supposed diseases before a proper diagnosis is made. In our series, nasopharyngeal symptoms were more common than those from intracranial involvement, probably because nine cases of benign tumors are included in the series.

The cervical lymph nodes most frequently involved are those situated beneath the mastoid tip under the upper end of the sternocleidomastoid muscle. Auditory symptoms, such as tinnitus and deafness, are present early as the tumor is often located next to the orifice of the Eustachian tube. When the tumor erodes the base of the skull, cranial nerve palsies develop.

The tumor may infiltrate the parapharyngeal space or pass through nearby foramina, particularly those in the base of the skull. Frequently invasion is through the foramen lacerum whereby the tumor gains access to the region of the carotid artery, the cavernous sinus, and the sensory and motor nerves to the globe.

Of the cranial nerves, the abducens and trigeminal are most commonly affected. Once the tumor has reached the middle cranial fossa, it may grow forward through the superior orbital fissure into the orbit, thus giving rise to the various ocular complications such as optic atrophy, choked disc, and proptosis. Systemic metastases are seen in one third of the patients, the skeletal system being most often involved with the liver and lungs next in order.[6]

TABLE 3

SIGNS AND SYMPTOMS PRESENTED ON ADMISSION BY 44 PATIENTS WITH NASOPHARYNGEAL TUMORS

Signs	Number	Percent
Cervical lymphadenopathy...	24	54.4
Nasal obstruction..........	20	45.5
Epistaxis..................	20	45.5
Hearing loss...............	15	34.0
Headache..................	11	25.0
Ocular symptoms..........	10	22.7
Dysphagia.................	8	18.2
Pain over face.............	6	13.5
Weight loss................	5	11.0
Hoarseness................	4	9.0
Fullness in throat..........	4	9.0
Tinnitus...................	3	6.8
Sore nose..................	2	4.5
Speech defect..............	1	2.2
Swelling of face............	1	2.2
Pain in arm and chest......	1	2.2
Post nasal drip............	1	2.2

DIAGNOSIS

In our series, diagnosis was made by direct visualization of the tumor in all cases and proved by biopsy in all but one case. On admission, 54 percent of the 44 patients had palpable cervical nodes. Nasal obstruction, epistaxis, and poor hearing were present somewhat less frequently. Headache and ocular symptoms were noted in approximately 25 percent of the patients in this series. Dysphagia, facial pain, weight loss, hoarseness, and a variety of other symptoms were noted in decreasing numbers (table 3).

OCULAR MANIFESTATIONS

Thirty-two percent of the 44 patients developed ocular manifestations at some time

TABLE 4

SUMMARY OF OCULAR MANIFESTATIONS SHOWED BY THE PATIENTS WITH NASOPHARYNGEAL TUMORS

Ocular involvement	Number
6th nerve.................	10
3rd nerve.................	7
Proptosis (all unilateral).....	4
4th nerve.................	2
2nd nerve.................	1
Choked disc..............	1
Horners syndrome..........	1
External ophthalmoplegia....	1
Corneal anesthesia.........	1
Pressure over eyes.........	1
Photophobia..............	1

Fig. 1 (Boyce and Bolker). W. F., a 50-year-old man, with epidermoid carcinoma of the naso-pharynx. He had slight exophthalmos on the right, 5th-nerve paresis, 12th-nerve paralysis, and 7th-nerve paralysis.

during the course of their disease. Most of those showing ocular signs were found to have malignant tumors. The ocular signs and symptoms were multiple in 54 percent of the patients. Involvement of the abducens was most common, while oculomotor and trochlear nerve palsies were noted in fewer cases. There were four cases of unilateral proptosis (table 4).

CASE REPORTS

The following three cases are typical of those showing ocular manifestations:

Case 1. E. F., a white man, aged 50 years (fig. 1), was first seen in August, 1947, because of deafness and a feeling of pressure in the right ear. Transient diplopia had been noted in October, 1946. Pain over the right side of the face and enlargement of the right cervical lymph nodes had been present for five months.

At examination, he was found to have an epidermoid carcinoma of the right naso-pharynx which produced a small amount of exophthalmos of the right globe, paresis of the ophthalmic branch of the trigeminal

nerve, and paralysis of the hypoglossa nerve. Roentgenograms showed erosion o the base of the skull. This patient was give a course of roentgen therapy. He returneu a few months later showing a right facial paralysis and an exposure keratitis.

Case 2. K. A., a 13-year-old boy (fig. 2), was first seen in December, 1947, at which time he had had nasal obstruction for 13 months, episodes of epistaxis for 12 months, and proptosis of the left eye for 1 month. He was found to have a juvenile fibroma of the nasopharynx.

Roentgenograms of his skull did not reveal any erosion, and the tumor was presumed to have extended through orbital foramina into the orbit. He received roentgen therapy and no recent increase in symptoms has been noted 6 months after treatment.

Case 3. J. Y., a 3-year-old girl (fig. 3), was seen in 1940. Her parents gave a history indicating that she had had nasal obstruction, abducens palsy, frequent nose bleeds,

Fig. 2 (Boyce and Bolker). K. A., a 13-year-old boy, with juvenile fibroma of the nasopharynx showing exophthalmos of the left eye.

and proptosis of the right eye for several months.

On physical examination, she was found to have bilateral choked discs. No abdominal masses were noted. After microscopic examination, the tissue from the nasopharynx was diagnosed as neuroblastoma. The exophthalmos decreased following roentgen therapy. Two months later, an abdominal mass became evident. The patient died three months after admission.

Although the nasopharynx is an unusual primary site for neuroblastoma, cases have been known to occur there, and the growth characteristics as seen at the time of exploration through both an orbital and nasopharyngeal approach would indicate this to be true in this instance.[6]

TREATMENT

The most generally accepted method of treatment of malignant tumors of the nasopharynx is roentgen irradiation. Radium is not often used as it is difficult to apply to this site. Since the lesions are deep, multiple ports are needed to deliver an adequate tumor dose without over-irradiating the skin. Highly penetrating beams, as produced by high voltages and heavily filtered rays, are essential to successful treatment. Care should be taken to shield uninvolved radiosensitive tissues such as the pinna of the ear and the structures of the anterior segment of the eye.

At this hospital the treatment of a malignant nasopharyngeal tumor varies, depending on the proposed effect of treatment, whether curative or palliative, and the response of the tumor to irradiation. A curative effort is made in every case without evidence of distant metastasis.

Skull involvement as demonstrated by roentgenograms is not considered a definite contraindication for a curative effort. The best results are obtained with patients who report for treatment before the appearance of enlarged cervical nodes.

A tumor dose of approximately 3,500 to 5,000 r is desired, and this is achieved by the

Fig. 3 (Boyce and Bolker). A 3-year-old girl with neuroblastoma of the nasopharynx. She showed proptosis of the right eye, bilateral choked discs, and paralysis of the 6th nerve on the right. She died three months after admission.

administration of 2,600 to 3,400 r in air to each of 2 or 3 fields. In a centrally located lesion, 4 fields may be used, both right and left lateral nasopharyngeal and right and left oblique maxillary fields. In addition to the primary tumor, the involved cervical lymph nodes are also treated.

Palliative treatment is administered to relieve pain and nerve palsy, decrease exophthalmos, nasal obstruction and epistaxis, and to improve the general condition of the patient when the extent of the disease precludes a cure. Treatment is stopped when these objectives are attained.

Following treatment the primary lesion usually regresses rapidly, the only evidence of involvement being a defect of the pharyngeal mucosa which closes over with epithelium. Ordinarily there is no recurrence at the primary site, but rather in the lymph nodes. Pain from nerve involvement is often relieved after the first few treatments. The radiation reaction of the skin is transient and leaves minimal changes with properly given treatment.

With two exceptions, all of the benign

tumors in our series were juvenile fibromas. The exceptions were sclerosing angiomas, a tumor which is histologically closely related to fibromas. Since juvenile fibromas regress spontaneously in a few years after puberty, the object of treatment is not so much eradication of the tumor as restriction of its harmful effects until they are physiologically remedied. Efforts are made to decrease the frequency of epistaxis and expansion of the mass. Surgical extirpation is contraindicated due to the exceedingly vascular nature of the tumor. In fact, biopsy may cause severe hemorrhage.

Again, external irradiation is the treatment of choice, the dosage varying with the response to irradiation and ranging from 1,000 r to 2,500 r tumor doses.

COMMENT

Tumors of the nasopharynx, while uncommon, should none the less be kept in mind by the ophthalmologist for he may be the first to be consulted by the patient. If he is aware of the usual findings in this type of tumor, he may make the diagnosis early and give the patient the benefit of more prompt treatment.

SUMMARY

Carcinoma of the nasopharynx is rarely diagnosed correctly early because of the silent nature of the primary tumor and the difficulty of adequately examining the area. Usually the secondary manifestations of the tumor achieve prominence before diagnosis is made.

Forty-four consecutive cases of nasopharyngeal tumors seen over the past 15 years are reviewed; 34 were malignant, 9 nonmalignant, and 1 of unknown type. Thirty-two percent of the cases showed ocular signs or symptoms at some time during the course of the disease. Abducens palsy was most common of this group. Proptosis and lesions of the optic, oculomotor, and trochlear nerves were present in lesser numbers. When ocular manifestations were present, the prognosis was poor. The treatment of choice has been roentgen therapy.

University Hospitals.

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A STUDY OF THE EFFECT OF RETROBULBAR ANESTHESIA ON THE OCULAR TENSION AND THE VITREOUS PRESSURE*

HAROLD GIFFORD, JR., M.D.

Omaha, Nebraska

Ever since Elschnig[1] popularized the use of retrobulbar anesthesia in 1925 it has been known that the ocular tension is lowered by this procedure. Atkinson[2] has pointed out that there tends to be a deepening of the anterior chamber. Icaza[3] and Levett[4] suggested the use of retrobulbar injection to relieve pain and lower the tension in acute glaucoma.

The studies of vitreous loss by Wright,[5] Lancaster,[6] Kirby,[7] and myself,[8] have shown that there is a posterior segment pressure which is an important problem in cataract surgery. Elschnig, DeGross,[9] Dunphy,[10] Greenwood and Grossman,[11] and my brother, Sanford Gifford,[12] all have reported that the use of retrobulbar injection reduces the amount of vitreous loss in cataract surgery.

Ferrer,[13] Bothman,[14] and Lombardo,[15] checked the ocular tension before cataract operations but made no special separation of ocular tension and vitreous pressure. Ferrer believed that a high preoperative tension was a danger signal. Lombardo demonstrated that a lower preoperative tension was a good prognostic sign. Bothman reported only 1 case of vitreous loss in 23 cases with a high preoperative tension, and 2 cases had inverted flaps or low vitreous pressure at the time of operation.

Ferrer[16] in a later paper pointed out the fact that ocular tension did not cease when the chamber was opened. He noted that some eyes had an increased tension but he did not attempt to analyze the difference between ocular tension and vitreous pressure.

It seemed to me that a detailed study of the mechanism that produces this lowering of intraocular pressure might bring to light some interesting physiologic facts which might lead to safer cataract surgery, and perhaps to a better understanding of the etiology of glaucoma. I have been working on a method to produce complete motor paralysis of the extraocular muscles. With this work I have collected a series of cases in which the intraocular pressure was measured on the operating table before the retrobulbar injection and five minutes after it. These cases and some others form the basis of this preliminary report. It is hoped that this report will stimulate the interest of others to study this problem, since it is an important part of the physiology of the eye that has received very little attention. I would like to say that this is by no means a controlled experimental study, but simply a review of clinical findings and an attempt to evaluate these findings in the light of our present knowledge.

The technique of the orbital injection varied slightly but in general 2 cc. of 2-percent novocain containing adrenalin 1:1,000 was injected deep into the orbit, using a 5-cm., No.-25 needle. In some cases 4-percent novocain was used and the exact amount of adrenalin was not measured carefully except in the later cases in which 0.4 cc. to the ounce was used. The patients all had some basal anesthesia, sodium ortal or morphine and scopolamine. Also 4-percent and 10-percent cocaine with pilocarpine (1 percent) and adrenalin drops were instilled in the conjunctival sac, starting 20 minutes preoperatively. The facial nerve was blocked as completely as possible, using both the O'Brien[17] and Van Lint[18] methods. In many cases the Klein[19] technique was also added.

The tension was taken with the Schiøtz tonometer (sterilized in zephiran (1:1,000) just before the retrobulbar injection and the second tension five minutes later. If the orbital injection is properly placed deep in

the base of the orbit, the motor block comes on almost at once and the patient is unable to move the eye in any direction when asked to look-up or down, right or left. This effect was graded on a percentage basis, counting 20 percent off for each rectus still functioning and 10 percent for each oblique still active. For example, if the eye rotated only laterally, the motor block was considered to be 80 percent perfect. If two muscles were still active, the block was considered to be 60 percent effective. If movement was good in all directions but one, the motor block was listed as only 20 percent. There were also slight gradations for partial functions.

In the cataract operations, it was possible to set up a standard for posterior segment pressure—or vitreous pressure, as I have called it. When the eye is opened with a Graefe knife, the lens and iris diaphragm moves forward in the majority of cases, just filling the anterior chamber. This was recorded *as normal vitreous pressure.* If this movement forward was sufficient to cause gaping of the wound, a prolapse of the iris, or a horizontal wrinkle in the cornea, this was considered to be evidence of *positive vitreous pressure.* If the cornea collapsed or if the iris diaphragm did not move forward to fill the anterior chamber and an air bubble filled the chamber spontaneously, this was considered to be evidence of *negative vitreous pressure.*

Before looking at the clinical findings, it will make things more understandable if we review our knowledge of what takes place when novocain and adrenalin are injected behind the globe. The depth of the injection, of course, has some effects on the results. The novocain when injected deeply blocks the motor nerves, which relaxes the extraocular muscles more or less completely. The novocain also blocks the sensory nerves entering the base of the orbit, chiefly the nasociliary branch of the trigeminal. This produces anesthesia of the entire globe with anesthesia of the conjunctiva surrounding the cornea. It should block *both* the sympathetic and parasympathetic activity coming to or from the ciliary ganglion. The pupil dilates with a simple paralysis of the third nerve, but in my cases the pupil remained small because the iris was under the influence of cocaine and pilocarpine. I do not know what happens to the ciliary muscle. I hope that Dr. Harold G. Scheie will be able to tell us. The anterior chamber, however, becomes noticeably deeper in most cases. Is this effect due to relaxing the tone of the ciliary muscle? What happens to the vessels in the choroid? Do they dilate or constrict? A definite correlation between deepening of the anterior chamber and drop in tension has not yet been made.

The novocain placed this far back in the orbit should also block the optic nerve but for some reason this does not take place. Perhaps the optic-nerve sheath protects the nerve. I have checked the vision in most of these cases and have found the optic nerve to be as fully active as the state of the eye would permit. That is, in the aphakic cases these patients could count fingers promptly and accurately at the close of the operation and there was no gross field defect.

It has been generally accepted that the adrenalin placed in with the novocain is the drug that produces the lowering of the tension. Dr. Walter Atkinson believes that the adrenalin produces its effect by constricting the small arteries entering the globe but not affecting the venae vorticosae, which are more forward. I will present some findings later which indicate that the answer to the effect of the adrenalin is not this easy. To my surprise, I found that the effect of the adrenalin was relatively small and I am still in doubt as to just where the effect takes place.

This present study is based on 65 cataract operations and 40 glaucoma operations which had complete records of the tension before and five minutes after a deep orbital injection. Also the amount of motor block and the vitreous pressure after the globe was opened were recorded. There should be some rela-

tionship between the percentage of lowering of the ocular tension, the percentage of motor block, and the state of the vitreous pressure. The age of the patient may be an important factor, since this influences the rigidity of the sclera and the expansibility or contractability of the vascular bed. The vitreous body also changes with age, tending to become more fluid and perhaps chang-

There were wide variations ranging from 60 percent to no drop at all. The chart also shows that, along with the rise in initial tension, the base pressure goes up, starting at 10 and increasing to 15 mm. Hg. This will be considered later when discussing the 40 cases of glaucoma.

In the cataract series there were 34 males with an average lowering of tension of 31.9
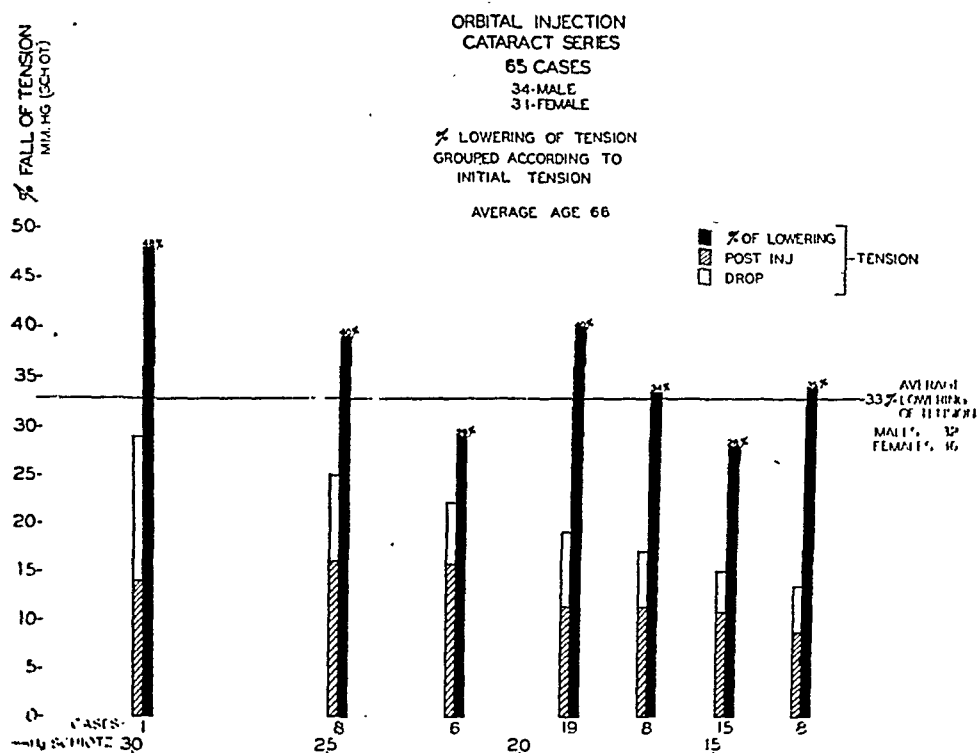
Chart 1 (Gifford). The percentage of lowering of the tension increases only slightly with an increase in the initial tension.

ing in other properties as well. It is obvious from looking at these variable factors that the problem is not a simple one.

It was noticed immediately that the actual amount of drop in tension depends on the initial level of the intraocular pressure and that the percentage of lowering of tension would give a better figure to use for this study. The amount of drop in tension was therefore changed to percentage of lowering of the tension. From Chart 1, it is seen that the percentage of lowering of the tension increases only slightly with an increase in the initial tension. The average percentage of lowering for the cataract series was 33.

percent and 31 females with an average lowering of 36 percent. This slight difference is probably not significant and would indicate that sex difference does not play a part in the tension-lowering mechanism.

The age of the patient did not influence the percentage of motor block. The average age of the 34 cases with more than 65 percent motor block was 65.9 years. For the 31 cases with less than 65 percent motor block the average age was 65.2 years. However, age seems to have some correlation with the state of the vitreous (Chart 2).

The average age for the cases with negative pressure was 69 years. The average of

the cases with normal vitreous pressure was 65 years, while the average of cases with positive vitreous pressure was 61 years.

was 37 percent. The average age for the entire group was 66 years. This is a relatively old group in which sclerotic vascular
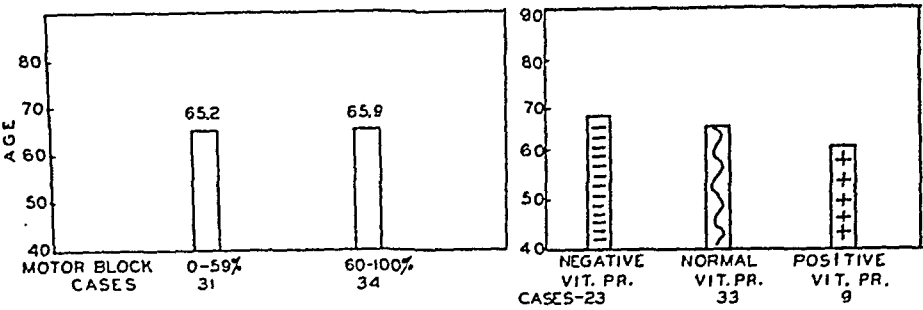
Chart 2 (Gifford). Age seems to have some correlation with the state of the vitreous.
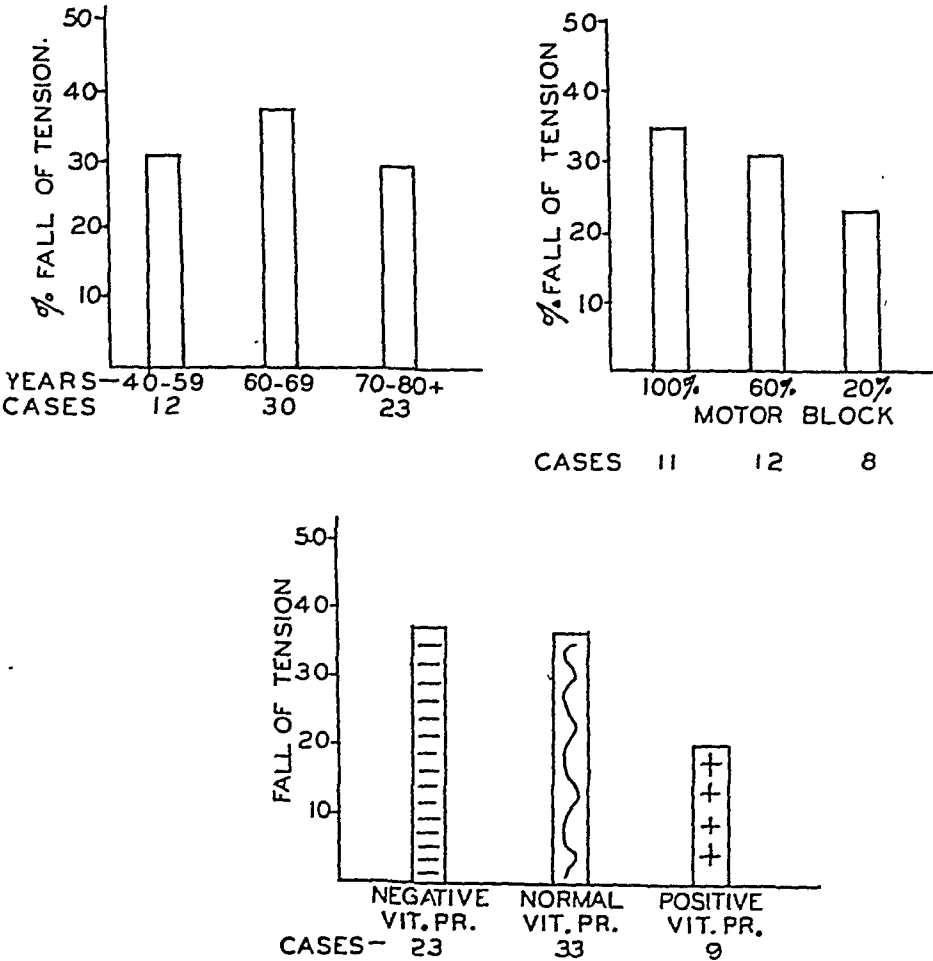
Chart 3 (Gifford). Effect of motor block on ocular tension and vitreous pressure.

The age of the patient does not seem to have a great effect on the percentage of lowering of tension.

The older and younger groups had slightly less fall—29 percent and 30 percent respectively—than the middle age group, which

changes are present. If a really young group were checked, they might show more difference or they might show a similar percentage of lowering due to the compensating effect of a more elastic sclera.

Chart 3 also shows the effect of the per-

centage of motor block on the percentage of lowering of tension.

Eleven cases with 100-percent motor block had an average lowering of tension of 34.6 percent, 12 cases with 60 percent motor block an average of 31 percent and 8 cases with 20 percent or less motor block showed only 25 percent.

The bottom part of Chart 3 shows that the percentage lowering of tension has only

when the percentage of motor block is poor the percentage of tension lowering is less (28). This would indicate that the extraocular muscles play a part in maintaining normal ocular tension and when they are relaxed by the orbital injection the percentage of lowering is greater. This chart also shows the effect of the motor block on the vitreous pressure. There were only two cases of positive pressure when the motor block was bet-
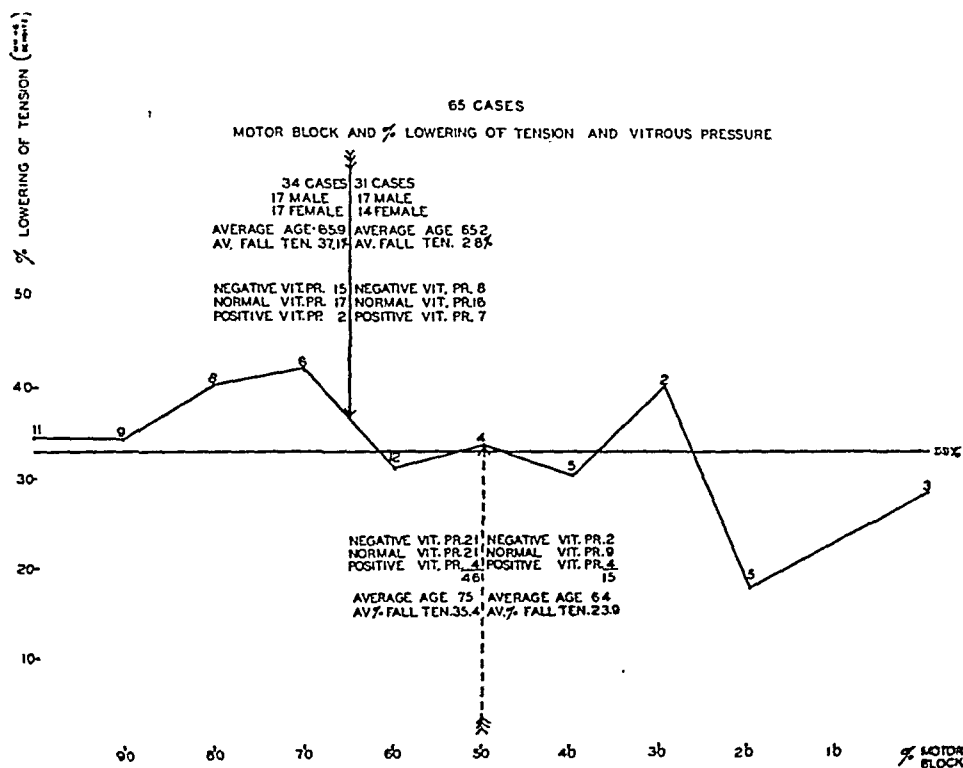
Chart 4 (Gifford). Correlation of the percentage of motor block with the percentage of tension lowering and the state of the vitreous pressure.

a little correlation with the negative and normal vitreous pressure, the average percentage of lowering being 37.6 and 36.6 respectively. The positive vitreous cases showed a percentage lowering of 19.9. This would indicate some correlation with positive vitreous pressure.

In attempting to explain the mechanism of the fall in intraocular pressure, the percentage of motor block was correlated with the percentage of tension lowering and the state of the vitreous pressure.

Chart 4 shows that as the percentage of motor block increases, the percentage of tension lowering increases (37.1), and also

ter than 65 percent. There were seven cases when it was less than 65 percent.

The effect of the motor block on the vitreous pressure and the percentage lowering of tension are shown graphically in Chart 5.

When the motor block was good there were more cases with negative pressure. The effect of the muscle tone was larger in this direction. When the percentage of lowering of tension was poor there were more cases of positive vitreous pressure. This is not an absolute correlation. There is some other factor operating. This appears to be the age of the patient. The three factors—age, percentage of lowering of pressure, and the
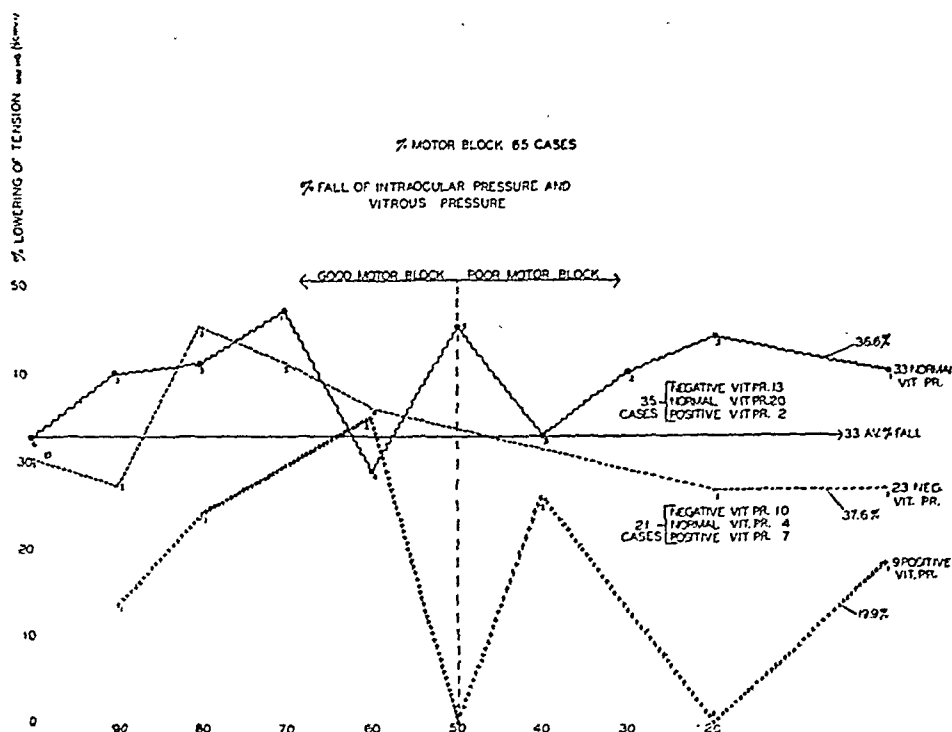
Chart 5 (Gifford). Graphic presentation of the effect of the motor block on the vitreous pressure and the percentage lowering of tension.
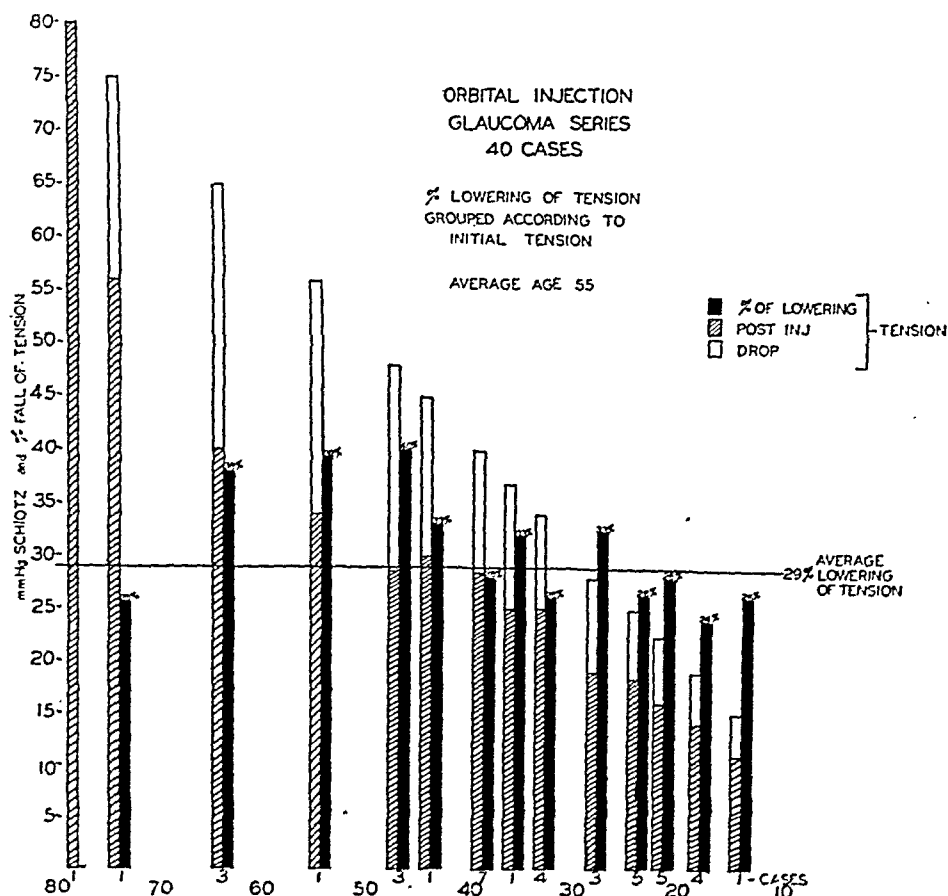
Chart 6 (Gifford). Percent of lowering tension grouped according to initial tension in a study of 40 glaucoma cases.

amount of motor block—all affect the vitreous pressure and in any individual case all three must operate in the same direction to be sure of producing either negative or positive vitreous pressure. Any one factor may overshadow the effect of the other. This was shown to be true in several individual cases. A patient, aged 73 years, with a small percentage drop, 15, had a negative vitreous pressure but a 90-percent motor block. The patient with the lowest initial pressure, 10

due to a continued rise in the base pressure. The rise in the base pressure is shown very clearly. It seems to me that this is the same base pressure brought out by Dr. A. B. Reese in his paper read before this society last year.

If this proves to be the case, an orbital injection would provide a quick and simple method for determining this base pressure. This would eliminate the "long-range perspective" that Dr. Reese feels is so desirable

TABLE 1
CATARACTS (2 PERCENT NOVOCAIN, NO ADRENALIN)

Age	Tension			Percent of Lowering	Motor Block
	Pre-injection	Post-injection	Drop		
73	15	11	4	27	60%
76	17	9	8	49	79
81	22	17	5	23	70 B.P. +8
56	15	9	6	40	70 B.P. −5
64	17	10	7	41	100 B.P. +12
				Avg. 35.6	

mm. Hg, had only a 20-percent drop and only 60-percent motor block, but negative vitreous pressure. He was 88 years of age. In this case, age was a deciding factor. For practical purposes in cataract surgery, youth, a low percentage of tension lowering, and poor motor block will tend to produce positive vitreous pressure. But if any of these three factors can be changed sufficiently, normal or negative pressure may be the result. Conversely, old age, a good motor block and a large percentage of fall will produce negative vitreous pressure, but if one of these is missing positive vitreous pressure may result.

The 40 glaucoma cases are shown on Chart 6. These are grouped according to the initial preinjection tension.

Like the cataract series, there is a tendency for the percentage of lowering of tension to be greater with a higher initial tension, but the average percentage of lowering was slightly less, being 29. This must be

to determine the choice of operation for each individual patient. A high base pressure would indicate a trephination or Lagrange sclerectomy. The oribtal injection might also prove to be a useful provocative test in preglaucoma patients. It will take considerably more study to set up normal percentage-lowering curves but I am sure such curves would be invaluable in understanding and treating glaucoma.

How does the orbital injection produce its tension-lowering effect? I have shown that relaxing the extraocular muscles has some influence on reducing the tension.

The adrenalin which has generally been given the credit for the tension-lowering effect, surprisingly, does not seem to be necessary (table 1).

Table 1 shows that it is possible to produce a slightly greater than average percentage of lowering of tension without any adrenalin in the orbital injection. The average for five cases was 35.6 percent. Saline

alone will not cause a lowering of the ocular tension but adrenalin alone has some effect.

Saline and adrenalin were injected the day before operation and the tension checked alone in the second, and about the same amount in the third. More of these cases will have to be done before the effect of adrenalin alone can be evaluated precisely.
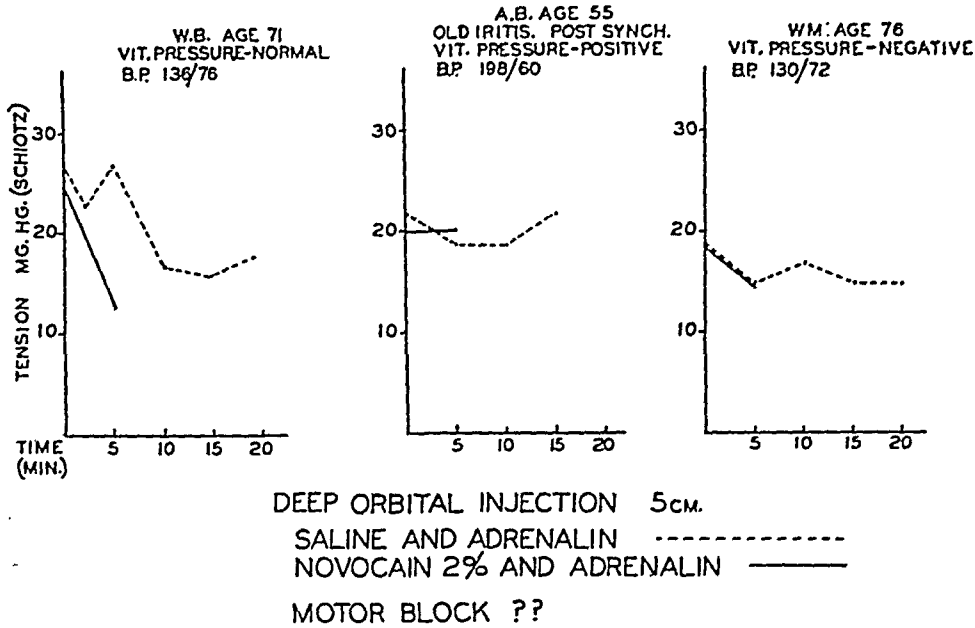
Chart 7 (Gifford). Tension curves produced by deep orbital injection.

(broken line). At the time of operation, the same amount of adrenalin was added to the novocain and the tension again checked (solid line). See Chart 7.

The effect of the adrenalin alone was not as great as when it was combined with novocain in the first case. There was slightly more lowering of tension with the adrenalin

A similar tension-lowering effect can be produced by sodium pentothal anesthesia (table 2).

This would indicate that there is a higher center in the brain for control of ocular tension. Since the amount of the effect is about the same as when an orbital injection is used, it would indicate that they both act

TABLE 2

GLAUCOMA. SODIUM PENTOTHAL

			Tension			
Age	Name	Eye	Pre-injection	Post-injection	Drop	Percent of Lowering
Acute Primary Glaucoma						
59	O. P.	O.D.	25	19	6	24 with sodium pentothal
		O.S.	40	29	11	27 with sodium pentothal
		O.D.	65	48	17	26 with retrobulbar
		O.S.	40	26	14	35 with retrobulbar
Acute Secondary Glaucoma						
42	R. H.	O.D.	48	48	0	0 with sodium pentothal
		O.S.	50	50	0	0 with sodium pentothal
		O.S.	48	48	0	0 with retrobulbar

by blocking or inhibiting certain nerve stim-
uli. Since the adrenalin acts by stimulating
the sympathetics and produces the same ef-
fect, it seems to me that the novocain must

The glaucomatous eyes, in general, seem
to respond to the orbital injection about the
same as normal eyes but with slightly less
percentage of tension lowering because the

TABLE 3
ORBITAL INJECTION FOR ACUTE GLAUCOMA

Age	Sex	Tension		Percent of Lowering	Time
		Pre-injection	Post-injection		
76	F.	65	40	38.4	20 minutes
78	F.	75	75	00.0	1 hour
82	M.	56	30	35.7	1 hour
41	M.	48	48	00.0	1 hour
72	F.	90+	90+	00.0	30 minutes

TABLE 4
TENSION OF ENUCLEATED EYES

Age	Sex	Name	Diagnosis	Pre-injection	Post-injection	After Muscles Cut	Eye Enucleation
52	F.	A. B.	Abs. Glau.	90+	76	90	30
39	M.	J. H.	Staphyl. C. Sec. Glau.	76	48	56	15
70	M.	C. L.	Mel. of Iris. Sec. Glau.	47	47	35	18
77	M.	E. K.	Hem. Glau.	90	62	75	90+
46	M.	R. O.	Mel. of Limb.	17	9	4	9
60	F.	M. C.	Mel. of Choroid	8	6	6	?

TABLE 5
ORBITAL INJECTION WITH NO DROP IN TENSION

Age	Sex	Tension			Percent Motor Block	Vitreous Pressure	Remarks
		Pre-injection	Post-injection	Drop			
55	M.	22	22	0	80	+	Old iritis. Post. synch.
47	F.	15	15	0	20	+	Loss of vitreous.
71	M.	15	15	0	20	0	Morgagnian cataract. Poor facial block.
71	M.	15	15	0	50	+	Japanese-shallow orbit. Orbital injection only 5 cm. deep; also block. Near vitreous loss.

produce its tension-lowering effect by block-
ing the parasympathetic activity of the third
nerve and the ciliary ganglion. How this
effect is produced is unknown. At present
this is not much more than a working hypo-
thesis but it seems to apply to the normal
eye at least.

base pressure has become elevated.

In acute glaucoma, however, there were
some exceptions (table 3).

There were three cases where no reduction
of tension occurred. These eyes had lost
their tension-lowering capacity. It seems that
the base pressure had simply become ele-

vated to a point equal to the initial pressure.

The tension was checked during and after enucleation in several cases (table 4).

Table 4 shows that the eyes with a high base pressure actually maintain some or all of this pressure after the eye has been removed from all nervous and circulatory control. It demonstrates that there may be an actual anatomic change in these eyes that is producing the elevation of the base pressure.

Some eyes failed to show any response to orbital injection, although the initial pressure was low. These eyes were not glaucomatous (table 5).

Table 5 shows four cases that did not show any drop in tension when the initial pressure was low. One eye had had a severe iritis but in the others the lack of drop in tension could be explained only on the basis of a poor motor block or some specific anatomic change that produces an eye that has no tension-lowering potential.

CONCLUSIONS

This study would indicate that in the normal eye there is a dynamic factor controlled by the nervous system that produces a certain amount of the ocular tension. This seems to be a relatively constant factor amounting to about 33 percent of the initial ocular tension. This dynamic factor is influenced by the tonus of the extraocular muscles and the parasympathetic activity of the third nerve. It can be separated from the total ocular tension by an orbital injection of 2-percent novocain, adrenalin, or sodium-pentothal anesthesia. This leaves a residual or base pressure that shows a tendency to increase slightly in the normal eye as the intraocular pressure rises. This base pressure is maintained by still-unknown factors but must in some way be associated with the hydrostatic pressure of the blood and the elasticity of the sclera.

This study would indicate that, in the glaucomatous eye, the base pressure has become elevated, in some eyes to such a degree that there is produced an anatomic change that resists all tension-lowering devices, such as drops, orbital injection, cutting the recti muscles, and even enucleation.

I feel certain that further clinical study and basic research on the choroid and its association with the ciliary body is necessary before the glaucoma problem can be solved. I know certainly that the percentage of vitreous loss in cataract surgery can be greatly reduced by using a deep orbital injection that produces a motor block of the extraocular muscles as well as more complete anesthesia, and a lowering of the intraocular pressure.

1620 Medical Arts Building (2).

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CHOICE OF A MIOTIC AGENT FOLLOWING RETROBULBAR ANESTHESIA*

HAROLD G. SCHEIE, M.D., AND GAYLORD OJERS,† M.D.

Philadelphia, Pennsylvania

INTRODUCTION

For some years it has been the custom in the Department of Ophthalmology at the Hospital of the University of Pennsylvania to instill physostigmine as a prophylactic measure against iris prolapse following delivery of the lens from eyes in which intact pupils have been preserved. Because an occasional prolapse continued to occur in spite of this and other precautions, the pupils of several eyes were examined at various intervals during the first 24 hours after extraction.

A significant number of pupils, in eyes which had received retrobulbar and subconjunctival injections of procaine hydrochloride, were found to have remained dilated for several hours after operation. This persistent mydriasis was surprising in view not only of the instillation of physostigmine but also of the added factor of trauma during operation. The pupils had been dilated preoperatively by homatropine hydrobromide.

In searching for a possible explanation, the phenomena described in the denervated pupil by Anderson[1] in 1905 was recalled. He found that, following removal of the ciliary ganglion from cats, the pupils on the operated side dilated widely. He demonstrated that with complete denervation, following such removal, physostigmine was ineffective in constricting the pupil. Furthermore, the pupil constricted normally or more actively than normal to pilocarpine solution.

Loewi, Dale, and other workers[2] subsequently explained these phenomena when they evolved the neurohumoral theory of transmission of nerve impulses. In part, this theory postulates that a nerve impulse stimulates an organ to its physiologic action by a chemical substance called the effector substance. This is liberated by the terminal nerve fiber upon the arrival at that point of the nerve impulse. The effector substance liberated by the nerve endings of the parasympathetic nervous system, which include those supplying the sphincter iridis, is acetylcholine. Stimulation of a muscle cell to contraction involves a special apparatus called the myoneural junction, which consists of the terminal nerve fiber and the muscle cell which has a specialized area called the motor end-plate. Acetylcholine, liberated by the nerve ending, has a special affinity for the motor end-plate and through it stimulates the muscle cell to contraction. Relaxation of the muscle cell is brought about by cholinesterase, constantly present in the tissues, which rapidly destroys the acetylcholine.

The various miotic agents in common use clinically depend for their effect upon their ability to intervene in the myonueral junction in various ways. Pilocarpine produces miosis by mimicking the action of acetylcholine. Physostigmine, on the other hand, stimulates the sphincter muscle only indirectly. It inhibits or inactivates cholinesterase, thereby preventing the destruction of acetylcholine which now accumulates in concentrations sufficient to give continuous stimulation of the sphincter iridis with resulting miosis. Physostigmine, therefore, must have acetylcholine available to be effective, and acetylcholine is produced only by intact nerve endings. The removal of the ciliary ganglion or destruction of the ciliary nerves peripheral to this ganglion destroys the source of acetylcholine in the sphincter iridis. This renders physostigmine ineffective and explains its failure to constrict the pupils of the cats used in Anderson's ex-

periments. On the other hand pilocarpine, which acts directly, as does acetylcholine, continues to be effective even after complete denervation.

It occurred to us that such a situation might account for the persistent mydriasis often seen in our patients following cataract extraction. A temporary postganglionic denervation of the sphincter pupillae might have resulted from the retrobulbar injection of procaine hydrochloride. This would of course render physostigmine ineffective when instilled postoperatively. The following experiments were therefore undertaken.

OUTLINE OF EXPERIMENTS

1. Observation of the effect of the retrobulbar injection of procaine hydrochloride upon the size and reaction of the normal pupil.

2. The effect of retrobulbar injections of procaine hydrochloride upon the pupillary response to miotic agents.

3. The effect of retrobulbar injection of procaine hydrochloride upon pupils previously rendered miotic by instillations of physostigmine or pilocarpine.

4. A comparison of the miotic effect of physostigmine and pilocarpine in overcoming homatropine and paredrine.

5. Determination of the most effective miotic agent for pupils previously dilated by retrobulbar injections of procaine hydrochloride and instilled homatropine or paredrine to simulate the clinical conditions encountered during cataract extraction under local anesthesia with retrobulbar procaine hydrochloride.

METHODS OF EXPERIMENTS

Unless otherwise stated, all experiments were carried out upon dogs anesthetized with nembutal. Ten eyes were used for each experiment. The term retrobulbar injection refers throughout to the injection of 2 cc. of 4-percent procaine hydrochloride. This was accomplished by rotating the eye upward with a fixation forceps and inserting

the needle through the lower eyelid. If the retrobulbar injection was to be repeated, the syringe was detached and the needle left in place between injections. The miotic agents used were physostigmine (0.5 percent), and pilocarpine (1 percent and 10 percent), and one tenth of 1-percent di-isopropyl fluorophosphate. To insure adequate administration they were instilled twice, five minutes apart. All pupillary measurements were estimated by the use of a millimeter ruler. Figures given represent the average for the 10 eyes. Pupils were arbitrarily said to be miotic when 3 mm. or less in diameter.

EXPERIMENTAL DATA

Effect of retrobulbar injection of procaine hydrochloride on the normal pupil.

The pupils of nearly all animals dilated widely within 30 to 60 seconds after retrobulbar injection. Occasional failure to dilate was due to a poorly placed injection, since a second injection with the needle properly inserted resulted in prompt mydriasis. The pupils were fixed to light. The mydriasis was found to persist for an average time of 160 minutes after retrobulbar injection.

Effectiveness of pilocarpine and physostigmine following retrobulbar procaine injection.

1. The effect of retrobulbar injection of procaine hydrochloride upon pupillary response to miotics:

The miotic effect of physostigmine, pilocarpine, di-isopropyl fluorophosphate (D.F.P.) on pupils rendered mydriatic by retrobulbar injection was tested.

Pilocarpine (1 percent) was found to constrict the pupils to 3 mm. in an average time of 24 minutes, while pilocarpine (10 percent) had a similar effect in 20 minutes (chart 1). This time interval was shorter than that found in the normal eye of unanesthetized dogs not subjected to retrobulbar injection. The effect of physostigmine (0.5 percent) on the other hand, was markedly delayed (chart 1). Miosis oc-

curred, but only after a time interval of 80 minutes as compared with 40 minutes in the normal control animals. D.F.P. also produced miosis, but like physostigmine only after a significant delay, which averaged 120 minutes.

Physostigmine and D.F.P. therefore both

10 percent), and a retrobulbar injection was given. No dilatation of the pupil ensued. Similar experiments were done with pupils constricted by physostigmine or D.F.P. The physostigmine-treated pupils dilated almost immediately following the retrobulbar injection of procaine, while 9 of the 10 pupils
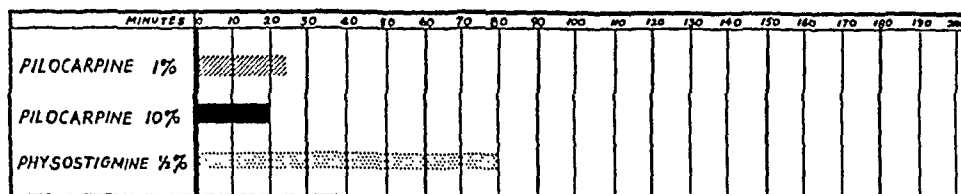
Chart 1 (Scheie and Ojers). Time required by pilocarpine and physostigmine to produce miosis in dog eyes with pupils dilated by retrobulbar injections of procaine hydrochloride.

became effective only after the effect of the retrobulbar injection began to wear off, a time previously found to be approximately 50 to 60 minutes following the injection.

After this interval, the pupils treated with physostigmine rapidly constricted. They became miotic twice as rapidly as the control eye which had had only a retrobulbar injection. These findings were compatible with those of Anderson and other workers with denervated sphincter muscle, and they indicated that a temporary ciliary ganglionectomy had been accomplished by the retrobulbar injection of procaine.

constricted by D.F.P. dilated following retrobulbar injection. There was more of a lag as indicated by a time range of 1 to 8 minutes.

3. Clinical observations on the pupil following retrobulbar injections of procaine hydrochloride:

Some of the experiments just described in dogs were repeated upon patients who were being operated upon under local anesthesia, and the results were found to be similar. No drops except pontocaine hydrochloride (1 percent) were instilled locally. Retrobulbar injections were made contain-
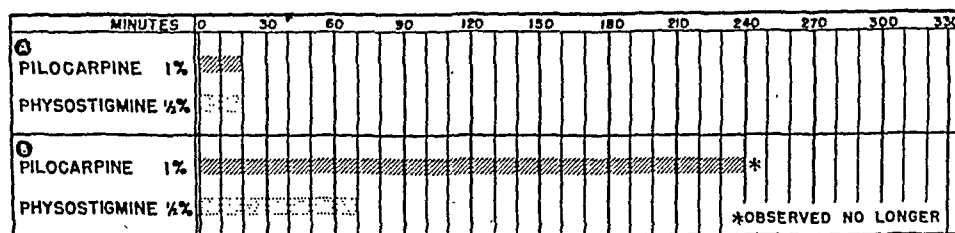
Chart 2 (Scheie and Ojers). Time required by pilocarpine and physostigmine to produce miosis in human eyes with pupils previously dilated by (A) paredrine and (B) homatropine.

2. Effect of retrobulbar injection of procaine hydrochloride on pupils previously constricted by pilocarpine, physostigmine, or D.F.P.:

Miosis was produced in dog eyes by the instillation of pilocarpine (1 percent or

ing 4-percent procaine hydrochloride. Adrenalin was not used either by instillation or injection. Several patients who were being operated upon for strabismus were given bilateral retrobulbar injections. Pupil dilatation was maximal in 40 to 50 seconds (figs.)
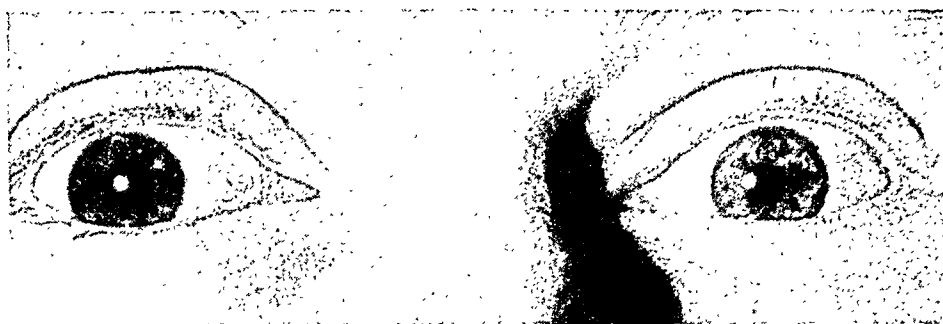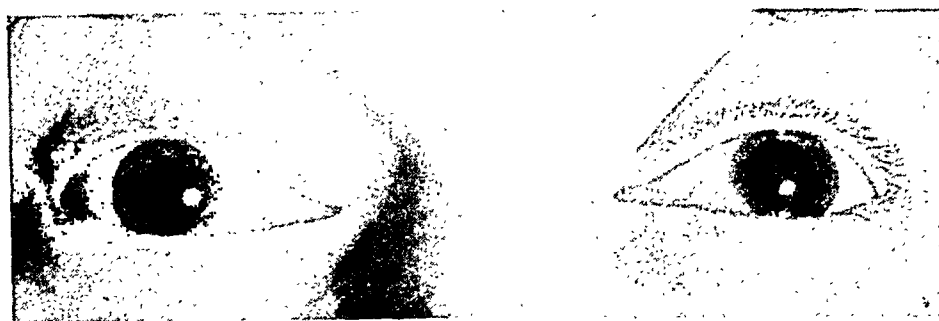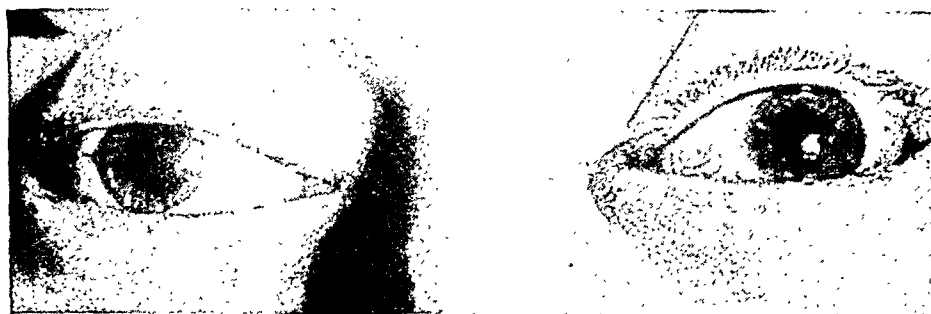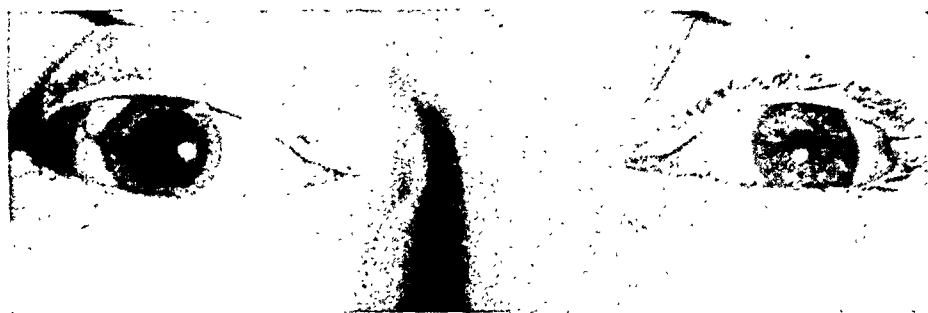
Fig. 1 (Scheie and Ojers). Photographs showing dilatation of pupils following retrobulbar injection of procaine hydrochloride and subsequent ineffectiveness of physostigmine. (A) Pupils prior to retrobulbar injection. (B) Mydriasis immediately following retrobulbar injection of procaine hydrochloride. (C) Pupils 15 minutes later, following instillation of physostigmine in the right eye and pilocarpine in the left eye. (D) Pupils 25 minutes later showing marked miosis from pilocarpine.

1A and 1B). Physostigmine (0.5 percent) was then instilled in one eye and pilocarpine (1 percent) in the other. Pilocarpine caused miosis which began in 5 minutes and was nearly complete in 20 minutes (figs. 1C and 1D). The pupils of several patients were then made miotic by instillations of physostigmine or pilocarpine prior to retrobulbar injections. Miosis was found to persist in the pupils constricted with pilocarpine, but those constricted by physostigmine promptly dilated.

Effectiveness of pilocarpine and physostigmine in constricting pupils previously dilated by homatropine or paredrine.

1. Pupils of 10 human eyes were dilated by two instillations of 1-percent paredrine five minutes apart. One-percent pilocarpine and 0.5-percent physostigmine were found to produce miosis with nearly equal rapidity (chart 2-A). Miosis of 3 mm. or less occurred within approximately 20 minutes.

2. Pupils of 12 human eyes were dilated by two instillations of homatropine (2 percent), five minutes apart. One-percent pilocarpine was then instilled and found to be quite ineffective in producing miosis. By the end of four hours, less than 1 mm. of contraction had occurred (chart 2-B). One-

Effectiveness of pilocarpine on pupils dilated by retrobulbar injections of procaine hydrochloride and the instillation of either homatropine or paredrine.

Having determined that pilocarpine, in contrast to eserine, produced prompt miosis in pupils dilated by retrobulbar injections, it seemed to be the miotic agent of choice following cataract extraction. However, because pilocarpine was relatively ineffective in counteracting homatropine dilatation, it was felt that paredrine would be the better agent for preoperative mydriasis whenever retrobulbar anesthesia was contemplated. The following experiments were performed to observe the effectiveness of pilocarpine in overcoming mydriasis produced by a combination of retrobulbar injection and homatropine or paredrine.

1. Because pupil dilatation was used as the criterion of a successful block, it was necessary to give the retrobulbar injection before instilling homatropine or paredrine. The needle was left in place as previously described to be sure subsequent injections were also properly placed. For some reason dog irides seemed refractory to homatropine and particularly to paredrine. Twelve instillations of one drop of 1-percent paredrine
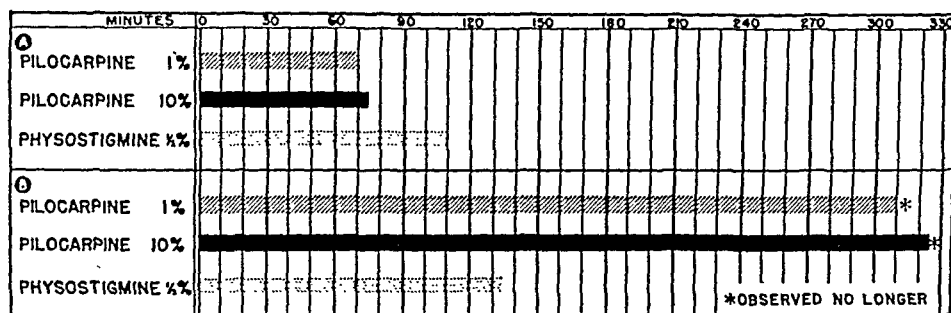
Chart 3 (Scheie and Ojers). Time required by pilocarpine (1 percent and 10 percent) to produce miosis in dog eyes with pupils previously dilated by retrobulbar injection of procaine hydrochloride and (A) paredrine or (B) homatropine to simulate clinical conditions during cataract extraction.

half-percent physostigmine, on the other hand, produced a miosis of 3 mm. in 12 human eyes after an average interval of about 70 minutes (chart 2-B).

were instilled into each eye at 5-minute intervals to be certain that the mydriatic would be absorbed. Two hours from the initial drop, a second retrobulbar injection was

made through the previously placed needles, and pilocarpine (either 1 percent or 10 percent) was instilled twice at 5-minute intervals. Miosis resulted in an average time of 70 and 75 minutes for each strength solution respectively (chart 3-A).

2. Using the same routine, six drops of homatropine (2 percent) were substituted for the paredrine in another series of dog eyes. In these experiments 1-percent and 10-percent pilocarpine were equally ineffective in that no significant miosis had resulted with either strength solution at the end of 310 minutes (chart 3-B). The eyes were not observed further.

DISCUSSION

Preliminary experiments with dog eyes showed that retrobulbar injections of procaine hydrochloride produced prompt pupillary dilatation of the ipsilateral eye. The pupil was fixed to light. These pupils responded to pilocarpine and eserine in a manner identical to that described by Anderson in animals from which the ciliary ganglion had been removed.

Prompt miosis was produced by the instillation of pilocarpine, but physostigmine was ineffective. Di-isopropyl fluorophosphate, which has physiologic properties similar to physostigmine, was likewise ineffective. The normal pupillary response of these drugs was regained after an average time of about 80 minutes at which time the effect of the retrobulbar injection of procaine had begun to wear off. Continued retrobulbar injection of procaine could prolong the mydriasis indefinitely.

Anderson in his experiments, however, found that physostigmine did not become ineffective for at least 24 hours after ciliary ganglionectomy; whereas, in our experiments with procaine this occurred within a period of seconds following the retrobulbar injection.

The explanation is obscure, but it seems likely that in Anderson's experiments the irritation of the severed nerves might have resulted in continued production of acetylcholine at the nerve endings. In the experiments with procaine, depression rather than irritation of the nerve fibers seemed likely. Acetylcholine was, therefore, no longer formed and physostigmine immediately became ineffective.

Experiments upon patients who were being operated upon under local anesthesia for strabismus gave similar results. Retrobulbar injections of procaine promptly produced mydriasis. Physostigmine was ineffective in producing miosis and remained so for 3 to 5 hours, but pilocarpine constricted these pupils normally. These experiments suggest that, in the presence of retrobulbar anesthesia, physostigmine is probably not the miotic agent of choice following cataract extraction.

Many surgeons believe the majority of iris prolapses occur during the first few hours after cataract extraction. During this immediate postoperative period the wound edges are very loosely coaptated and the anterior chamber probably forms and empties several times; meanwhile the aqueous tends to force the iris through the wound. Prompt postoperative miosis with retraction of the iris from the wound is therefore desirable, and from these experiments pilocarpine would seem to be the agent of choice.

Another factor which greatly influences the rapidity of postoperative miosis is the preoperative mydriatic agent employed. It is well known that the preoperative accidental instillation of atropine predisposes to iris prolapse because neither the trauma of operation nor miotics promptly constricts such pupils. For this reason homatropine and paredrine are the most commonly used preoperative mydriatics. We, therefore, tested the effectiveness of physostigmine and pilocarpine in counteracting homatropine and paredrine.

Pilocarpine was found to be quite ineffective in overcoming homatropine. Miosis had not occurred at the end of three hours.

Physostigmine produced miosis in such pupils in an average of 1¼ hours. On the other hand, these miotics were equally effective in overcoming mydriasis produced by paredrine. Such pupils were constricted within approximately 20 minutes by either substance. Because pilocarpine seemed to be the miotic of choice following retrobulbar anesthesia, we tested its effect following dilatation produced by combinations of retrobulbar injections of procaine and instillations of homatropine or paredrine. Prompt constriction of the pupils dilated by retrobulbar injection and paredrine occurred, whereas constriction occurred only after five hours when homatropine had been used. These findings would suggest paredrine should be employed rather than homatropine for preoperative mydriasis.

A miotic pupil is desirable throughout the corneoscleral trephining operation for glaucoma because it facilitates the performance of a peripheral iridectomy with the maintenance of an intact sphincter muscle. Experiments demonstrated that pupils constricted by pilocarpine remained undilated following the retrobulbar injection of procaine while those constricted by eserine dilated rapidly. Thus pilocarpine should be used preoperatively before a trephining operation, if miosis is to be maintained throughout the procedure when retrobulbar anesthesia is employed.

Retrobulbar injection of procaine hydrochloride, as suggested by Icaza[3] in 1946, has been employed in the treatment of acute congestive glaucoma. In view of the experiments just described, pilocarpine or some substance which acts similarly upon the myoneural junction should be used prior to the injection to avoid pupillary dilatation. Failure to do so, or the use of eserine alone, would result in wide mydriasis and possible aggravation of the glaucomatous state by further narrowing of the angle of the anterior chamber.

CONCLUSIONS

1. Retrobulbar injection of procaine temporarily produces an effect identical to the removal of the ciliary ganglion. The pupil is dilated and fixed and fails to constrict to eserine but does so promptly to pilocarpine.

2. Evidence therefore suggests that, if a miotic is to be employed following cataract extraction done under retrobulbar anesthesia, pilocarpine is preferable to eserine because eserine is rendered ineffective by the injection.

3. Paredrine is theoretically a more ideal preoperative mydriatic agent than homatropine because it is much more readily counteracted by pilocarpine. Although ordinarily a weak mydriatic, the retrobulbar injection of procaine adds to its effectiveness through paralysis of the sphincter pupillae.

4. If mydriasis is to be prevented following retrobulbar injection of procaine, particularly as used in the treatment of acute congestive glaucoma, pilocarpine should be used beforehand.

313 South 17th Street (3).

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DEGREES OF CORRECTION PER MILLIMETER OF SURGERY*

RICHARD G. SCOBEE, M.D.
Saint Louis, Missouri

The title of this paper suggests little of interest for the orthoptic technician. It is the ophthalmic surgeon who should be interested in such a discussion. Unfortunately, many an orthoptist has been forced against her will into the position not only of saying when surgery should be done on a patient with heterotropia but also what operation should be done.

The blame for such a lamentable situation, when it exists and it is unhappily all too common, lies entirely with the surgeon. The oculist that is too lazy to delve into the intricacies of dysfunctions of the oculorotary muscles has no business attempting the surgical correction of such cases. There are many surgeons, however, who do exactly that.

A patient with crossed eyes will enter their consulting room. Their first step after refraction is to refer the patient to an orthoptist and then sit back and wait. The orthoptist will refer the patient back to the ophthalmologist's office at intervals during orthoptic training but nothing happens. It finally becomes obvious that the surgeon is going to do nothing until he is forced into it and the conscientious orthoptist will, therefore, usually suggest surgery when it is indicated. The surgeon usually agrees with surprising alacrity and will ask in an off-hand manner for the orthoptist's opinion as to what should be done.

Make no mistake about this seemingly casual question for it is more frequently than not asked in dead earnest. Any suggestion that the orthoptist makes is usually followed to the letter. If the results are not good, the surgeon then blames the orthoptist rather than himself. If the results are good, he considers it a clever bit of surgery and often forgets the source of the advice. Actually, he has only himself to blame and he has taken an unfair advantage of the orthoptic technician and placed her in a very embarrassing position.

DIAGNOSTIC DIFFICULTIES

Every ophthalmologist who does surgery is confronted with one or more patients with heterotropia early in his career of private practice. Diagnostic procedures which seemed quite reliable during a residency quickly assume an alarming air of uncertainty in private practice when the responsibility for the case is his and his alone.

It is a simple matter to measure the number of degrees in the deviation of a patient with heterotropia. The problem is what to do once the amount of the deviation is known. It is an established fact that there are 360 degrees in a circle and that the circumference of the adult eyeball is in the neighborhood of 72 mm. If one divides 360 by 72, it will be found that each millimeter represents five degrees. The mathematical principle here is sound. However, the surgeon who expects to obtain 5 degrees of correction per mm. of surgery is doomed to many disappointments in dealing with the oculorotary muscles.

The young surgeon begins a search of the literature for some indication of exactly how much surgery to do when the heterotropia amounts to so-and-so many degrees. He will find some paper published on the subject with no great difficulty and will apply the figures given therein to his own case or cases. The results will be sometimes

gratifying but more often bewildering and bitterly disappointing.

After one or two such unfortunate occurrences, he will begin to search the literature anew until he finds another paper on the subject. Here again, some authority is saying that for so many millimeters of recession he usually obtains so-and-so many degrees of correction. The young surgeon applies these new and, we might add, different figures to subsequent cases but again the results will be confusing.

The surgeon finally concludes that no one knows a great deal about the subject and consequently that he knows as much as anyone. His technique in dealing with patients with heterotropia is from that time onward a trial-and-error one and is far from satisfactory.

AVERAGES MISLEADING

There is one basic fallacy in all papers which report on "degrees of correction per millimeter of surgery" and it is that the figures given are always *averages*. Such averages can be, and usually are, highly deceptive.

A good analogy may perhaps be found in a survey, let us say, of wages in various small industries. One industry may employ 20 persons whose salaries range from $100 to $300 per month; the *average* wage in this industry might be $200 per month. Another industry, also employing 20 persons, might have two high-powered publicity men with salaries of $1,600 per month while the rest of the employees get no more than $150 per month; the *average* wage in our second example might be $260 per month.

The conclusion implied by a knowledge of only the average wage figure per month with respect to the actual incomes of the individual workers in the two industries is obviously false. In exactly the same way, average figures for the results of muscle surgery are prone to be deceptive.

No TWO CASES ALIKE

It is extremely rare to find two patients with heterotropia whose conditions are identical, and yet innumerable patients can be found who have, let us say, 30 degrees of esotropia. The point to be recognized and emphasized is this: the 30 degrees of deviation is not particularly important; much more important is *why* the 30 degrees of deviation are present.

About the only thing that any two patients, both having 30 degrees of esotropia, share in common is the degree of their deviation and even that may vary from time to time. From an intimate knowledge of only one of these cases, we can say little or nothing about the other. A lizard and an elephant have little in common except that they are both vertebrates. An intimate acquaintance with a lizard does not enable us to say anything intelligent about the elephant unless we have also seen and studied the elephant.

Admittedly there is nothing new nor particularly startling in the foregoing considerations. The mere realization that there is much variation between two patients with identical amounts of heterotropia is small consolation to the surgeon who is faced with the necessity of correcting the deviation surgically.

CONSIDERATIONS IN PLANNING SURGERY

There are a number of points to be taken into consideration in planning surgery in the patient with crossed eyes and no one of them alone yields sufficient information to enable an accurate decision to be reached. Let us review these considerations briefly.

1. Age. How old is the patient? The same operation on a child will usually result in far more correction than on an adult.

2. Duration. How long has the tropia been present? The same operation will produce more correction on a tropia which has been present for a short time than on one that has been present for a number of years.

3. How variable is the deviation? The patient whose tropia measures 10 degrees on one visit, 30 degrees on another visit, and 20 degrees on a third visit will show far more correction from the same operation than will a patient whose tropia measures 30 degrees on every visit.

4. Do glasses reduce the deviation? The same operation will produce more correction in a patient whose tropia is reduced by glasses, that is, in which there is an accommodative element, than in one whose tropia is affected not at all by glasses.

5. How large is the deviation? The same operation will produce more correction in a patient whose tropia measures 45 degrees than one whose tropia measures only 25 degrees.

6. Is there obvious paresis? A patient whose tropia is the result of a mild paresis combined perhaps, with other factors will show more correction following the same operation than will a patient whose deviation is solely the result of a severe paresis.

7. What is the near point of convergence? If the convergence near point is poor, that is, remote, in a patient with tropia, secondary convergence palsy is present. The immediate postoperative effect of a recession of the medial rectus muscle is much less in a patient with secondary convergence palsy than in one with no such palsy.

8. What degree of fusion is present? Even small amounts of second-degree fusion will appear to increase materially the correction effected by an operation in the patient with heterotropia. This is true for obvious reasons.

9. Which are the offending muscles? There is no substitute for an accurate identification of the muscle or muscles involved in the patient with heterotropia. One will occasionally hear a surgeon remark that ". . . it makes no difference which eye one selects for surgery in heterotropia because the two eyes are conjugated and work as a team." Actually, nothing could be farther from the truth. Surgical attack on the correct muscle will give far more correction than the same operation performed on an improper muscle.

10. Which is the dominant eye? The deviation which is present with the dominant eye fixing is the deviation at whose correction the surgeon must aim. This is true whether it be primary or secondary deviation, although it is imperative that the type of deviation be known. The same operation will go much farther toward correcting secondary than primary deviation.

11. Is the tropia monocular or alternating? The same operation will usually result in greater correction in the patient with monocular heterotropia than in one with an alternating type of deviation.

12. Is the tropia constant or intermittent? The same operation will have a greater effect in an intermittent heterotropia than in a constant one.

PROBLEMS AT OPERATION

The points so far enumerated can be determined as easily by the orthoptist as by the surgeon. If these were all that mattered, the orthoptist would be perfectly competent to make detailed suggestions about the surgery to be performed in the patient with heterotropia. There are other factors to be considered, however—factors which can be properly evaluated only in the operating room. Let us consider them.

1. Effect of general anesthesia on the deviation. What happens to the deviation under general anesthesia? A patient whose esotropia disappears almost entirely or entirely under general anesthesia will show far more correction from the same operation than will a patient whose deviation is changed little if at all under the same circumstances. It should be stated here that the general anesthesia must be deep before the position of the eyes is evaluated; under shallow general anesthesia, esotropia often appears exaggerated while exotropia often seems to decrease in amount.

2. *What are the results of the forced duction test?* The forced duction test* may be used as an indicator, in the majority of cases, not of how much surgery to perform but of which muscles to attack. It should be obvious that the results of surgical attack on a primary offender will be greater than the same attack on a secondary offender. This point, which may seem vague, should be clarified in the next item for consideration. It does not refer to primary and secondary deviation.

3. *What anatomic anomalies are present?* The size, extent, and consequent significance of various anatomic anomalies found in connection with the oculorotary muscles in the patient with heterotropia should determine to a large extent the effect of surgery on these muscles. Anatomic anomalies frequently encountered are extra and thickened check ligaments, fused check ligaments, posterior check ligaments, foot-plate insertions, abnormal insertions, abnormal muscle slips, and abnormalities of the intermuscular membrane.*

4. *Elasticity of the muscle.* How elastic is the muscle which is being subjected to the surgical procedure? When severed from the globe, does it retract promptly into the orbit or does it retract slowly and incompletely? The greater the elasticity of a muscle, the greater the correction which will follow a recession of that muscle.

5. *Size of the muscle.* How large is the muscle? Recession of a large muscle will result in much more correction than recession of a small muscle for the same distance.

6. *Operative technique.* What is the technique of the surgeon? It might be thought that the operation of recession, for example, is a fairly well-standardized procedure. It is quite surprising, therefore, how many actual differences in technique may be found between two surgeons performing the same operation.

The surgeon who divides the check ligaments will get more correction than one who does not. The surgeon who severs the intermuscular membrane will get more correction than one who does not. The surgeon who finds and deals properly with anatomic anomalies will get more correction than one who does not. The surgeon who, inadvertently or not, strips the muscle of its sheath will get less correction than one who preserves it carefully intact. And yet both may be doing a recession operation.

Under the heading of operative technique should come the choice of the operation. Rather than attempting to perform many operations of different types and never performing any one procedure with a fair degree of skill, it is much wiser for the surgeon to practice one or two operations in order that he may master them. A perfectly suitable armamentarium is composed of one lengthening operation and one shortening operation. The recession and the resection will serve the average surgeon faithfully and well and neither is difficult.

7. *Postoperative care.* Immediate postoperative care in heterotropia is almost as important as is the operation itself. What might otherwise be a good result can be lost by lack of proper postoperative care. One is referring here to the use of atropine, glasses, orthoptics, or the prohibition of close work when any of these are indicated, either separately or in combination. The period of postoperative bandaging of the eyes is important with regard to the amount of correction to be obtained from the operation performed.

COMMENTS

It is obviously impossible for the orthoptist to evaluate any of the points listed in the second group for the very excellent reason that she is nowhere near the operating room. Such a decision must be made by the surgeon himself on the operating table. This point has been recognized by such leaders as Jameson, White, Kirby, and Prangen in the past 25 years.

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* Scobee, R. G.: Anatomic factors in the etiology of heterotropia. Am. J. Ophth., 31:781, 1948.

It is surprising how many surgeons are prone to ignore this latter group of points. They concentrate on the first group of findings and preoperatively formulate a rigid plan of procedure for the operating table— a plan from which they refuse to deviate one iota, irrespective of the findings at operation.

The situation is similar to that of a man who decides to drive to a neighboring community by a certain one of several possible roads and insists on taking that road even though he is told that the bridge has been washed out at the last minute. He is, of course, riding for a fall and deserves no particular sympathy.

It is not at all unusual to obtain as much as 25 or occassionally even 30 *degrees*—not prism diopters—of correction from a recession of a single medial rectus muscle in the patient with esotropia, provided the operation is properly done. On the other hand, a recession operation on the same muscle, when improperly performed, may yield no more than 4 degrees of correction.

With all of the points mentioned for consideration, two facts should by now be obvious. The first is that *average* figures for "degrees of correction per millimeter of surgery" are worthless. The second is that no two cases of heterotropia are alike and each must be treated on the basis of its own individual pecularities if the treatment is to be rational and thus successful.

The orthoptist can and should be a tremendous help to the surgeon in considering the first group of points, but he must consider the second group alone. It is distinctly unfair to the orthoptist if the surgeon seeks to force her to make suggestions about surgery when she cannot possibly know all of the important factors concerned prior to the actual operation itself.

Diagnosis and some forms of nonsurgical therapy may well be within the province of the orthoptist in handling cases of dysfunction of the oculorotary muscles. Surgical therapy for such conditions is in the province of the ophthalmologist alone. The orthoptist will readily agree with the latter fact. It is the surgeon who must be occasionally reminded of it.

640 South Kingshighway (10).

DISCUSSION OF DR. SCOBEE'S PAPER

WENDELL L. HUGHES, M.D.
Hempstead, New York

Dr. Scobee kindly sent me a copy of this timely, important, and constructive paper prior to his presentation. A great many points have been emphasized. Anyone who has read any of his papers must realize the background of research behind the opinions expressed. His opinions are not a rehash of opinions he has read or heard others express. They are an honest attempt to get at and present the truth. Whether all of his conclusions will bear the test of time, only time will tell.

For those of you who are liable to feel that it is the place of the orthoptic technician to advise as to how much of a shortening or lengthening procedure should be done in any specific case, it is well to bear in mind that there are a great many variables in the technique of the surgical procedures.

In a resection for instance, should one measure the distance from the front of the clamp to the position of insertion of the sutures through the stretched muscle as it is pulled forward at the time of insertion of the sutures or should one measure the unstretched muscle? The latter is obviously the

theoretically accurate measurement but it is the usual custom to measure the distance on the stretched muscle.

With this in mind, it is obvious that one is taking out more muscle tissue in a case where there is little stretching than in a case in which the muscle is weak and thin and stretches a great deal and, therefore, more correction will result in the case of the more rigid muscle from the same recorded amount of excision.

1. Where the forceps are applied to the muscle is a factor. There is a variation of a couple of millimeters in the location of choice of various surgeons. The portion anterior to the forceps is usually omitted from calculations. This portion retracts to the clamp as soon as it is severed. Some men will leave a millimeter or two of the tendon at the stump still attached to the eye, others will cut the muscle very close to the insertion.

2. The manner in which the sutures are placed and their number may cause variations. If the sutures are placed through the muscle and then the section of muscle cut off before pulling up the sutures, as in the original Reese technique, there will be a certain amount of longitudinal slipping of the sutures in the muscle and the effect will be only about two thirds of the effect produced by holding the muscle forward by the clamp and tying the sutures before excising the muscle section. Whether or not the same sutures are used to close the conjunctiva that are used in the muscle will account for some variation as compared to the technique where the conjunctiva is closed by a separate suture.

3. Whether or not the fascia is stripped entirely from the muscle is also a factor which was touched upon by Dr. Scobee.

4. In the recession operation many points of variation in technique will alter the results.

   a. Whether or not a clamp is used to place the sutures and how far back in the tendon the sutures are placed, or whether or not the fascia is included or is stripped back from the tendon or widely severed, as Dr. Scobee has mentioned, will all affect the amount of correction.

Anatomic variations have already been covered by Dr. Scobee in this and other papers.*

You are all very familiar with functional analysis and many points have been mentioned by Dr. Scobee. When convergence excess is present a weakening of the muscles that have to do with convergence, prorated as to the convergence-divergence relationship, will produce the most satisfactory result. Usually, there is a combination of convergence overaction combined with underaction of the divergence function. Then a combined surgical procedure designed to weaken the muscles having to do with convergence and strengthen the muscles having to do with divergence is best. The amount of surgery to be done on one set of muscles will be prorated according to whether the findings are more abnormal on near or on distance fixation. If the findings are more abnormal at near range, the muscles having to do with active convergence (the medial recti) will be adjusted particularly.

Of course, when one runs across anatomic variations one must also take them into consideration in determining what and how much surgery to do.

One could continue for hours on a more or less futile compilation of the difficulties that beset the attending surgeon in cases of strabismus, but I believe more will be accomplished by the summary of some exemplary cases than in any other way.

In cases of convergence excess combined with a secondary divergence in sufficiency, with a moderate amount of latent hyperopia (over 1.500), and 20/30 vision or better with each eye, the following amounts of recession and resection are planned.

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* Scobee, R. G.: Am. J. Ophth., 31:781, 1948.

With an esotropia of 35△ for distance and 45△ for near, which is reduced to 25△ for distance and 35△ for near by the use of a nearly full correction of the latent hyperopia present, I have been in the habit of doing first a recession of 4 mm. on one medial rectus and a resection of 5 mm. of the lateral rectus of the same eye.

The technique of the recession was to dissect the conjunctiva and fascia down to the tendon and sever the fascia along the muscle for about 12 mm. and to sever the check ligament as well. One double-armed, 3-0 catgut suture was looped transversely over the central fibers at a point about 2 mm. back from the actual insertion and then the tendon was cut off at the insertion. The needles were then inserted into the outer one third of the sclera at a point 4 mm. back from the insertion.

Strictly speaking this is a recession of only about 3 mm. when the extra amount of tendon in front of the suture is considered and allowance is made for the slight amount of slipping of the suture longitudinally in the fibers of the muscle.

The conjunctiva was then closed with a separate continuous mattress 5-0 catgut suture.

The lateral rectus was likewise cleaned and the check ligament cut. Then a resection forceps was applied to the muscle about 2 mm. back from the insertion. The muscle was then cut off leaving about 0.5 mm. of tendon as a stump. The muscle was then stretched moderately forward and the central needle of a triple-armed suture* was passed from without in through the muscle 5 mm. back from the front of the blade of the resection forceps and then passed forward to the insertion stump.

The end needles of the suture were then passed through the respective margins of the muscle at the same distance back from the blade of the forceps and then passed through the margin of the tendon stump. The suture was then cut at the position of the central needle thus making two sutures. The muscle was then pulled forward and the stump pulled back so there would be no longitudinal slipping of the suture in the muscle. Each suture was then tied, pulling the muscle tightly to the tendon stump. Then the muscle was cut transversely in front of the sutures and the conjunctiva united by a continuous mattress 5-0 catgut suture.

If, in the above case, there had been 45△ of esotropia for distance and 60△ for near, I would have chosen to do a similar recession of 4 mm. and a resection of 7 mm. If more effect is needed an additional recession of 3.5 to 4 mm. on the medial rectus of the other eye would be done.

These figures may serve as a guide, if the above mentioned technique is followed. One could continue this discussion for days but I think that the points that Dr. Scobee has brought out are particularly important. This discussion is specifically prepared from the surgical standpoint since you are all quite familar with the orthoptic points which he has brought out.

131 Fulton Avenue.

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* Lisman, J. V.: A triple-armed suture for resections. Am. J. Ophth., 31:466, 1948.

THE CLINICAL ASPECTS OF SYMPATHETIC OPHTHALMIA*

HAROLD H. JOY, M.D.

Syracuse, New York

There is evidence that sympathetic ophthalmia was recognized nearly 1,000 years ago, but its first accurate description was given by McKenzie in 1840. Although a vast amount of clinical and experimental investigation has been carried on during the past century, its pathogenesis is still unsolved. Consequently, there is no method of determining individual susceptibility or of ascertaining the imminence of its onset, and there is no specific therapy for its prevention or cure. Attempts to produce the disease experimentally and to find an offending organism have been unsuccessful. The two most generally accepted pathogenic theories are that it is produced by an exogenous infection or that it is the result of an allergic reaction to uveal pigment, or that both processes are involved.

INCIDENCE

Its occurrence is relatively infrequent with an estimated general incidence of about 0.15 percent of all eye diseases and an incidence of 1 to 2 percent of all perforating injuries. It may occur at any age and, although it is most frequent in children, their particular susceptibility has not been proved.[1] Males are much more frequently affected than are females, probably due to their greater exposure to injury.

It has been suggested that certain individuals have an acquired or hereditary sensitivity, and that others, such as Negroes who are rarely affected, have an immunity. Several authors have commented on the rarity of sympathetic ophthalmia in arid climates and have noted the greater likelihood of its occurrence during the wet and cold seasons. For some reason, during times of war, the incidence is lower in the armed

forces than in the civilian population. This has been ascribed to the prompt and proper care of eye injuries of the military personnel, to their better physical condition, and to the possible prophylactic value of the various sera which all receive. It has been stated on numerous occasions that the incidence of the disease has decreased in recent years. However, a review of the literature of the older writers, in which all manner of varieties of ocular inflammation have been diagnosed as sympathetic ophthalmia, indicates that the decrease is more apparent than real.

PREDISPOSING CAUSE

The predisposing cause is almost always a perforating wound involving the ciliary body or the root of the iris, particularly if there is incarceration of uveal tissue or lens material. In such cases the wound does not heal promptly, and the danger of late infection is added to that of immediate contamination and uveal constriction. On the other hand, perforating wounds of the cornea, with a nonprotruding iris prolapse anterior to the limbus, and clean, promptly healing wounds of the sclera behind it, are relatively safe. As a rule, large limbal wounds offer more danger than small ones, since they remain open longer and the uveal prolapse is apt to be more extensive. Strangely enough, sympathetic ophthalmia rarely follows the spontaneous rupture of corneal ulcers. In these cases, the inflammatory reaction produces a fibrinous exudate which soon seals off the exposed area.

The disease seldom occurs unless there is a frank opening in the globe. However, it may follow nonperforating trauma or, more rarely, a disintegrating melanoma of the uvea. In either case there is almost always a subconjunctival scleral rupture, and it is possible that the offending agent enters the

eye through minute abrasions of the conjunctiva, or that it penetrates the uninjured conjunctiva.

The presence of pyogenic bacteria in the globe lessens the hazard of sympathetic involvement by tending to destroy the uveal tissue and whatever is the causative agent. However, it does not provide insurance against its occurrence for some uveal tissue may be retained and, as the globe becomes phthisical, it may become a potentially exciting eye.

About 85 percent of cases result from perforating wounds, and about 65 percent are accidental.[2] The nature of the object causing the injury is relatively unimportant so long as an iridocyclitis is produced. An analysis of 436 proved cases of sympathetic ophthalmia showed that 20.9 percent were attributed to intraocular operations.[3] This relatively high incidence is understandable in view of the fact that most operations involve the iris, and many also involve the lens. Moreover, as the presence of inflammatory or degenerative changes possibly increases the danger, cataract and glaucoma may be of some importance as predisposing causes.

Although it is occasionally impossible to discover an extenuating circumstance to account for postoperative sympathetic inflammation, it is probable that some such cause is frequently present. This was found to be true in 58 percent of 44 confirmed postoperative cases which I studied.[3] In some cases a predisposing pathologic process was found in the exciting eye preoperatively, in others an accident occurred during the operation or shortly afterwards, while in some a second operation was performed. De Grosz[4] has called attention to the fact that repeated operations add to the danger of sympathetic involvement.

Cataract extraction is the most common predisposing cause of postoperative sympathetic ophthalmia. Statistics are not available to show how much of this is due to the frequency of cataract operations, and how much is due to any particular danger of the condition. Extracapsular extraction offers more danger than if the lens is removed in its capsule, because of the greater likelihood of delayed wound healing as a consequence of incarceration of uveal tissue or lens material.

Another important predisposing factor is the development of phaco-anaphylaxis caused by retained lens cortex in the anterior chamber. This is probably the most frequent cause of sympathetic ophthalmia after discission of congenital cataracts.

Although the intracapsular method of extraction obviates the danger caused by lens material, the necessarily large incision favors the occurrence of iris prolapse which, after all, is the most important element in producing sympathetic disease.

Glaucoma operations would seem to offer a favorable field for the development of sympathetic inflammation. For most of the operations which have been devised to relieve intraocular pressure permanently expose the uvea to infection, while the inclusion operations offer the added hazard of iris incarceration.

It has been frequently stated that sympathetic disease does not often follow iridectomy, for generally the operative trauma to the ocular tissues is not marked, iris prolapse is infrequent, and a keratome incision heals promptly and securely. However, three cases followed iridectomy in my series.[5]

Although the deliberate incarceration of the iris seems contrary to good surgical procedure, iris-inclusion operations have become increasingly popular in recent years because of their efficacy in reducing intraocular pressure. Surprisingly enough, it does not appear to be a frequent cause of sympathetic ophthalmia. However, some ophthalmologists have abandoned its use because of this danger. Its substitution by trephination lessens somewhat, but does not eliminate, the hazard; and it offers the added possibility of late pyogenic infection and subsequent loss of the globe.

So long as a glaucomatous eye remains

hard after operation, the chance of sympathetic involvement is remote. However, the very low postoperative tension that sometimes follows may not always be due to filtration, but may be the result of postoperative iridocyclitis. Such a globe is approaching atrophy and may be the precursor of sympathetic inflammation.

Cyclodiathermy and operations for retinal detachment do not favor the development of sympathetic ophthalmia, for the uvea does not prolapse. The reaction causes the openings to close almost immediately and the tissues tend to shrink away from the wound because of their elasticity.

INCUBATION PERIOD

One of the most confusing aspects of this disease is the extreme variability in the interval between injury and the onset of inflammation in the fellow eye. Apparent authentic cases are on record in which this interval ranges from a few days to as long as 49 years. However, in the vast majority of cases, the incubation period extends from 1 to 3 months, with the greatest incidence occurring during the second month. There is usually little to fear after three months have passed, and practically no danger after one year. The diagnosis should be scrutinized closely if the fellow eye becomes affected in less than 14 days after injury or if the interval is greater than one year. Close study of many cases with an apparent extremely long incubation period will show some extenuating circumstances, such as a more recent second injury or operation.

CLINICAL PICTURE IN INJURED EYE

Although there is no characteristic clinical picture in the injured eye to give warning of the onset of sympathetic inflammation, there is usually more or less evidence of the likelihood of impending danger. Eyes which should be viewed with most suspicion are those which, after a penetrating wound involving the ciliary body or the root of the iris, are followed by a prolonged low-grade uveitis which is resistant to treatment and is subject to occasional exacerbations with a tendency to recurring ciliary pain and to phthisis. The danger is in close proportion to the incidence of prolonged inflammation.

On the other hand, the injured eye may give little or no indication that sympathetic ophthalmia is threatening, for the type and degree of inflammation which may be present is almost limitless. It may exhibit the clinical signs of a severe acute traumatic uveitis, or those of a mild inflammatory process that is apparently subsiding without complication. Although the inflammatory signs may be slight, careful examination will show evidence of congestion, for it is always present when sympathetc uveitis appears.

Once sympathetic ophthalmia has started, the congestion in the exciting eye increases and, according to Irvine,[6] runs a parallel course, with exacerbations and remissions occurring coincidentally in the two eyes.

CLINICAL PICTURE IN SYMPATHIZING EYE

Sympathetic ophthalmia may originate posteriorly in the choroid, but it almost always appears first as a mild iritis which gradually develops into a prolonged plastic uveitis, characterized by massive cellular reaction, and subject to exacerbations and recurrences. The iris soon becomes thickened and rigid and more and more resists dilatation. In spite of comparatively mild inflammatory symptoms, exudation is marked, and there is early and persistent development of posterior synechias, and gradual secondary involvement of all the ocular tissues.

With the exception of defective vision the subjective symptoms are notable for their mildness. Ciliary tenderness may be present throughout the course, and pain may occur as the result of an accompanying scleritis or of secondary glaucoma.

The onset is insidious without premonitory signs. Dimness of sight is almost always the first symptom and is usually due to a mild serous cyclitis. Examination at this time reveals bedewing of the corneal en-

dothelium, a few posterior corneal precipitates, and slight clouding of the aqueous. According to Irvine,[6] the corneal precipitates appear in this eye before or simultaneously with their occurrence in the exciting eye. Within a day or two, ciliary congestion can be observed, the iris shows slight furring, a few fine posterior synechias can usually be seen, and the disc is frequently blurred. At the outset, the vitreous is usually clear, but small opacities soon appear and rapidly increase in number, causing a generalized cloudiness and, later, disintegration.

Meanwhile, the inflammation in the anterior segment has continued to progress. The corneal precipitates increase in number, the aqueous becomes more turbid, and the posterior synechias further develop, tending to produce seclusion or occlusion of the pupil. Even if there is partial mydriasis, peripheral adhesions may form, binding the entire posterior surface of the iris to the lens, which shows early capsule clouding and frequently later cataract formation. At this stage the iris has a muddy, velvety appearance and the stroma loses its fine details. Woods[1] describes a characteristic change which usually appears not earlier than the second month in which the iris and lens capsule become almost confluent, with vessels from the iris invading the pupillary membrane.

The media usually become so cloudy after a few weeks as to obscure fundus details. But in arrested cases, small yellowish lesions of chorioretinitis are sometimes seen scattered about the periphery. The intraocular pressure is often reduced and the globe may become very soft but usually some degree of glaucoma occurs as the result of the posterior synechias or of the increased protein content of the intraocular fluids. If this is not relieved, vision is destroyed and phthisis bulbi follows.

Fortunately, early and well-directed treatment usually checks the progress of the inflammation before vision is destroyed. And occasionally there are mild cases which seem to recover regardless of treatment. However, the course is usually long drawn out, characterized by exacerbations and relapses, and lasting 9 or 10 months in the well-treated and favorable cases, and sometimes extending for years in those which progress to blindness.

DIAGNOSIS

The clinical diagnosis cannot be made with absolute certainty since the picture in the exciting eye is not characteristic and may be masked by the results of trauma and infection; and symptoms identical with those found in the sympathizing eye can be due to other causes. The various serologic diagnostic aids, which have been advocated from time to time, have not proved constant; hence, the presumptive diagnosis must be made by ophthalmic signs alone.

The diagnosis will be more likely the more closely the case fulfills the following conditions: (1) The presence of uveal inflammation in the injured eye caused by exogenous infection, particularly if there is inclusion of uveal tissue or lens matter in the wound. (2) A reasonable interval (usually 2 to 3 months) between injury and the onset of inflammation in the fellow eye. (3) The presence in the fellow eye of the rather characteristic plastic uveitis with early development of keratic precipitates. (4) Proof that this inflammation is not due to some other cause such as focal infection, syphilis, sarcoid, or tuberculosis. While a presumptive diagnosis may thus be made, the only means of making a positive diagnosis is by histologic examination of uveal tissue.

PROPHYLAXIS

Sympathetic ophthalmia is much easier prevented than cured. The salient prophylactic measures comprise prompt and proper treatment of accidental perforating wounds, correct procedures in intraocular surgery, and particularly if the progress is not satisfactory, careful and repeated slitlamp studies of both eyes until all danger has passed.

Above all, it is of paramount importance to remove the injured eye promptly if indicated.

Evisceration is not an effective prophylactic measure, probably because of the occasional retention of uveal tissue. Owing to the possiblity of extraocular extension of the process, the enucleation should be done freely, including removal of the muscular insertions and as much of the optic nerve as possible. On the assumption that potentially active material may still be left behind, Samuels[7] has suggested postoperative radiation of the socket.

Although no definite criteria for prophylactic enucleation can be laid down, there are certain rules which, if followed, will lessen the danger of sympathetic ophthalmia. Hopelessly injured eyes and those with vision destroyed by suppuration should be promptly removed. It is also usually advisable to remove blind eyes resulting from old injuries, and even those with light perception but with faulty projection, for they are potentially dangerous. This is particularly true if they are subject to recurrent ciliary congestion and lowered intraocular pressure.

As a rule, prophylactic enucleation is contraindicated if there remains any degree of vision. However, if vision is reduced to light perception in the injured eye and is good in its fellow, enucleation may be indicated in the following conditions: (1) In patients who cannot be controlled. (2) If there is marked ciliary tenderness and low intraocular pressure persisting for as long as three weeks after injury. (3) In extensive wounds involving the ciliary body accompanied by uveal and vitreous prolapse, if not seen within 24 hours after the injury, and in which there is little hope of useful vision.

Sympathetic ophthalmia can always be prevented if the injured eye is removed before the appearance in it of the specific pathologic changes, and it can usually be prevented if removed before such changes occur in the fellow eye. Hence, the shorter the interval between injury and enucleation the greater the prophylactic value. Removal of the exciting eye within two weeks after injury almost always prevents sympathetic involvment, but further delay lessens or nullifies the favorable effect.

If sympathetic inflammation does not follow within two weeks after enucleation of the exciting eye, the chance of it occurring is slight, and it almost never occurs after one month. However, because of the fact that it may appear after a longer interval, it is advisable to make repeated slitlamp studies of the fellow eye for a considerable period after removal of a suspected eye.

If the onset of sympathetic ophthalmia is feared, the pupil of the uninjured eye should be fully dilated in anticipation of inflammation, systemic treatment started, and daily examinations made with the slitlamp.

TREATMENT

To be at all effective, treatment must be started early, and it must be thorough. It is quite generally agreed that enucleation of the exciting eye has little or no favorable effect after sympathetic uveitis is once established. However, cases are occasionally reported which tend to refute this opinion. So, until it has been definitely proved ineffectual, a blind exciting eye or one with grossly faulty projection should be promptly removed, at least in early cases. On the other hand, if it offers any hope whatever of retaining or regaining any degree of vision, it must not be sacrificed, for in the end it may be the better eye.

Practically all that can be done in treating the sympathizing eye is to attempt the establishment of maximum mydriasis. This is usually most difficult, due to extensive posterior adhesions, and to a lesser extent the rigidity of the iris. The development of secondary glaucoma, while potentially very serious, need not necessarily cause undue alarm since, as a rule, the sympathizing eye withstands increased intraocular pressure

fairly well. In many mild cases, particularly if due to increased protein content of the intraocular fluids, the period of hypertension is brief and subsides during the continued use of mydriatics. In others, repeated corneal paracenteses may tide over the acute phase. Any surgical measure involving the uvea should be postponed if possible, for it is notoriously sensitive to operative interference.

No form of systemic treatment has proved entirely adequate. The use of massive doses of salicylates and nonspecific foreign-protein therapy, particularly in the form of diphtheria antitoxin, appear to be the most effective, especially if supplemented by desensitization through uveal pigment. The intravenous injection of arsenicals, tuberculin therapy, and autoserum therapy have many advocates, but have proved of doubtful value. The sulfonamides and penicillin have, on the whole, been most disappointing; and it is yet too early to assess the value of streptomycin.

Because of the devastating nature of the disease, its uncertain etiology, and the lack of a truly adequate form of treatment, there is a tendency to use too many therapeutic agents and to use them excessively. This not only results in confusion of values but may lower resistance to the specific infection. "Shot-gun" treatment must therefore be avoided.

Since the course of the disease is long drawn out and debilitating, the bodily resistance should be aided in every possible way. A complete physical and serologic examination is mandatory, and proper attention must be given to any abnormalties, with particular attention to foci of infection. Bed rest is essential during the inflammatory episodes, and hospitalization is necessary until well after complete subsidence of inflammation in favorable cases, and only when all hope is abandoned in those with an unfavorable outcome. After hospital discharge, repeated follow-up examinations with the slitlamp are most important, for

recurrences and exacerbations are characteristic of the disease.

Even in successfully treated cases the battle with sympathetic ophthalmia is not always won with the subsidence of inflammation, for cataract and glaucoma are frequent complications or sequelae. No conditions tax the judgment and skill of the ophthalmic surgeon more, for while the exciting eye tolerates operations well, the sympathizing eye is extremely sensitive even after a long period of quiescence. This sensitivity may often be reduced by uveal-pigment therapy or by injection of diphtheria antitoxin before the operation. If surgical intervention is necessary, it should be done with a minimum of trauma, particularly to the uvea. Except in a grave emergency, it is advisable to delay the operation for at least one year after all signs of inflammation have disappeared.

PROGNOSIS

The prognosis of sympathetic ophthalmia is always uncertain, chiefly because of variation in degree of severity, the reasons for which are unknown. Many authors have maintained that generally the course is unusually severe and the outcome less favorable in children and after cataract extraction. However, there are too many variable factors present to ascribe importance to any particular type of case. The prognosis is viewed today with much more optimism than in former years, principally because of the earlier recognition of the disease and to a better understanding of the importance of starting treatment promptly. Indeed, the most important prognostic factor over which we have control is the early institution of prompt and proper therapy.

The statistics of various authors indicate that a favorable prognosis may be expected in two thirds of the cases in which therapy is prompt and adequate. The results of my studies would seem to bear this out, for useful vision resulted in 73 percent of the patients for whom treatment was started within two weeks of the onset, compared

with 37.5 percent in those for whom it was delayed for one month or more.[2] Unfortunately, a great many patients are not seen until the disease is well advanced, and the outcome in these cases is likely to be unfavorable in spite of all treatment. Considering all cases, vision of 20/200 or better may be expected in a little over one half.

- *504 State Tower Building.*

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ARIBOFLAVINOSIS

WITH A CASE REPORT ON PARENCHYMATOUS KERATITIS FOLLOWING RIBOFLAVIN DEFICIENCY

B. K. DAS GUPTA,* M.B.

Calcutta, India

It is barely eight years now that riboflavin has attracted the attention of the ophthalmologists of the world. Since the publication of the paper by Sydenstricker, Sebrell, Cleckley, and Kruse[1] in which they described the ocular signs of ariboflavinosis in man, several workers in different parts of the world attributed different types of lesions of the eye either to riboflavin deficiency or to vitamin-B–complex deficiency. Up until now, no clear-cut picture of ocular manifestations due to riboflavin deficiency has been made out and it is clear that, as the years go by, with the advancement of knowledge, reports of various types of ocular manifestations, which will be attributed to riboflavin deficiency, will pour in.

The components of the vitamin-B–complex group probably act as synergists. In the series of cases described by Sydenstricker, nicotinic acid, thiamin chloride, ascorbic acid, and cod-liver oil were added to the diet in order to make the deficiency of riboflavin a dominating one. Ocular signs may be noticeable before the disorders make their appearance.

Subjective symptoms, such as photophobia and dimness of vision, seem to appear first and on examination circumcorneal injection is seen. The description given by Sydenstricker and others is: "The earliest change that can be recognized with the slitlamp is marked proliferation and engorgement of the limbic plexus with the production of great numbers of very narrow capillary loops which outline the extreme margins of the scleral digitations and obliterate the narrow avascular zone between the plexus and the sclerocorneal junction. . . . Such capillaries lie just beneath the epithelium and soon anastomose to form a tier of loops from which more single capillaries arise, extending centripetally."

Bessey and Wolbach[2] showed that ocular signs of ariboflavinosis could be produced experimentally in rats, and pointed out that the earliest detectable sign is corneal vascularization. Some observers include congestion or engorgement of the normal loops in this category, and Gregory[3] pointed out, in 1943, that there was no discrimination in the literature between a full limbic plexus and an actual invasion of the cornea by new vessels.

Mann[4] says that it would be unwise to include the full limbus among signs of riboflavin deficiency, the earliest certain signs of which would seem to be a budding out

* Professor of Ophthalmology, Medical College, Calcutta.

of new capillaries from the limbal loops at their apices, with extension on to the true cornea.

McCreary, Nicholls, and Tisdall[5] photographed the sclerocorneal junction with the ophthalmic camera and found that the results obtained were not significantly different from slitlamp examination of the corneoscleral junction. Out of 41 individuals studied, who had been provided with a ration containing 2.9 mg. of riboflavin per day for a period of one year, 50 percent were given a supplement of 3.3 mg. of riboflavin three times a day for two months. They did not find any consistent change in corneal vascularization in either the treated subjects or the controls.

Day, Langston, and O'Brien[6] reported on the clinical manifestations in experimental animals on diets deficient in riboflavin. These mainly consisted of alopecia around the eyelids and excessive lacrimation. Pappenheimer reported on the histologic examination of the cornea of one of these rats and found "a very slight keratitis and some newly formed blood channels."

Day, Langston, and O'Brien reported, in 1931, on ocular changes in 37 rats fed on a diet deficient in riboflavin. They found anterior interstitial keratitis in 100 percent and cataract in 94 percent. Microscopic examination revealed an inflammatory process in the anterior stroma. The epithelium was normal but there were subepithelial small lymphocytic and leukocytic infiltrations accompanied by new blood-vessel formation.

In 1935, Bourne and Pyke,[7] in similar experiments, were able to produce cataract in only 31 percent of the animals after a period of 79 days on the diet, and they stated that the most consistent ocular sign was "superficial keratitis," which occurred in 92 to 100 percent of the rats within 70 days.

Das Gupta,[8] in 1943, described a case of parenchymatous keratitis following riboflavin deficiency. In his case the endothelium of the cornea and deeper parts of the substantia propria of the cornea were affected, but there was no new vessel formation at the sclerocorneal junction which invaded the cornea. The patient was given 4 mg. of riboflavin daily and the whole cornea cleared up in 29 days.

Cosgrave and Day,[9] in 1942, reported on 28 patients with corneal diseases treated with riboflavin. The results varied considerably. Cases of interstitial keratitis associated with hereditary syphilis responded much more rapidly when riboflavin was administered along with antisyphilitic treatment than when the antisyphilitic treatment alone was given.

Sebrell and Butler[10] described in detail the general signs of ariboflavinosis in man. The lips may become abnormally red and cracks may appear at the angles of the mouth. There is seborrhea and follicular keratosis of the forehead, malar and chin eminences. The tongue shows signs of glossitis and there may be fissuring of the tongue.

Johnson and Eckhardt,[11] in 1940, reported that rosacea keratitis improved with riboflavin therapy; whereas, recently Fish[12] has contradicted the statement. Karunakaran and Nair[13] described a condition of the skin of the scrotum, in which it becomes dry and scaly and causes considerable itching in cases of riboflavin deficiency along with the eye and mouth lesions (oro-oculo-genital syndrome).

CHEMISTRY AND PHYSIOLOGY OF RIBOFLAVIN

Riboflavin has long been known to be combined with phosphoric acid and a protein to form Warburg's yellow enzyme (Johnson).

A.

A. Riboflavin

B.

$$CH_2-O-PO(OH)_2$$
$$HO-C-H$$
$$HO-C-H$$
$$HO-C-H$$
$$CH_2$$

Protein

H₃C, N, N, C=O

H₃C, N, NH, C=O
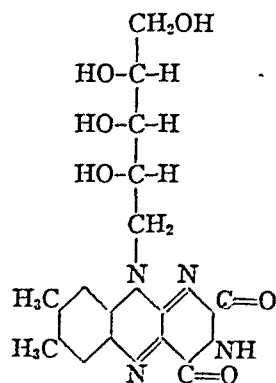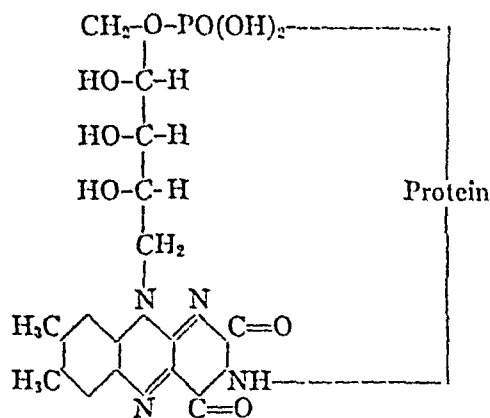
B. Warburg's yellow enzyme

Sydenstricker, Kelly, and Weaver[14] maintain that riboflavin, nicotinic acid, and thiamin are the reactive components of several co-enzymes necessary for the fractional dehydrogenating process, which results in the utilization of energy from carbohydrate. Riboflavin is also necessary for intracellular respiratory processes and, like other vitamins, is supposed to be present in every living cell.

It is believed that, if hemin substances are not present in a tissue (for example, avascular cornea), the oxidation within the cell is accomplished by Warburg's yellow enzyme. A deficiency of riboflavin seriously impairs the intracellular oxidative process. Proliferation of capillaries from the limbic plexus seems to be an attempt to combat localized anoxemia by bringing hemin substances into close proximity with the tissues. When riboflavin is administered in sufficient amounts, regression of the proliferated capillaries occurs.

OCCURRENCE OF RIBOFLAVIN IN THE BODY

Riboflavin occurs largely in a free state in secretions such as milk and urine. In tissues it occurs in a combined state with adenylic acid, a phosphate group and a specific protein, most of which do not fluoresce. Prolonged dialysis may release riboflavin from tissues but this is probably due to breakdown of flavoproteins. Estimation of riboflavin depends either on its property of fluorescence, a method described by Najjar,[15] or on the microbiologic method, as worked out by Snell and Strong,[16] that depends on the growth rate of certain bacteria, which varies with the concentration of riboflavin in the medium. The Snell and Strong method of estimation is the one of choice, at the moment, for it enables an accurate estimation of very small amounts of riboflavin. It has been estimated that an adult man requires about 3 to 5 mg. of riboflavin per day.

CASE REPORT

History. P. C. B., a Hindu businessman, a native of Howrah, was seen on October 30, 1947. He gave the history of a slight redness in the right eye followed by gradual loss of vision during the last five months. He was seen by several eye specialists of Calcutta, who gave him atropine drops for his right eye along with milk injections. Wassermann and Kahn tests were negative but still he was given a course of arsenic and bismuth, and to no effect. His vision was very much reduced and he said that his eye was getting worse day by day.

On examination, the right eye showed slight circumcorneal injection. There was slight watering from the affected eye. The photophobia was of moderate degree and there was slight ptosis.

Except for a small rim at the periphery on the temporal side, the cornea was grayish white. There was no encroachment of the limbic plexus on to the cornea. The opacity was almost homogeneous. No keratic precipitates were seen. Vision was 1/60 in the right eye. In the left eye, vision was 6/6 and the fundus was healthy.

On slitlamp examination, it was found that all of the cornea except the epithelium was densely infiltrated. No blood vessel was seen. There were no keratic precipitates. The endothelium was very ragged in outline. Infiltration was much more dense in the posterior part of the stroma than in the anterior part.

General examination. The patient was rather thin but looked quite healthy otherwise. He lived on an average Bengali diet
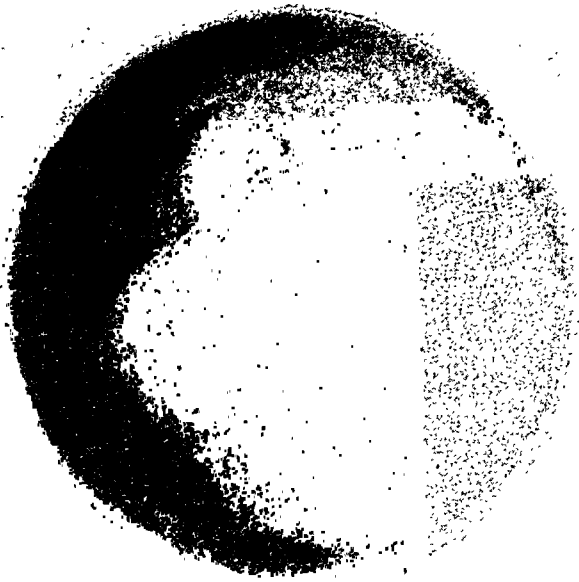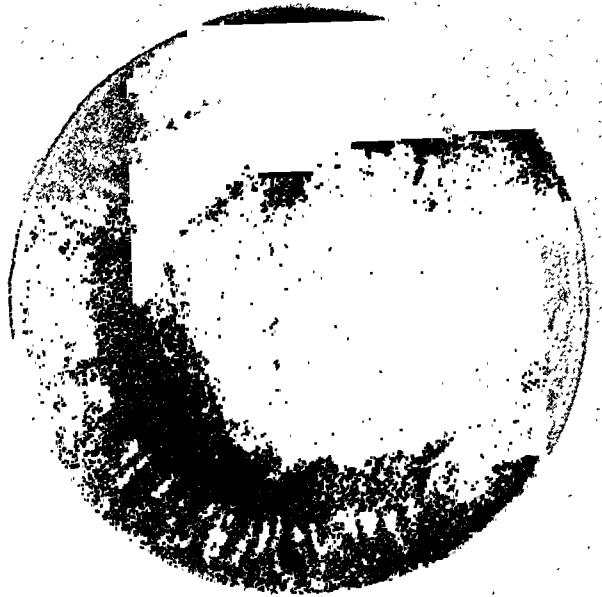
FIRST STAGE   SECOND STAGE
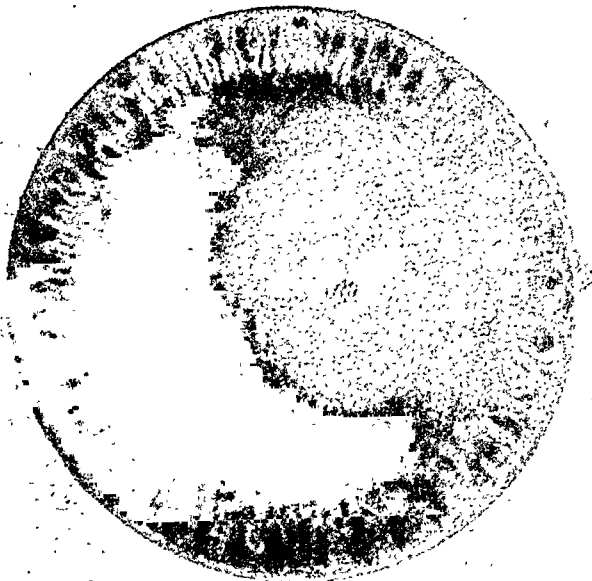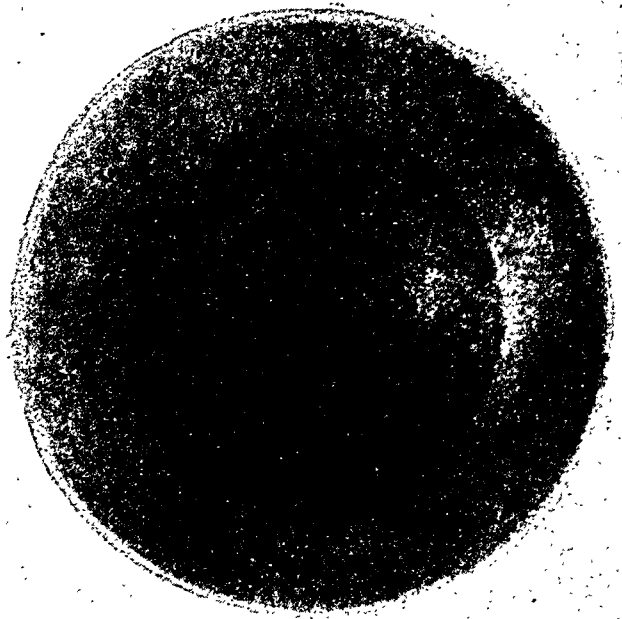
THIRD STAGE   FOURTH STAGE
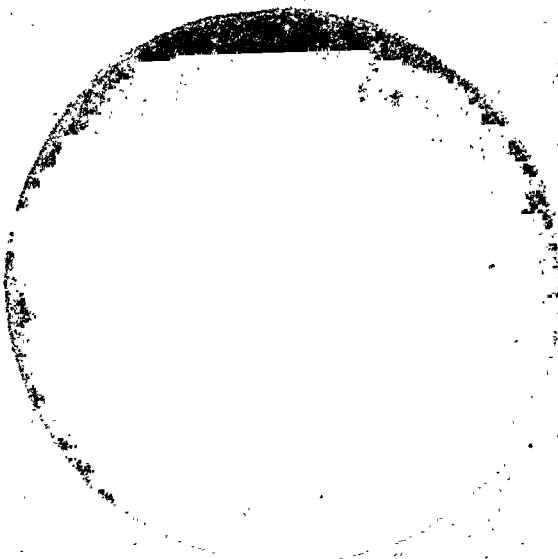
Fig. 1 (Das Gupta). Drawings showing the appearance of the eye at various stages during riboflavin treatment. (1st stage) Before treatment was started. (2nd stage) 12 days later after 120 mg. of riboflavin had been administered. (3rd stage) 30 days after treatment was started and after the administration of 300 mg. of riboflavin. (4th stage) After the administration of 520 mg. of riboflavin—at the end of 52 days of treatment. (5th stage) 65 days after treatment was started. 650 mg. of riboflavin had been administered.

FIFTH STAGE

consisting mainly of rice, dal, fish, and vegetables. There were no other signs of ariboflavinosis—no angular stomatitis, glossitis, fissuring of tongue, or scurfiness of the skin of the scrotum.

Treatment. Locally, atropine ointment (1 percent) was applied once every day. He was advised to put on dark goggles. One ampule of Beflavin (Roche) containing 10 mg. of riboflavin was injected intramuscularly every day.

After about 12 injections (120 mg. of riboflavin), the patient showed signs of improvement. The photophobia and epiphora were much less and the corneal haziness looked less dense. Beflavin was continued and, after about 25 injections (250 mg. of riboflavin), the opacity started to clear from the periphery. The patient was given 78 injections (780 mg. of riboflavin) before the whole cornea cleared up. The central part of the cornea was last to clear.

Before the cornea had cleared up completely, the central opacity became fragmented. If anyone had seen the case at this stage, he would have mistaken it to be an old case of superficial punctate keratitis. I personally gave the injections and watched the progress of the case from day to day.

The patient now has a normal cornea, possibly a bit thinned, and his vision is about 6/9.

SUMMARY

1. General ariboflavinosis is reviewed
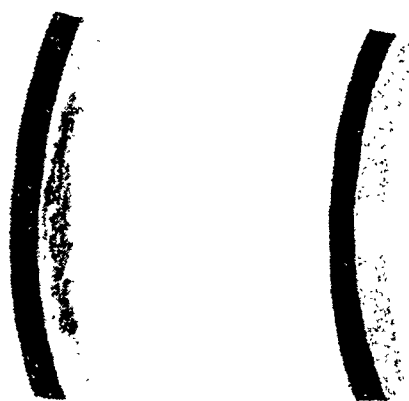
Before Treatment   After Treatment

Fig. 2 (Das Gupta). Slitlamp appearance of the eye before and after treatment.

with special reference to ocular manifestations.

2. A case of parenchymatous keratitis, which improved markedly with riboflavin given parenterally as the only therapy, is described.

3. Notable features of the case are that there was no abnormal growth of blood vessels from the limbic plexus on to the cornea and that all the layers of the cornea except the epithelium were involved.

Medical College Hospitals.

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FURTHER STUDIES IN AMBLYOPIA

J. B. FELDMAN, M.D.
Philadelphia, Pennsylvania

In a previous paper,[1] I suggested a new device for an easier, as well as more rapid, treatment of amblyopia. Since that time, more experience has been gained both in the use of the instrument and in the phenomena of amblyopia.

Ordinarily the great majority of cases with refractive errors but with normal fundi are corrected by glasses. By comparison the amblyopic cases are few, and these patients are instructed to use either a patch or a mydriatic to the good eye depending on the extent of the refractive error. Unfortunately these instructions are not always rigorously adhered to, and the treatment is discontinued by the patient until the time for the next refraction. When the patient returns after 1 or 2 years for reëxamination and shows a persistently poor monocular vision, the previous tentative diagnosis of congenital amblyopia naturally appears verified, and little more attention is paid to the amblyopic eye.

Undoubtedly amblyopia is a condition far more prevalent than is ordinarily realized. With the aid of the telescopic amblyoscope, one can easily arrive at a prognosis. This will eliminate undue hardship in that the eye need not be patched continuously, and will relieve the examiner of embarrassment because the treatment was not effective anyway.

Associated with amblyopia there may often be a muscular imbalance, suppression, abnormal correspondence, and some or all of these together, with or without strabismus. As a result of these, or possibly independent of these obstacles, there may be a psychologic background, the correction of which may materially affect the improvement or cure in a number of cases.

TREATMENT

Briefly the initial examination consists in taking the vision on four or more different Snellen charts, including the vision through the telescopic amblyoscope. If the latter instrument shows normal vision for the amblyopic eye,* treatment is suggested. An orthoptic examination should be made in order to recognize all the obstacles present. An attempt is then made to correct these obstacles at the same time. The visual acuity is corrected to the best vision obtainable.

Lessons on the telescope are given once a week, with daily lessons for work at home. Twelve lessons are given followed by a month's rest period to assure the permanency of the visual improvement. The patch and some exercises may be used during this rest period. If, on return, the case is not entirely improved, but an examination by the telescopic amblyoscope shows a possibility of further improvement, another course of treatment is suggested. Ordinarily two courses of these treatments have proved beneficial; rarely, are more advisable.

The recession of a line on the Snellen chart on return after the rest period is no bar to further treatment provided the reading on the telescopic amblyoscope approaches normal vision.

It should be remembered that just the attainment of normal vision in an amblyopic eye is not sufficient. The permanency of good visual acuity is assured only when good duction is firmly established, and thus fusion with amplitude is gained. For this reason, associated orthoptic training is necessary.

OBSERVATIONS
AMBLYOPIA ASSOCIATED WITH SUPPRESSION

Ocular, like auditory suppression is a condition often found in normal individuals.

It was interesting to observe what part, if any, suppression played in the presence of

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* The instrument is more valuable for prognosis in children than in adults.

amblyopia or in delaying cure when treatment was instituted.

Suppression is not an ever-existing obstacle in severe amblyopia, even though one might expect this to be so.

One of my cases will, I believe, illustrate this fact. H. N., aged eight years, with a visual acuity of: O.D., 20/30; O.S., 20/200, took three series of treatments (over a year's treatment including rest periods). Her final vision was: O.D., 20/20; O.S., 20/30. Never during any lesson did she show the slightest evidence of suppression.

On the other hand suppression may be persistent, and yet the patient with amblyopia may have the vision improved in spite of this obstacle. An outstanding case was B. B., aged 32 years. Vision was: O.D., 20/50; O.S., 20/20. She obtained normal vision in five lessons, although she had strong suppression. She could not be persuaded to return for treatment of suppression, a condition of which she was not actually aware.

There were 42 cases of amblyopia, each of which had suppression only. Their ages ranged from 4 to 60 years. Sixteen, or 39 percent, obtained normal vision. In some of these cases, the suppression cleared. Among these, 39 percent of the cases, the suppression varied from mild to alternating to absolute. A number of cases took 2 courses of 12 treatments each with an interval between treatments of one month.

Of the 61 percent of uncured cases, 9 patients had absolute suppression, and the balance varied, like the visually corrected amblyopics, between mild and alternating.

VERTICAL IMBALANCE ASSOCIATED WITH AMBLYOPIA

Any form of muscle imbalance may be asymptomatic, and an individual may also have normal visual acuity of both eyes in spite of either vertical or horizontal muscle imbalance.

Of the various types of muscle imbalance, possibly the only one likely to retard improvement in amblyopia would be the vertical imbalance. White and Brown[2] have called attention to the fact that disregard of the study of the vertical imbalance in a case of squint may result in an unsuccessful operation. Refractionists have seen a number of alternating squints with normal vision in spite of the deviation present.

During the time that the cases of amblyopia were studied, it was interesting to observe that actual improvement in vision came to those patients who, during their treatment, acquired good duction.

The following is corroborative evidence, I believe, that hyperphoria plays a small role, if any, in either the causation of, or as a deterrent factor in the cure of amblyopia.

Hyperphoria can be observed in several types of patients: (1) Those with normal visual acuity and who are asymptomatic; (2) those who attain normal vision and yet have symptoms of muscular asthenopia, such as pain in the eye, dizziness, nausea, and so forth; (3) cases of hyperphoria in squint with normal vision; (4) cases of hyperphoria in squint associated with poor vision.

1. *Hyperphoria* can be present in normal visual acuity as illustrated in this one case. A patient, T. R. S., aged eight years, with a vision of 20/20 of both eyes, came to be refracted. She was examined on three different occasions. There was present during her examination a hyperphoria of between 3 to 9 prism diopters, with alternating suppression. Her vision was normal and, therefore, she did not require glasses.

2. *How little hyperphoria* influenced either the causation or retardation of visual correction is demonstrated by the case of M. S., aged 28 years, who suffered a great deal as a result of her vertical imbalance. She had a left hyperphoria of between 5 and 8 prism diopters, and she wore prisms prescribed for her by several ophthalmologists. Her vision was always corrected to normal in spite of her hyperphoria.

3. *In cases of normal visual acuity*, even in hyperphoria with strabismus, the patient

does not suffer from interference with his vision because of a vertical imbalance. T. A., aged eight years, had an alternating squint of 45 prism diopters. During her orthoptic treatment, her hyperphoria varied from 4 to 14 prism diopters. She even had cyclophoria. In spite of all this, her vision was always normal.

While treating the amblyopic patients, five patients were treated for the improvement of their strabismus. They all had normal vision in spite of the fact that their vertical imbalance ranged up to 13 prism diopters.

4. *Hyperphoria in squint associated with poor vision.*

There were nine patients of this type whose ages ranged from 6 to 16 years, and who had vertical imbalances of from 4 to 13 prism diopters. Their squints ranged to 70 prism diopters. Their vision improved in spite of the hyperphoria present.

In a few other cases which might have been included in this group but were not, there was abnormal correspondence. In these cases, to be reviewed later, the vision did not improve, more likely on account of the abnormal correspondence than the hyperphoria.

STRABISMUS ASSOCIATED WITH AMBLYOPIA

When strabismus is associated with amblyopia there are usually also present other obstacles such as muscle imbalance, suppression, and so forth. These cases were divided into two groups for evaluation: (1) Those with normal correspondence; (2) Those with abnormal correspondence.

1. *Normal correspondence.* There were 22 cases of squint with normal correspondence. Their ages varied from 4 to 44 years. In some cases the squint was as low as 6 to 8 prism diopters* and in others ranged up to 25 prism diopters. Nine patients obtained full correction in spite of the associated ob-

stacles. Of the remaining 13, 5 patients showed no improvement whatever; a few might have improved, but they stopped treatment for one reason or another. Among the patients who did not improve, was 1 with vision of 20/200, and 3 with visions of 20/70.

In the group of improved cases, 2 patients had 20/100 vision and 3 had 20/70 vision in the amblyopic eye. The remaining few had almost the same visional range distribution as the uncured cases in those cases of squint with abnormal correspondence.

2. *Abnormal correspondence.* In this group the ages ranged from 4 to, in several cases, 46 years. The highest angle of squint was 80 prism diopters, yet several squints were as low as 4 prism diopters. One patient had vision as low as 5/200; another, 20/300; 4 had 20/100 vision; and vision in the other cases was between 20/70 and 20/40 for the amblyopic eye.

There were 35 cases of abnormal correspondence. Nine obtained normal vision. Of the 26 cases who did not get well, 5 had a resulting vision varying from 6/200 to 20/200. It is questionable whether the few patients who did show improvement could ever definitely obtain normal vision and, if they should obtain normal vision, whether the cure would be permanent.

Not any of these patients had normal vision on the telescopic amblyoscope on their first or any other examination, so that little hope was expected for these cases from the very beginning. A number of these cases were given 3 or 4 series of lessons, but with no final cure.

AMBLYOPIA ASSOCIATED WITH DIVERGENT SQUINT

There were 4 cases of divergent squint in the group treated; 2 of these cases, with the angle of squint up to 15 prism diopters, were improved to normal.

In the other 2 cases the results were not so good. The angle of squint was 30 prism diopters for each.

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* For the purpose of uniformity, all measurements were on the synoptophore and are given in prism diopters.

One of these patients, W. E., aged 6 years, had 20/200 vision in the left eye. He took three series of lessons, but vision never improved beyond 20/70. He had a low grade anisometropia.

The other case, H. S., aged 17 years, had an alternating suppression with a hyperphoria up to 5 prism diopters on occasion. Her original vision in the poor-seeing eye improved from 20/50 to 20/40 + 3. She also took three series of lessons. On several rechecks at bimonthly intervals, her vision showed a tendency to recede.

NYSTAGMUS WITH ITS ASSOCIATED AMBLYOPIA

Nystagmus is included in this group only because of the high refractive error in these patients. One could hardly expect amblyopic treatment to improve the visual acuity in a case of nystagmus; there was, however, one exception. The patient had a lateral nystagmus. He came to see me 2½ years ago at which time vision was: R.E., 20/200; L.E., 20/50. He obtained one series of treatments with vision in both eyes improved to 20/40. He returned in five months for a check-up, and the vision was the same. He was not heard from for two years; he then returned because the teachers complained about the poor work he was doing. His vision was 20/70 for both eyes.

A course of treatments was given with resulting vision of 20/40 for the right eye and 20/30 −4 for the left eye. Unfortunately it is impossible to get a true measure of his fixation. However, he feels better and does better work in school, as observed by the teachers.

In the four other cases, the patients claimed that their vision "cleared" and that they felt more comfortable.

PSYCHOLOGIC EXAMINATION AND TREATMENT

When, in the course of treating cases of amblyopia, it was noted that some cases made little progress because of psychologic diffi-culties, I referred 12 of my patients for psychologic examination and treatment. Four of these cases have shown marked improvement in their amblyopic exercises. These amblyopic cases and others to be added will be reported at a later date.

TAKING OF FIELDS AND VISUAL ACUITIES

A number of fields and visual acuities on at least four different test charts were taken on each patient.

The fields, taken in the main on a tangent screen, varied from large central scotoma, to fleeting suppression scotoma of various dimensions, to various-sized scotomas peripherally in the 10- to 30-degree area. A few cases even had a clear-seeing central field up to as far as 10 to 25 degrees, beyond which they did not see.

When such bizarre fields are found for amblyopia, one questions their validity. It is to be remembered that, in the main, the patients are children who, when examined, are apprehensive, and do not give exact findings.

In reviewing the amblyopic records, it was learned that the visual acuities were taken on the most common Snellen charts: (1) Illiterate (E) charts; (2) letters on white charts; (3) numbers on white charts; (4) white letters on black charts. When taking visual acuities with Snellen charts, there may be a personal element involved. Some patients read letters more easily, others numbers. In a majority of the cases, the visual acuity was somewhat less with the number chart than with the other Snellen charts.

ANISOMETROPIA ASSOCIATED AMBLYOPIA

The frequency with which one sees anisometropia in amblyopia is well known. In my cases, 63 patients had an anisometropia of more than 1 diopter; 25 had an anisometropia up to 1 diopter.

It was interesting to observe, in reviewing several thousand records taken at random from my files, that 68 patients had anisometropia and 20, a milder form; that is, a varia-

tion in refraction of up to 1 full diopter. All these were amblyopic.

In addition to this number, there were 49 patients with anisometropia among 2,000 patients. Not a single one of these 49 patients had amblyopia, showing that anisometropia, unless of high degree, is not the sole cause of amblyopia.

The degree of anisometropia or the vision present were not always indications as to whether the case would not respond to treatment. Some cases with a high visual error improved faster then those with better vision, and the same was true in anisometropia.

SUMMARY

A review of 108 cases of amblyopia is given; 36 (32 percent) were cured.

Directions are given for the use of the telescopic amblyoscope as a prognostic instrument and for the treatment of amblyopia.

Obstacles are diagnosed by orthoptic examination.

To obtain permanency of the improved vision in an amblyopic eye, it is important to obtain, in addition to the improved vision, fusion with amplitude. Vision should be rechecked on a number of occasions for a number of months.

Suppression, muscle imbalance, squints with or without normal correspondence are discussed as to their relative importance in the causation or delay of cure of amblyopia; excepting the cases of congenital amblyopia which are always incurable.

Anisometropia and squint with abnormal correspondence, or amblyopia with a high angle of squint, may be instrumental in either the causation, the prolongation, or failure of cure in amblyopia.

It appears that if the adult past the age of 45 years and the conditions just mentioned are excepted, there is some hope for the amblyopic.

With the telescopic amblyoscope, or some such devise, a prognosis for the case can be given, especially for a child. The telescope has an added advantage—that of being used in treatment.

Poor visual acuity (less than 20/200) is not always an indication of a poor result. A patient with a visual acuity of, for example, 20/40 in some instances has no better assurance of improvement than another patient with vision of 20/70 or 20/100. The same is true of anisometropia. Amblyopia with a very low degree of anisometropia may sometimes take longer to cure than when a slightly higher degree of the same condition is present.

37 South 20th Street (3).

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CLINICAL EVALUATION OF D.F.P. IN GLAUCOMA THERAPY*

MORGAN B. RAIFORD, M.D.

Atlanta, Georgia

Since its introduction for the treatment of glaucoma, D.F.P. has proved a most potent anticholinesterase drug and a powerful miotic. Its action is quite prolonged and, according to Scholz and Wallen in their studies in normal human eyes, signs and symptoms of its spasm of accommodation and miotic effects varied from 3 to 7 days following a single instillation.

D.F.P. in the concentration of 0.05, 0.1, and 0.2 percent produces blurring of the vision, headache which may be over the eye, or orbital discomfort. Spasm of accommodation and pericorneal injection are frequently encountered. McDonald stated that the ciliary spasm and occasional rise in tension following its administration apparently is the result of arteriolar dilatation and an action of the drug upon the ciliary body. In the concentrations already mentioned, it produces its greatest number of undesirable symptoms during the first few days of its use. Because of these effects, there has been a tendency to discredit the use of D.F.P. in the clinical care of glaucoma patients. In the toxicologic studies reported, no dangerous side reactions have been noted when the concentrations usually given in glaucoma cases have been administered.

Leopold and Comroe reported two instances in which a rise in intraocular pressure followed instillation of D.F.P. In one of the cases, an iridectomy was required before the tension fell spontaneously.

In the 82 patients with 122 glaucomatous eyes, reported by McDonald, 57.4 percent had a tension of lower than 30 mm. Hg (Schiøtz). In McDonald's series, 0.1-percent D.F.P. was used in daily instillations. He also noted that the correct dosage must be determined for each patient.

The use of D.F.P. (0.05 percent) following intracapsular cataract extraction through a round pupil and in cyclodialysis is recommended by Lebensohn as a miotic of choice at the conclusion of surgery.

PRESENT STUDY

Since D.F.P. has such prolonged action and is a most capable antagonist of cholinesterase, a series of 22 patients with 42 glaucomatous eyes were studied, using varied concentrations of the drug. The period of investigation covered a period of 10 months.[†] The patients, with two exceptions, had had glaucoma for a period of from 10 months to 9 years.

When first used, D.F.P. (in each case 0.05 percent or 0.1 percent in peanut oil) was instilled as one drop at bed time every night. This was continued for 2 to 4 weeks, and the effects as to signs and symptoms were recorded. The D.F.P. was then discontinued for a period of 4 to 6 weeks, during which time miotics previously used were given. Then D.F.P. of lesser concentration was used, 0.01 percent and 0.005 percent in peanut oil), one drop being instilled nightly at bed time. This was continued for the remainder of the 10 months of observation with the exception of two cases.

Of these exceptions, one patient was found to be sensitive to peanut oil (Case 20), and another (Case 17) was probably refractory to the drug and was returned to 5-percent pilocarpine which was instilled 5 times a day in each eye.

SURVEY STATISTICS

In this series of 21 patients with 41 glaucomatous eyes, the age varied from 39 to 84

TABLE 1

TABULATED CLINICAL FINDINGS WITH ADMINISTRATION OF D.F.P. IN THE TREATMENT OF GLAUCOMA

No.	Name	Age	Type and Duration of Glaucoma	Vision	Intraocular Pressure with Previous Miotics (mm. Hg Schiotz) Lowest	Highest	Average	Previous Therapy	Visual Fields	D.F.P. Administration	Length of Observation (Months)	Intraocular Pressure with D.F.P. (mm. Hg Schiotz) Highest	Lowest	Average	Visual Fields	Comment
1	E.H.	78	Chronic simple (1942)	O.D. 6/12 O.S. blind	19	34	22	Pilocarpine 2% gtt.i, t.i.d.	O.D. within 20° central.	0.1% slight pain and ciliary reaction 1 wk. 0.01% no reaction.	8	19	13	17	No change	More comfortable with 0.01% H.S. gtt.i, O.D.
2	A.S.	67	Chronic simple; diabetic; O.D. aphakic.	O.D. 1/60 Aphakic. O.S. 6/12	17 18	38 36	20 22	Pilocarpine 3%; Eserine ½% O.U. t.i.d, gtt.i	O.D. 13 central. O.S. 25° central.	0.1% pain in eyes. 0.01% no reaction.	9 9	22 19	15 14	18 17	No change No change	Comfortable 0.01% gtt.i, O.U., H.S.
3	M.D.	54	Chronic simple; corneoscleral trephination—O.D. 1942, O.S. 1943; allergic.	O.D. 6/60 O.S. light perception.	12 19	29 61	17 40	Pilocarpine 3%; Eserine ½% q.i.d. gtt.i, O.U.	O.D. 5° central. O.S. light perception.	Began with 0.01% H.S. gtt.i, O.U.	5 5	18 36	11 24	16 26	No change No change	0.01% very satisfactory, holds tension lower, less fluctuation.
4	R.D.	51	Chronic simple (1942); corneoscleral trephination, O.D. 1944.	O.D. 6/6 O.S. 6/6	19 17	37 29	24 21	Pilocarpine 2% gtt.i, O.U. and occasionally Eserine ½%.	O.D. & O.S. maintained central 15-20° past 3 years.	0.05% H.S. gtt.i for 2 wks. Then to 0.01% D.F.P. H.S. gtt.i, O.U.	8 8	25 26	17 17	19 19	No change Slight increase.	Slight increase of tension first 4 days with little headache. D.F.P. free interval of 5 wks. and began 0.01% with no symptoms.
5	W.E.	71	Chronic simple (1939); trephination, O.D. 1941, O.S. 1944; cataract surgery, O.D. (1948); O.S. (1947).	O.D. 6/12 O.S. 6/15+2	13 After trephination 15 After trephination	31 35	19 20	Pilocarpine 2% gtt.i, 5X daily O.D., 3X daily O.S.	Decrease in superior O.D. 25° central O.S. since trephination.	0.1% D.F.P. H.S. caused pulling sensation in eyes. 0.01% no reaction gtt.i, H.S., O.U.	9 9	26 17	15 12	17 14	No change No change	D.F.P. free interval for 6 wks. changed to 0.01%. No reaction.
6	W.G.	60	Chronic simple (1941) O.U.; O.D. surgery (1943) and cataract surgery O.S. (1947).	O.D. 6/30 O.S. 6/12	11 After trephination 17 After trephination	48 34	19 19	Pilocarpine 2%; Eserine ½% 4X daily gtt.i O.U.	O.D. field stabilized since trephination. O.S. contracted.	0.1% caused blurring vision and aching for 1 wk.	8	24 22	16 16	19 18	Slight increase No change	10 days of 0.1% D.F.P., stopped for 4 wks. Began 0.01% D.F.P. No reactions.
7	E.H.	55	Cataract surgery O.D. and O.S. (1944); O.D. vision went bad 1 yr. later, optic atrophy now. Pain in eyes for 2 mo.	O.D. 6/9+1 O.S. hand movements	21 41	29 59	23 44	Pilocarpine 2%; Eserine 1%; gtt.i t.i.d. O.U.	O.D. 12° central. O.S. hand movements	Began with 0.01%. No reactions. No change O.S. when reduced X1 daily.	6	26 41	19 28	20 32	No change No change	Fluctuations in tension better controlled with D.F.P. more than once daily did not change tension O.S.
8	S.G.	39	Noted pain O.S. Feb. 1948, more at night; O.D. occasional aching; chronic simple, wide angle.	O.D. 6/6+2 O.S. 6/5	22 24	32 30	27 26	Pilocarpine 1% gtt.i, t.i.d. Had pain at night in both eyes.	Increase relative scotoma about blindspots. Decreased in 2 wks. after miotics.	0.1% H.S. Some blurring of vision. 0.02% then used, gtt.i, H.S., O.U.	5 5	26 29	18 22	22 23	Slight decrease	Decrease in central fields. Advised trephination. Wants to continue D.F.P. More even tension.
9	M.S.	65	Chronic simple (1943); trephination—O.D. 1943, O.S. 1944.	O.D. 1/60 O.S. 6/12	11 after trephination 11 after trephination	78 30	17 22	Pilocarpine 2% gtt.i, t.i.d, O.U.	O.D. 5° central. O.S. 12° central.	0.1% no reaction other than few days of blurring vision. 0.01% kept tension down as well. H.S. gtt.i, O.U.	10 10	22 24	15 19	17 20	No change No change	Just prior to D.F.P. % tension O.U. up. 0.01% H.S. O.U. gtt.i acts well in controlling.
10	G.G.	84	Cataracts (1939); O.D. operated (1940), O.S. (1911); glaucoma (1942) postoperative.	O.D. light perception O.S. 6/15	14 15	40 40	26 24	Pilocarpine 2%; Eserine ½% gtt.i, t.i.d. O.U. since 1942.	O.D. light field 10°. O.S. 7° central.	0.1% caused slight aching O.D. No symptoms O.S. 0.01% no symptoms.	5	27 26	21 20	22 22	No change No change	0.01% holds tension evenly. Reduced to 0.01% after free interval of 2 wks.

No.	Initials	Age	History	Vision	Tension			Treatment	Fields	Reaction	Days	Tension			Change	Remarks
11	C.W.	66	9/18/47 chronic simple, seen because pain in eyes and blurring of vision	O.D. 6/9+1 O.S. 6/9+3	21 21	35 32	29 23	Pilocarpine 2% gtt.i, t.i.d., O.U.	O.D. 3° contracture O.S. 11° central.	0.1% caused pain in eyes. No rise in tension. Changed to 0.01% after 16 days.	10 10	29 26	19 19	21 21	Slight decrease / No change	Patient hypertensive, mentally slow. D.F.P. keeps tension more stable. Less administration each day aids patient.
12	M.A.	69	Followed since 1942, chronic simple, cataracts, no surgery desired.	O.D. 1/60 O.S. 1/60	19 22	44 50	26 30	Pilocarpine 2% gtt.i, t.i.d. O.U. Eserine ½%. Not too regular with miotics.	Light fields peripheral 40-50° all meridians.	0.05%, no symptoms, 0.01% holds tension just as well.	7 7	25 29	17 19	19 22	No change / No change	By miotic once daily, patient finds more convenient. D.F.P. controls tension better at lower level.
13	J.S.	77	Removal cataract O.D. (1927), O.S. (1930) with vascularization of cornea (1937).	O.D. 6/15 O.S. 6/60	17 13	30 35	21 22	Pilocarpine 2% gtt.i, t.i.d., O.U.	O.D. 25° central O.S. 3° central	0.05% gtt.i. H.S. O.D. Slight blurring O.D. 0.01% holds tension equally well. No reaction.	10 10	35 22	17 13	19 22	Slight improvement in central field / No change	Beta radiation O.D. for vascular cornea. Tension higher than (Jan. 1948). Lower afterward.
14	A.P.	58	Chronic simple (1945) O.U.	O.D. 6/12 O.S. 6/2	17 17	48 29	22 22	Pilocarpine 2%; Eserine ½% gtt.i. O.U.	O.D. 25° central, enlarged blind spot. O.S. 15°	0.1% blurring symptoms. 0.01% no symptoms.	9 9	22 21	17 19	19 19	Slight increase O.D. / O.S. no change.	0.01% kept tension same level with less fluctuation.
15	B.S.	54	Chronic simple—O.D. narrow angle, O.S. old old iridocyclitis (1941).	O.D. 6/9+4 O.S. blind	17 35	35 78	24 48	Pilocarpine 2%; Eserine ½%, gtt.i, t.i.d., O.U. Prostigmine 5% and Mecholyl 5% did reduce O.S. tension.	10° central O.D. Blind O.S.	0.05% headache and blurring .0.01% for 10 days no reaction.	10	24 48	15 35	22 42	No change	After reducing to 0.01% no complaints and no change in tension level. Decreases fluctuation.
16	B.H.	64	Chronic simple (1/15/45); O.D. trephination (1946); diabetic.	O.D. 6/22 O.S. 6/9-2	13 13	35 29	18 20	Pilocarpine 2% gtt.i, t.i.d., O.U.	O.D. 20° central, O.S. Rönne step 15° field	0.1% blurring of vision. 0.01% no reaction.	9	22 29	17 21	19 22	No change	0.01% no reaction. Tension variation less.
17	J.W.	53	Chronic simple O.S. (1942); Loss O.D. trauma.	O.D. enucleated O.S. 6/15	— 11	— 55	— 21	Pilocarpine 5% 5X daily O.S.	O.S. 5° field.	0.01% gtt.i. H.S. O.S.	1	56	28	37	No change	Stopped. Patient probably refractory to... D.F.P. Did best on 5% pilocarpine.
18	W.W.	70	Old keratitis O.S. (1921); senile cataract and chronic simple O.D.	O.D. 1/60 O.S. 6/30	15 17	25 29	22 21	Pilocarpine 2% gtt.i, t.i.d. O.U.	O.D. light perception. O.S. depression lower half.	0.1%, headache. Blurring 0.01% no reaction.	10	26 26	19 19	22 21	No change	0.01% gtt.i., H.S., O.U. lessened tension variation. Beta radiation O.D. corneal vascularization.
19	C.T.	62	Old bilateral luetic choroiditis and glaucoma, pains and ocular aching.	O.D. 6/12 O.S. 6/22	19 18	31 29	24 23	Pilocarpine 1% gtt.i., t.i.d.	O.D. and O.S. 12° central.	0.1% pain and regular aching for 4 days. No reaction to 0.005%.	5	22 24	17 17	15 15	Improved O.U.	0.005% less variation in tension curves... Fields improved.
20	M.S.	56	Chronic simple (1945); O.S. cataract extraction; optic atrophy O.D.	O.D. 6/30 O.S. 6/12	29 17	56 34	28 19	Pilocarpine 2% gtt.i., t.i.d., O.U.	O.D. 25° central. O.S. 10° central.	Sensitive to peanut oil. Had to stop D.F.P.	2 weeks	34 22	19 11	24 13	No change	Conjunctivitis with peanut oil. D.F.P. stopped after 2 weeks.
21	H.W.	49	Bilateral senile cataracts; O.D. extraction (1948); secondary glaucoma; O.S. aphakic and normal.	O.D. light perception O.S. 6/12	17 19	35 24	24 22	Pilocarpine 1% gtt.i., t.i.d. O.U.	O.D. 20° central. O.S. normal.	0.1% used O.D. Only headache first 5 days.	9 9	32 22	17 19	22 20	No change	O.D. 0.01% D.F.P. held tension just as well. No reaction O.S. No miotic used.
22	I.S.	46	Chronic simple (1945); bilateral iridectomies (1945 and 1946).	O.D. 6/15 O.S. 6/9	11 11	35 40	25 22	Pilocarpine 2% gtt.i, 4X daily.	Superior portions both fields lost 10°-50° below normal.	0.1% ciliary spasm with conjunctival injection. 0.005% no reactions.	10 10	29 22	19 13	21 17	No change	0.005% proved best. No reaction and H.S. X1 daily. Tension variations less.

years. Chronic simple glaucoma was present in 17 patients or 33 eyes; secondary glaucoma was present in 4 patients or 8 eyes. The secondary glaucoma followed postcataract extractions in 4 eyes, an old keratitis in 2 eyes, and iridocyclitis in 2 eyes. The duration of the glaucoma in this series varied from 10 months to 9 years.

EYE EXAMINATIONS

Visual acuity. This was the best vision obtainable with the patient's correction. All cases were refracted before the survey began and again during the last three months of the study.

Gonioscopic examination. A gonioscopic examination was made of each patient at the beginning of the investigation. When administration of 0.05- and 0.1-percent of D.F.P., was started, gonioscopic examination was again done. No noticeable change was noted in the iris structure under gonioscopic vision after use of D.F.P.

Tension. Intraocular pressure was recorded (Schiøtz) before the D.F.P. was given, and tension curves since the patients were first seen were reviewed. After D.F.P. was begun, both in the first series (0.05 percent and 0.1 percent) and the second series (0.01 percent and 0.005 percent), tension readings were taken every day for 4 days, and signs and symptoms noted; then they were taken each week. The highest, lowest, and average tension readings were recorded for previous, as well as D.F.P., therapy.

Visual fields. Central fields were taken in each case before D.F.P. therapy was begun. The fields were all done under 7 foot-candles in artificial light (light was standardized and checked at monthly intervals with a light meter). Visual fields were done every two months. An evaluation of the field changes was made at the end of the 10-month period of investigation (table 1).

SUMMARY

In a series of 41 glaucomatous eyes followed over a period of 10 months, 33 eyes had chronic simple glaucoma and 8 secondary glaucoma.

In 13 patients (25 eyes) one drop of 0.1-percent D.F.P. was instilled at bed time. With the exception of two eyes (Case 3), the patients noted headache, ocular discomfort, blurring of vision, and extension to the sensation of pain. A concentration of 0.05 percent in 8 eyes (Cases 4, 12, 13, and 15) caused only slightly less reaction of similar nature, with the exception of Case 4 in which only a slight rise in intraocular pressure was evident during the first two days. One case (7) was begun with 0.01-percent D.F.P., and no reactions occurred of any type throughout the period. One patient (20) was sensitive to peanut oil, determined by instilling it in each eye after a 4-week free period of D.F.P. Only one individual (17) proved to be what was considered refractory to D.F.P. and the intraocular pressure went up to 56 mm. Hg at the end of five days. The tension returned promptly to an average of 21 mm. Hg and was maintained well with 5-percent pilocarpine.

After an interval of 4 to 6 weeks in which the patients were returned to pilocarpine or eserine therapy, they were placed upon 0.01-percent D.F.P. in 19 cases or 36 eyes. Two patients (13 and 15) or 4 eyes used 0.005 percent D.F.P. with similar results. In two eyes (Case 8), the optimum concentration of D.F.P. to control the tension properly proved to be 0.02 percent. In 18 eyes, 0.005-percent D.F.P. proved just as effective in maintaining proper tension as the 0.01-percent solution.

The tension curves were better maintained with 0.01- or 0.005-percent D.F.P. in all cases with exception of one eye (Case 8). The entire study showed that fluxations of intraocular pressure were decreased by 28.5 percent and an overall reduction in level in tension of 17.4 percent.

The visual fields were not expected to change too much. One case (19) showed the greatest single increase of the central fields. In Case 8 the presence of Seidel's sign dis-

appeared in both central fields, which is attributed to the more stabilizing effect of D.F.P.

The most frequent comment of the patients was in praise of the ease and need of less frequent instillation when D.F.P. was used. Since D.F.P. was given at bed time, the film created by the peanut oil was less annoying. With the exception of Cases 17 and 20, the patients have been pleased with this miotic and prefer it to previous medicants. They stated that their vision was clearer throughout the day when D.F.P. was used.

CONCLUSIONS

1. The use of D.F.P. in lower concentration (0.01- and 0.005-percent) has proven it a most valuable miotic in the clinical care of *glaucoma patients.*

2. The maintaining of a lower and less fluctuating intraocular-pressure curve has been constantly demonstrated throughout the entire 10-month period of this study.

3. The prolonged effect of the drug lessens the frequency of instillation, and the use of more than one drop daily did not lower the tension curves.

4. No detrimental reactions have been manifested in the concentrations of 0.01- and 0.005-percent D.F.P.

Grady Clay Memorial Clinic,
Emory University.

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OPHTHALMIC MINIATURE

The subdivision of manual labour manifestly tends to perfect the operations of art; but to limit the sphere of Science by the detachment of its parts, is to destroy the foundation upon which it rests. With respect to that of Medicine, however beneficially we may observe the labours of individuals to be occasionally exerted in the selection of particular branches, as the more exclusive objects of their study and attention, yet this can only occur to those who have first investigated this science as a whole; and we may be assured that others who assume a superior knowledge of any branch of medical practice, on the ground of comparative ignorance of, or indifference to the rest, are but little indebted for whatever reputation they acquire, to the actual benefit they are able to effect.

JOHN VETCH, *A Practical Treatise on the Diseases of the Eye,* 1820.

NOTES, CASES, INSTRUMENTS

THE EFFECT OF DI-ISOPROPYL FLUOROPHOSPHATE (D.F.P.) ON THE PUPIL OF THE DARK-ADAPTED EYE*

Edwin B. Dunphy, M.D.
Boston, Massachusetts

Englehart[1] in 1931, using rabbits and cats, showed that, when the third nerve was stimulated, a substance was liberated in the aqueous, which had the properties of acetylcholine. It was found to be greatly increased when the eye was exposed to bright light, but it was absent in the dark-adapted eye even

Fig. 1 (Dunphy). Normal appearance of the eyes of subject used in the experiment.

after eserine had been instilled to destroy the cholinesterase.

This being the case, one might infer that the anticholinesterase miotics would have little, if any, effect on the pupil of the dark-adapted eye, since no acetylcholine would be formed in the dark to stimulate the sphincter muscle of the iris. However, Englehart also demonstrated the presence of acetylcholine in extracts of the iris or ciliary body not only of eyes that had been exposed to light, but also of those which had been kept in the dark.

It is true, of course, that during sleep the pupils are miotic, but this might be the result of unconsciousness in which the stronger sphincter tonus prevailed over the dilator tonus due to the removal of inhibitory sympathetic stimuli.

It has already been shown[2] that, if a human eye is exposed to D.F.P. vapor and immediately dark-adapted for one hour, the miosis persists in the dark in spite of the fact that no reflex impulses from light stimulation are travelling over the third nerve. This suggests that the acetylcholine formed in the tissue just prior to dark adaptation cannot be eliminated in the absence of cholinesterase.

A search of the available literature failed to show whether or not an anticholinesterase miotic would produce any miosis if instilled into an eye *in the dark* after complete dark adaptation. The following experiment was therefore devised to ascertain the answer to this question.

A young individual with normal pupillary responses (fig. 1) was dark adapted for 30 minutes in front of a high-speed camera already focused to take a flash photograph of the pupils. At the end of this period of dark adaptation, one drop of D.F.P. (0.05-percent solution) was instilled in the left eye. This was accomplished by means of a special eyecup originally devised by Heath,[3] and modified so that the subject could instill the drop in his own eye in complete darkness without fear of injury to the cornea. Dark adaptation then continued for another 30 minutes, the flash photograph being taken at the end of this period (fig. 2). This shows the right pupil widely dilated, but the left pupil miotic.

Fig. 2 (Dunphy). Appearance of eyes after dark adaptation and instillation of D.F.P.

It is obvious from this experiment that D.F.P. will produce miosis when instilled in complete darkness in a dark-adapted eye when no reflex impulses (at least from light stimuli) are traveling along the third nerve. This seems to corroborate the belief generally held among pharmacologists and physiologists that acetylcholine is constantly being formed at all parasympathetic nerve endings as the result of normal muscle tonus.

243 Charles Street (14).

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PROGRESSIVE RETINOPATHY ASSOCIATED WITH MENSTRUATION

GEORGE R. LAUB, M.D.
Columbia, South Carolina

History. E. H., a 13-year-old white girl, was seen for the first time on August 9, 1944, with the complaints of slightly diminished vision. She was brought by her parents in order to have some glasses fitted. The examination at that time showed a visual acuity of 20/20 in the right eye and less than 20/800 in the left eye. The external findings for the right eye were perfectly normal, with normal eyegrounds.

The left eye showed some yellowish pinpoint spots between the disc and the macula. They had a peculiar arrangement in so far as they were all within a triangular field with the base at the disc and the apex of the triangle at the macula. The best description of these spots would be that they looked like beginning miliary tubercles.

No diagnosis could be made at that time. The patient was given some simple eye wash for psychologic reasons and was asked to return in a week.

Second examination. On August 16, 1944, the right eye was unchanged, the vision of the left eye was 20/228, the already described spots in the eye had practically disappeared. Her mother told me that during the last week my patient had had her first menstrual period.

On August 30, 1944, she was reëxamined and the vision of the left eye was 20/80. No spots at all were on the retina. On September 13th, the second menstrual period had not yet started, and vision of the left eye was 20/200, with the spots like they were at the first examination.

At that time, the child was admitted to the Columbia Hospital for thorough examination. The medical findings were all negative. X-ray films of sinuses, skull, and chest were all within the normal limits. Urine, blood count, Wassermann, tuberculin, and undulant-fever agglutination tests were negative. Glucose-tolerance test was normal. B.M.R. was normal.

Course. On November 15, 1944, vision in left eye 20/320, the spots reappeared, and at the upper side of the triangle a slight grayish tissue like a fold could be seen. The right eye, during the entire period of observation up to the present time, had always been normal.

Because of trouble with her menstrual periods, which were very irregular, she received at the advise of her diagnostician (Dr. F. E. Zemp) Antuitrin S and some Theelin injections. Her eye condition kept on changing with each period, worse just before the menstruation, best shortly afterwards.

For many months the parents did not return her, but, in February, 1946, when she returned, an entirely different picture was presented. The left eye showed that "the

disc is somewhat paler than the right and, extending out into the vitreous body from the disc towards the macula at an angle of perhaps 10 degrees with the retina, is a gray-

Fig. 1 (Laub). Eyeground of the left eye. (Published with the kind permission of Dr. B. Anderson, Duke University Hospital.)

ish white sheath. This is not associated with a vessel. It is approximately a fourth of a disc diameter in width and appears almost as a fibrous cylinder with tenestra or dehiscences at irregular intervals in the walls. The tip extends well over the center of the macula and from the tip a few darker strands dip down to the macular area. The retina in the macular area is drawn upward toward this tip almost like a tent.

"As viewed with a giant binocular ophthalmoscope, one gets the impression that this tubular whitish sheath hangs out in a cranelike fashion from the disc and, at its tips, raises the retina in a tentlike fold over the macular area. Beneath this tentlike fold in a roughly oval disc about the diameter of which is a dark-brown or black area that is interpreted as being choroidal or subretinal hemorrhage. Extending from the disc vertically to the 3-o'clock position is a fold of retina which would ordinarily be interpreted as a congenital anomaly (retinal septum)."

This quotation is from a report of Dr.

B. Anderson at Duke University Hospital, who saw her in consultation and took the photograph at that time (February, 1946), which he kindly permitted me to use for publication (fig. 1). The vision of the left eye was 20/200.

A year later, in March, 1947, the findings of the eyegrounds were apparently unchanged, although the vision dropped to 20/400−. In June, 1948, when I saw this girl last, her vision was unchanged (20/400) but practically no central vision was left. The "tent" as described by Dr. B. Anderson, which used to have a veil-like appearance, increased in density and progressed somewhat further encasing practically the entire macula. The upper part of the tent had an especially dense appearance.

Comment. This case is a very unusual one. There is no heredity factor involved. We had the chance to examine the eyes of the parents, as well as other members of the family, none of whom showed any sign of a pathologic condition of the eyes.

The picture of the eyeground as it appears now could easily be mistaken for that of retinitis proliferans. However, having observed the entire development of the disease over a period of more than four years, having seen the changes of the eyeground with each menstrual period, at first only "miliary tubercles" later the development of fibrous tissue, makes the diagnosis completely obscure. A search of the entire literature and personal discussions with some of the leading ophthalmologists did not throw any light on this case.

SUMMARY

The case of a young girl, whose eyesight as well as eyegrounds changed with each menstrual period is reported. She is gradually loosing the sight of one eye. No description of a similar disease could be found in the literature. It is hoped that, if any ophthalmologist can throw light on this case, he will communicate with me.

1627 Bull Street (1).

DIFFERENTIATION OF CONJUNCTIVAL TUMORS

CLINTON WILSON, M.D.
Los Angeles, California

It is sometimes difficult without histologic study to different pinguecula and early pterygium from early malignancy of the conjunctiva. Missed diagnoses are not unknown. Therefore, some practical means of giving at least a hint of possible malignancy should be useful.

One such means is the use of the Hildreth or the Woods lamp. The ultraviolet light emitted by these lamps causes fluorescence of the lipoid-bearing pingueculas and pterygia but not of the lipoid-free but otherwise similar-appearing structures which may be malignant.

Attention is directed to the matter at this time because of: (1) Confirmation of preoperative diagnoses of cancerous or precancerous lesions made on the basis of nonfluorescence, and (2) the need for widespread investigation, histologic and otherwise, in order to evaluate the worth of this simple procedure.

Such a study might disclose that some fluorescent lesions are malignant and that some nonmalignant lesions are nonfluorescent.

It is good clinical practice at this time, in my opinion, to be suspicious of and therefore to excise thoroughly the nonfluorescent conjunctival lesions. The reports of histologic study of such material would be valuable.

3875 Wilshire Boulevard (5).

A PENLIGHT PROJECTOR FOR THE LANCASTER RED-GREEN MUSCLE TEST*

JOHN M. HILL, M.D., AND
FENN T. RALPH, M.D.
New York

This test, devised by Lancaster[†] for the measurement and interpretation of muscle
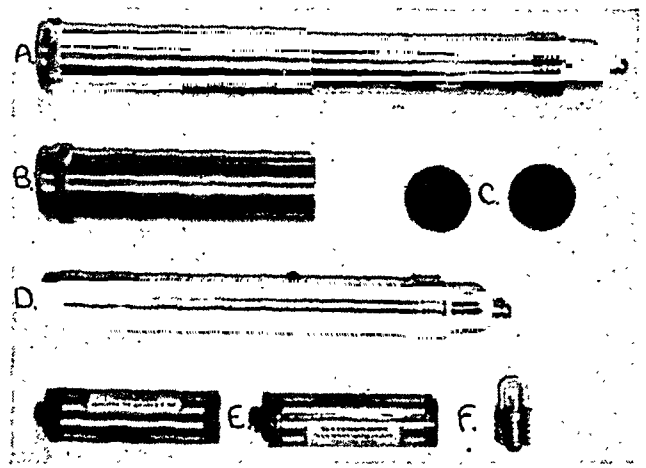
Fig. 1 (Hill and Ralph). (A) Assembled penlight. (B) Focusing sleeve. (C) Red and green disks. (D) Penlight barrel. (E) Penlight batteries —size AA Eveready. (F) Reid-streak retinoscope bulb.

deviations, involves the use of two flashlight projectors. However, the fact that the commercial projectors are cumbersome, expensive, and not readily available discourages the use of this test by the ophthalmologist.

In attempting to overcome this difficulty, the following inexpensive penlight projector was devised. A simple two-cell penlight is utilized, with a straight filament bulb[‡] as the source of the illuminated streak. Two condensing or focusing sleeves,[§] one fitted with a small round disk of red plastic, the other with green, slip over the barrels of the penlights and focus the streaks thus produced, at the desired distance of 1 or 2 meters.

In addition to its primary use with the Lancaster red-green test the projector has a secondary function. By removing the red or green plastic disk in the focusing sleeve, the projector, with its illuminated streak, can be used for external eye examination. It may also be used in conjunction with a loupe as a hand slitlamp for examination of the cornea, anterior chamber, and lens.

Second Avenue and 13th Street (3).

SOCIETY PROCEEDINGS

Edited by Donald J. Lyle, M.D.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

December 6, 1948

Dr. Benjamin Esterman, *president*

BIOMICROSCOPIC OBSERVATIONS OF THE CHAMBER ANGLE WITH THE GONIOPRISM

Dr. Harvey E. Thorpe said that the first goniobiomicroscopy was performed by Koeppe in 1920 with the aid of his contact lens, a special mirror, and the slitlamp microscope. The technique was difficult and was usually limited to the examination of the nasal and temporal portions of the anterior-chamber angle. Clinical interest in this region of the eye dates back to Leber's demonstrations, in 1873, that the trabecular portion of the angle was the chief exit channel for the aqueous fluid. Further interest was aroused when Knies, in 1876, having discovered the anterior-chamber angle to be obliterated in glaucoma, postulated the closure of the angle to be due to inflammation. One year later, Weber brought forth the view that edema of the ciliary body and processes was responsible for occlusion of the angle.

Trantas of Athens, in 1900, and Saltzman of Graz, in 1914, were the first to publish chamber-angle studies. In this country Troncoso was first to call attention to the contact-lens method for clinical examination of the angle in 1921. It was really Troncoso's work and his invention of aids to gonioscopy which gave this subject its clinical basis. Castroviejo, Reese, and Bruce were among the early workers in this field. Friedman simplified the method of filling the space beneath the contact lens with fluid. Kronfeld, McLean, Sugar, and others have shown the value of gonioscopy for anterior-chamber surgery.

It was Barkan, however, through his studies of the angle and his new approach to glaucoma surgery, who gave this subject further impetus in the 1930s.

Since then, the advent of the Goldman contact lens and more recently the Allen gonioprism have facilitated the examination of this region with the aid of biomicroscope. Two drops of 0.5-percent pontocaine are instilled in the conjunctival sac. A drop of 1-percent methyl cellulose is placed on the concave surface of the plastic gonioprism and the instrument, with its flat reflecting surface below, is inserted between the lids while the patient is seated at the slitlamp.

The slit illumination is thrown into the prism mirror surface and the microscope is focused in the same area to observe the magnified view of the upper angle. The prism is readily rotated within its plastic speculum carrier to observe the entire circumference of the angular drainage area.

Narrowing of the angle, adhesions between the iris root and peripheral cornea, pigmentation or debris or exudate in the trabecular zone are readily recognized by this means. Small foreign bodies hidden behind the limbus within the angle, small pathologic conditions of the peripheral iris, and trauma can only thus be recognized. Moreover, inflammatory corneal processes and keratic precipitates can thus be seen from the posterior view. If corneal edema presents a problem, a drop of glycerine usually dehydrates the cornea sufficiently to facilitate both angle and fundus studies. One of the benefits resulting from this technique is the ability to study our own handiwork after glaucoma and cataract surgery. We can thus tell why we fail in one cyclodialysis or trephination and succeed in another, and why a cataract extraction with delayed chamber restoration frequently results in subsequent

glaucoma. Gonioscopy has aided in our understanding of the pathologic processes of the visible angle and helps in planning the medical and surgical management of cases in which the chamber angle is concerned.

CIRCULATORY ASPECTS OF THE GLAUCOMA PROBLEM

DR. JOHN N. EVANS delivered the annual Mark J. Schoenberg Memorial Lecture. He discussed certain aspects of ocular circulation. He called attention to the fact that the aqueous and the vitreous might be termed the "fourth circulation." (The "third circulation" was a term created by Harvey Cushing in referring to the cerebrospinal system fluid.) He presented illustrations from original work which lent strength to the idea that the vitreous is probably much more active in a nutritive and dynamic sense than is usually recognized. He suggested that the remains of the vitreous vascular fetal system may act as cleavage planes to help conduct the aqueous element of the vitreous to the posterior drainage system by way of the perivascular spaces.

He pointed out that the choroid in health is much thicker than we are led to believe from the study of histologic preparations. He discussed the possible mechanism of vitreous-chamber fluid pressure associated with the rapid changes in volume of the choroid which take place in nervous shock, and so forth. The mechanism taking part in such changes is related to the action of the so-called capillary sphincter muscles, the structure which he described in a communication about a year ago. He stressed the point that therapeutic and surgical measures should be designed especially for the relief of vitreous pressures in cases of glaucoma. Dr. Evans illustrated his paper with numerous slides from original studies. (The lecture will be published in an early issue of the JOURNAL.)

Bernard Kronenberg,
Recording Secretary.

LOS ANGELES OPHTHALMOLOGICAL SOCIETY

December, 1948

DR. WILLIAM ENDRES, *chairman*

THE TEXTBOOK RETINA AND THE REAL ONE

DR. GORDON L. WALLS of Berkeley (by invitation) presented an illustrated lecture correcting many of the errors and half truths concerning the retina as described in most textbooks.

The retina does not end at the ora serrata, but at the margin of the pupil. In lowly vertebrates the sensory retina degenerates if the opticus is cut, but a new retina regenerates from the ciliary epithelium, which is actually retinal tissue.

The retina is not a mere part of a sensory organ. It is the visual sense organ, and more. All other parts of the globe are as much accessory as are extraglobar orbital structures. The retina is homologous with the whole thickness of the brain wall, and is more a sense organ since it contains its own associational systems mediating facilitative and inhibitional phenomena, and can almost "think."

The retinal layers traditionally taught have no meaning. Functionally, the retina has only four layers: (1) the purely nutritive pigment epithelium; (2) the visual-cell layer; (3) the layer of internuncial neurons; and (4) the ganglion, so thinly distributed that it forms a "layer." At either side of the internuncial layer, funneling and spreading of excitation and inhibition are mediated by the horizontal and amacrine cells and by the diffuse dendrites of large bipolar and ganglion cells.

Rods and cones are neither nerve cells nor neuro-epithelium, but modified ependymal cells which were formerly flagellated, as is shown by their cytogenesis as well as by their situation in the developing optic cup.

The rods are not historically older than the cones, as is generally taught (and as is

assumed in the Ladd-Franklin theory of color vision). But the first cones did not mediate color vision—nor did the first rods contain visual purple, which is by no means a primitive visual photochemical but an ingenious one which conveniently decolorizes in bright light (preventing dazzlement).

Cones have secondarily given rise to rods, and vice versa, through evolutionary transmutations. The two are not immutable structural types. Pure-cone, diurnal animals have had nocturnal descendants with duplex and even pure-rod retinas. Human cones were derived from lemuroid rods and are not homologous with cones outside of the Primates.

Human cones are not conical. Adequate micrologic methods show their outer segments to be cylindrical and as long as those of rods. Moreover, each cone outer segment is ensheathed by (and possibly continuous with) a tubular process from the nearest pigment-epithelium cell. This trophic arrangement, demanded by the elevated metabolism of the cones (as opposed to rods), explains why vision never returns perfectly after a detachment is repaired.

The cones are not most numerous in the extramacular fundus and fewest at the ora; nor are the rods most numerous at the ora. Østerberg found the densest rod population in a zone only 5 to 6 mm. from the fovea. The rods are actually denser here (160,000/sq. mm.) than are the cones in the fovea.

What the textbooks call the "macula" is actually the *area centralis*. The fovea, properly, is the depression in this area. The macula lutea is by definition the region containing a yellow pigment. With a purple filter described by Walter Miles, the macular pigmentation can be seen entoptically. It is found to be actually smaller than the foveal pit, though textbooks describe the fovea as occupying a small portion of the macula. The human area centralis may have a diameter of 10 to 12 degrees, the foveal pit 6 to 7 degrees, the macula lutea 2 to 2.5 degrees; and, the rod-free spot is only 50 minutes of arc in diameter. The cones in this spot are slenderized to promote acuity and elongated to preserve their sensitivity.

The center-to-center separation of adjacent foveal cones is 24 to 28 seconds, which happens to be about the value of the smallest resolution thresholds reported for Landolt-ring targets. But this is mere coincidence. Resolution thresholds may be made as small as desired with parallel-line targets, simply by increasing the thickness of the lines. The resolution target then intergrades with one presenting a bright line on a black field, and for such a line there is no minimal visible width.

Resolution of lines does not require an unstimulated row of cones between stimulated rows, hence is not limited by the diameter of one cone. It is only necessary that the rows of cones be differentially stimulated; so, it is the intensity-discrimination function that sets the limit upon visual acuity: in resolution, one is discriminating intensities within the diffraction retinal image of the target. The conception of the mental image as being made up of dots, each contributed by a cone, is fallacious and outmoded.

The "retinal local signs" so important in space perception are neither retinal nor local, but cortical and directional. The stimulation of a retinal point arouses a cortical point which now has information regarding oculocentric direction but not of distance, hence not of place. Space is more finely graduated than is the visual-cell mosaic (as vernier and motion acuities show), since the multiplication of paths between the cones and the cortex makes a great number of cortical elements correspond to two adjacent cones. Differential illumination of these cones can cause activity to "peak" in any one of many cortical cells, so that the spatial point may be directionalized between the produced axes of adjacent cones. Visual space is thus made subjectively "continuous."

Orwyn H. Ellis,
Recorder.

OPHTHALMOLOGICAL SOCIETY OF MADRID

May 14 and June 18, 1948

HYDATIDIFORM CYST OF ORBIT

DR. MARIN AMAT AND DR. BENZO, in discussing the surgical cure of a hydatidiform cyst of the orbit, referred to the case of a 5-year-old boy who had had intense pain in his left eye for 2½ months and awoke one day to find his lids greatly swollen. During the 2 or 3 days that the lids remained swollen, the pain was gone. The cycle repeated itself every 3 or 4 days.

Examination of the left eye showed a pronounced, irreducible exophthalmos; very marked edema of both lids, especially the upper; slight erythema of the skin of the lid; almost complete limitation of ocular movements; sensation of a fluid wave in the upper inner angle of the orbit; and visual acuity of ¼. The fundus showed a white papilla, with sharply defined borders and normal vessels, that is, a developing, simple (descending) atrophy. Laboratory findings gave a red blood count of 5,040,000; leukocytes, 10,700; eosinophiles, 6; lymphocytes, 50. The Arneth index showed a deviation to the right, the intradermal reaction of Cassoni was positive after 6 hours, and positive after 24 hours.

A Krönlein operation was performed and, at the apex of the orbit, situated between the superior rectus and the inferior rectus, was a cyst, the size and shape of a small date, having a thin covering which broke during the dissection and poured out a colorless transparent liquid. The operation was completed by repositioning the osteo-musculo-cutaneous tissue.

The postoperative course was followed by an intense inflammatory reaction (of an allergic nature) which lasted nearly a month. At the end of this time, a cure was obtained with conservation of vision and a perfect cosmetic result.

Discussion. Dr. Mario Esteban opened the discussion by saying that Dr. Marin Amat had reviewed the symptomatology and differential diagnosis of hydatidiform cysts of the orbit so completely that there was nothing to add. He only pointed out that one must not ascribe an absolute role to the eosinophilia, since it is absent in some cases, and on the other hand may be present in tumors, as in sarcoma. Puncture for diagnostic purposes must not be done without taking precaution against an anaphylactic shock.

As for treatment, surgical extirpation is better than injection of modifying substances. The latter method should be reserved, as in the early days of marsupialization, for those cases where the extirpation is difficult or where, because of the situation and adhesions of the cyst, important organs have to be sacrificed in the operation. However, he recommends to puncture the cyst with a syringe before the operation in order to remove some of the contents, taking care not to spill any of the hydatid liquid on the tissues and, without retracting the needle, inject some formalin into the cavity before detaching the membrane, which ruptures easily. Evacuating the contents of the cyst leaves the membranes flaccid, which facilitates the extirpation, and the injection of formalin is useful for its sterilizing effect.

CYSTICERCUS OF THE VITREOUS

DR. MARIN AMAT AND DR. MARIN ENCISO presented a man, aged 39 years, who had lost the sight of his right eye a year and a half before, after a period of violent pain and acute inflammation, and who for the past several days has noticed complete, momentary lapses of sight in his left eye.

Examination showed in the vitreous of his left eye a cylindrical shaped vesicle fairly large and of a bluish color, with a rounded end at the upper part of the fundus and at the other end a thin and long, necklike structure which ended in a rounded area, like a head. The vesicle displayed lively movements of displacement and contraction, especially of the head and neck of the parasite, which reminded one of the antennas of a snail.

The right eye showed an atrophic iridocyclitis, perhaps also of a parasitic origin. Laboratory tests were negative to the Wassermann, urine, Weinberg, and Cassoni tests. Erythrocytes were 3,650,000; leukocytes, 4,800; eosinophiles, 2; and lymphocytes, 27 percent. The patient was seen by other members of the staff who agreed with the diagnosis.

CORNEAL OPACITY WITH MICROCORNEA

DR. MARIN AMAT presented a 5-month-old girl who, shortly after birth was treated with injections of Hepabismuth. She received 36 intramuscular injections twice weekly, and no results were obtained. The child's eyes were turned upward all the time, hiding the cornea under the upper lid, as is found in those born blind. She was given a subconjunctival placental injection (Filatov's method) in hope that it might stimulate the biologic development of the fetal cornea tissue.

RETINAL EDEMA

DR. MARIN AMAT presented a patient who showed a quadrangular zone of retinal edema between the macula and the papilla apparently due to a disturbance of the circulation. He thought the condition was due to a spasm of a cilioretinal vessel whose exit from the papilla at the border of the scleral opening was compromised and appeared thin and threadlike.

An examination of the patient showed, in addition to the edematous zone, a slight clouding of the retina in the upper half, the upper branch of the central artery of the retina was thin, almost threadlike. Perimetric examination showed a loss of vision in the lower half of the visual field, although central fixation was retained.

Treatment with vasodilating drugs (acetylcholine, vasil, eupaverine, nicotinic acid) prevented a spasm of the inferior branch of the central artery, which usually occurs. By using intramuscular injections of organic iodine, a satisfactory cure was obtained, the patient having a visual acuity of 1.00 (20/20) in the eye and only a slight peripheral reduction of the visual field in the lower part. However, there remained a slight pallor of the papilla and a slight reduction in the caliber of the arteries in the upper half of the retina as compared to those of the lower half. The favorable outcome of the case is shown by the visual field charts taken during the course of the disease. In addition to this result, which is worth while reporting, the case offered the unusual opportunity of following ophthalmoscopically the evolution of a retinal arterial spasm.

PTOSIS OPERATION

DR. MARIN AMAT showed a girl who was operated on for congenital ptosis of the upper lid by the procedure of Friedenwald and Guyton. The simplicity and effectiveness of this method deserve its widespread application (published in the AMERICAN JOURNAL OF OPHTHALMOLOGY, 31:411 (April) 1948).

EPIBULBAR EPITHELIOMA

DR. MARIN AMAT AND DR. MARIN ENCISO presented the case of a woman who, following the embedding of a foreign body in the cornea, developed a wartlike structure in the upper-outer portion of the corneal limbus. It was removed three times, but rapidly reformed. She entered the Provincial hospital of Madrid where the authors diagnosed the lesion as an epithelioma.

Operation consisted of complete extirpation of the neoplasm with treatment of the region of the implantation at the corneal limbus by diathermy and a conjunctival covering. Histopathologic examination showed the lesion to be a prickle-cell epithelioma, a type most refractory to radiotherapy. Four months after the operation there was no recurrence. Visual acuity was normal and the globe was not affected.

LEUKOSARCOMA OF IRIS

DR. MARIN AMAT AND DR. MARIN ENCISO presented the case of a 46-year-old

woman who had had a circumscribed lesion in the iris for a period of 10 years which gave her no trouble until the beginning of the year when she showed a hemorrhage in the anterior chamber. This was absorbed in a few days, but shortly thereafter there occurred a more extensive hemorrhage which alarmed the patient considerably. The examination showed a neoplasm, the size of a grain of rice, white and surrounded by many thick capillaries, and in addition a deposit of dark brown blood (the remains of the last hemorrhage) in the anterior chamber. The condition was diagnosed as leukosarcoma, and the treatment consisted of excision of a large section of the iris which contained the neoplasm. Histopathologic examination confirmed the clinical diagnosis of a leukosarcoma. The postoperative course was uneventful, and resulting vision was 20/20.

The authors then discussed the apparent rarity of a leukosarcoma in a pigmented organ like the iris, the slow evolution of the neoplasm, the uncertainty of the time period for the development of metastases in distant organs, and the great advantage of being able to preserve the eye and normal vision whenever possible.

Discussion. Dr. Carreras Matas said that this case was a typical example of a sarcoma of the iris which is curable by extirpation of the iris. More delay might have proved too late and the patient should be congratulated on having been treated so wisely and in time. That the lesion was a leukosarcoma is rather curious. One must remember, however, that, although it originated in a tissue very rich in melanophores, the melanoblasts in the adult eye are very scarce, being found almost exclusively at the corneal limbus.

RETINITIS PUNCTATA ALBESCENS

DR. B. CARRERAS MATAS referred to an observation of a patient with retinitis punctata albescens who, having had hemeralopia of a half hour's duration, began to notice at the age of 18 years absence of the dis-

turbance on rainy days although not consistently. This indicates a shortening of the time of adaptation and an evident improvement.

Discussion. Dr. Marin Amat said that the interesting thing about this affection were the points which this condition has in common with pigmentary degeneration of the retina and the points wherein the two conditions differ.

The points in common are: (1) Both are congenital, (2) appear in the first years of life, (3) are found in several members of the same family, and (4) the patients show difficulty of adaptation to low illumination.

The differences are (1) In the progress (pigmentary degeneration is always progressive, whereas retinitis punctata albescens very rarely increases), (2) the fundus shows completely opposite pictures (black spots in one and white spots in the other, with alteration in the retinal vessels and atrophy of the papilla in the advanced stages of retinitis pigmentosa), (3) alteration in the visual field in retinitis pigmentosa begins with a large annular scotoma with preservation of the peripheral and central fields and in retinitis punctata there is a concentric contraction.

Dr. Matas, in closing, said that the ophthalmoscopic pictures described by Japanese authors on hemeralopia due to dietary deficiencies are very suggestive. The observations of Dr. Tena Ibarre refer to the progressive form of the disease. But there certainly exist benign forms which tend to get better. Our patient is one of them.

PLASTIC SURGERY OF LID

DR. TENA IBARRE presented a case of blepharoplasty of the upper lid. The method of Fricke (tissue taken from the temple) and the method of Snydacker (taken from further parts) were used, and the result esthetically and functionally was perfect.

Joseph I. Pascal,
Translator.

ACTH IN MYASTHENIA GRAVIS

One of the functions of the editor of an ophthalmic journal is to bring to the attention of his readers discoveries in other fields of medicine that may be of significance in his specialty and to point out lines of investigation that may be fruitful in his field.

Since last May when the Mayo Clinic announced the spectacular results that had been procured by treating rheumatoid arthritis with Compound E, or cortisone, the medical world has been impressed, stimulated, and exhilarated. Ophthalmologists share in this excitement for ocular signs and symptoms, even blindness, are fre-

quently associated with rheumatoid arthritis and rheumatic fever. To cite some examples, phlyctenular conjunctivitis, scleritis, iritis, keratoconjunctivitis, scleromalacia perforans, Reiter's disease, Behçet's syndrome, and others.

Cortisone, prepared solely form bile acid, is difficult and expensive to produce and the quantity for experimental studies is restricted. The newer drug, adrenocorticotropic hormone, called ACTH at present, presumably stimulates the adrenal glands to secrete more cortisone. ACTH is an extract of the pituitary of hogs. It is said that about 200,000 hogs are required to produce half a

pound of the drug. It is, therefore, costly to produce and extraordinarily difficult to prepare. The clinical work that is necessary to prove the usefulness of this product cannot be done until an adequate supply is available.

The United States Public Health Service is attempting to discover new sources of supply, and has reason to believe that the African Strophanthus sarmentosus seed may provide more of the remedy. A joint expedition sponsored by the Public Health Service and the Department of Agriculture has been dispatched to Africa, Malaya, Liberia, and China to obtain specimens of various plants. The synthesis of the drug will require much effort and time. Thus, we see that the physicians in daily practice and their patients have a long wait ahead before an adequate supply of either cortisone or ACTH is available for daily use.

In the meantime, as is usual when any new and startling remedy is announced, the drug is being tried in conditions other than that for which it was first employed, in this case rheumatoid arthritis. Dr. Torda and Dr. Wolff report in the *Proceedings of the Society for Experimental Biology and Medicine* (71:432, 1949) on the effects of adrenocorticotropic hormone on neuromuscular function in patients with myasthenia gravis.

It was administered by these investigators to patients with myasthenia gravis mainly on the basis of the following observations and inferences: (1) The immediate cause of the symptoms of myasthenia gravis is a decrease of acetylcholine synthesis; (2) administration of ACTH increased acetylcholine synthesis in vivo; (3) increase of the lymphatic tissue, round-cell infiltration of various organs, mainly striated muscle, and hyperfunctioning thymus have been found in patients with myasthenia gravis (studies have shown that one of the sources of the substances that inhibit acetylcholine synthesis is the thymus—administration of ACTH induces reduction of the mass

of the thymus and the lymphatic tissue); (4) removal of the pituitary gland in rats induces changes in the electromyogram that closely resemble the abnormalities noted in patients with myasthenia gravis; and (5) the pituitary gland of several patients who died of myasthenia gravis showed accumulation of an eosinophilic colloid material suggesting altered function of the gland.

Torda and Wolff administered 400 mg. adrenocorticotropic hormone in amounts of 20 mg. every six hours to five patients moderately to severely ill with myasthenia gravis. "Changes that may indicate the beginning of an incomplete remission occurred after completion of the injections. These changes consisted of decrease of the symptoms and outward manifestations of muscle dysfunction, disappearance of the abnormalities noted in the electromyogram, increased work performance in the ergograph, and increase to normal of the ability of serum to support acetylcholine synthesis. The incomplete remission appears to be long standing."

The authors of the report exhibit a praiseworthy restraint in reporting their findings. Those who take the trouble to read the paper will be impressed with the high scientific caliber of their work and presentation, quite different from many reports of the results obtained from other "biogenic stimulators."

One can foresee in the near future the employment of ACTH in all sorts of chronic and hitherto unexplained maladies, even retinitis pigmentosa, for example. This is praiseworthy and necessary; but it is to be hoped that, like those of Torda and Wolff, such clinical experiments will be conducted on the highest scientific plane and the results modestly and properly presented.

Derrick Vail.

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LIGHTING FOR TRAFFIC SAFETY

Visual impressions register more slowly as the level of illumination drops. Consequently, motor accidents at night entail a

severer toll in deaths, injuries, and property damage since the driver is allotted less time and space to avoid contact or reduce the force of impact. Per accident at night the bodily injuries are more serious and the property damage 50 percent higher than in daytime.

Night driving is being facilitated by more efficient headlights and more adequate illumination on streets and highways. In daylight, an obstacle is distinguished by the detail revealed by its reflected light. Enough artificial light to allow such discernment is not generally practicable nor indeed necessary except for crowded business areas.

Satisfactory visibility is obtained if the background is brighter than the object (silhouette discernment), or if the object is brighter than the background (reverse silhouette). Adequate pavement brightness permits all important pavement details to be seen and makes silhouette discernment effective.

Pavement brightness depends on the illumination and the pavement reflectance. The diffuse reflection factor of a 10-year-old concrete pavement is 22 percent; of similar asphalt and brick pavements, 7 percent. The more-reflecting surface gives a greater distance of road visibility. Pedestrians are the most important of obstacles, and the reflectance of their clothing ranges from 2 to 15 percent, the average for men's clothing being 5 percent.

When electric lighting was first applied to headlamps in 1914, the single all-purpose beam provided a compromise between road illumination and glare. The dual beam became necessary as operating speeds increased, and was introduced in 1930. The driving beam of 50,000 candle power allowed seeing at a sufficient distance to stop a car travelling 45 miles per hour in about 200 feet. This apparently fulfilled the requirements, since the motorist's line of sight usually centers at a point approximately 200 feet ahead of the car. But, because of the

time factor in vision, decreased visibility accompanied further speed. For each increment of one mile per hour in speed, a driver perceives an unexpected obstacle at two feet less distance.

Since 1940, the driving beam produced by a pair of headlights has been increased to 75,000 candle power. The depressed beam for the reduction of glare now directs more light to the right edge of the road which aids vision during the approach of another car. The reflector, filament, and lens are aligned and hermetically sealed during manufacture to insure perfect and permanent focus. The "sealed beam lamps," now in universal use, maintain almost their initial output throughout the life of the car. When driving in dense fog, the depressed beam must be used as the layer of lighted fog between the roadway and the driver's eyes is then thinner and so causes less interference with seeing.

On city streets and on roads with high traffic density, headlamp lighting alone is insufficient. Fixed lighting is necessary which should give a minimum value per square foot of street surface of 0.4 to 1.2 foot-candles, according to the density of pedestrian and vehicular traffic. Controlled light direction is obtained by the reflector-type pendant luminaire. Glare is avoided by raising the lamps high above the street level. The glare effect at the height of 20 feet is double that at 30 feet. The entrances of long tunnels must have supplementary lighting for daytime operation to avoid a too abrupt light change. At 25 feet from the tunnel entrance, the illumination should be 100 foot-candles; at 100 ft., 25 foot-candles.

With the same amount of light similarly distributed, equal visibility is produced by sodium-vapor, mercury-vapor, and filament lamps.

The filament lamp is best adapted for general use. It produces light of pleasing color and is available in a wide variety of sizes. Globes of clear rippled glass are

preferable because of the low light absorption.

Mercury-vapor lamps for street lighting are made in 250- and 500-watt sizes. Although costly to install, their high efficiency makes maintenance economical. The color contrasts well with the display lighting of business districts. In Los Angeles, the obsolescent arc lamps on Broadway were recently replaced with 16,000 lumen mercury-vapor units. The new lighting gives the street two foot-candles as compared with 0.31 foot-candles of the old system at 20 percent of the operating cost.

Sodium-vapor lamps are only in 10,000 lumen units. This attention-getting light is especially good for underpasses, bridges, railroad crossings, sharp curves, and dangerous intersections. The yellow light gives complexions an unnatural appearance and hence is not desirable for city streets. Sodium-vapor lamps are much more costly than equivalent filament globes but give nearly three times as much light per watt.

City lighting systems were originally designed for protection against robbery and other crimes; lighting to enhance business areas followed; but only lately has lighting for traffic safety become a goal. Since 1910, the expenditures for street lighting have gone up but 60 percent while the speed of cars has doubled and the traffic density has increased fivefold. The main traffic arteries in towns and cities, although one tenth of the total street mileage, account for half of all urban fatalities. The National Safety Council asserts that 35 percent of all night traffic accidents are traceable to inadequate lighting. The overall ratio of night to day fatalities has increased from 1.0, in 1930, to 1.4, at present, due to the lag of night lighting in relation to the growth of traffic.

In Chicago, a 1940 study showed that 35 percent of the total traffic fatalities occurred in 4.4 percent of the total street milage, and that more than 62 percent of the fatalities happened at night. After five dangerous

insections were provided with improved lighting, the total night accident rate dropped 37 percent. In Detroit in 1936, the average illumination on the main thoroughfares was 0.2 foot-candles. When this was increased to 1.2 foot-candles the ratio of night to day fatalities on these streets decreased from 6.9 to 1.4. Since November 1, 1946, when Indianapolis revised its prewar lighting, the annual night accidents on a typical busy street fell from 23 to 14. In Los Angeles, the improved street lighting inaugurated in 1947 reduced night pedestrian fatalities by 33 percent over the previous year. A decade of good lighting in Hartford, Connecticut, showed, in comparison with the previous decade, a reduction of 76 percent in night fatalities, 78 percent in pedestrian injuries, and 58 percent in all types of accident.

During the depression of 1932, Detroit reduced its lighting 35 percent, and, as a consequence, the proportion of night to day fatalities doubled. The cost of caring for the victims of traffic accidents more than exceeded the savings. In the dim-out of 1942 the ratio of night to day fatalities in New York City and Long Beach, California, rose from 1.33 to 2.15. In Connecticut the night accident rate that year increased 35 percent.

Automobile accidents are brought about by a combination of circumstances, and the removal of one factor often results in avoiding the accident. The more certain seeing provided by good lighting reduces the accident quota previously attributed to inattention, carelessness, fatigue, speeding, or drunkenness. At minimum visibility drivers reacted to an unexpected obstacle at 20 to 80 percent of the distance noted when warned of its presence. Hence a safety factor of 2 to 5 is required for the variation in driver attention alone. In reading with 10 foot-candles, as compared with the minimum illumination necessary (0.1 foot-candles), the safety factor is 100. In instruction signs on the road the color combinations chosen should be those seen best under

minimal illumination, such as black on aluminum, white on dark green, black on yellow, or black on white.

Accidents preventable by good lighting cost the nation annually 10,000 lives and $187,000,000. Modernized lighting is expensive, but it can be had at half this dollar loss and would, moreover, expedite pedestrian and vehicular traffic, increase property values, reduce crime, and promote civic pride.

James E. Lebensohn.

CORRESPONDENCE

Professor Meller's Birthday

Editor,
American Journal of Ophthalmology:

Many of the readers of the Journal will be interested to hear that Prof. Joseph Meller's 75th birthday will be celebrated at the University of Vienna on October 22, 1949. Somewhat older than when seen last by most of his American friends, but unbroken in body or spirit by the trials and tribulations of the last decade, Professor Meller will receive the international group of well-wishers and congratulators with the multilingual warmth and sparkling wit for which he is so widely known.

Joseph Meller was born in the town of Stein on the Danube on October 22, 1874, attended primary and middle school in the nearby town of Krems, and university and medical school in Vienna. During his undergraduate years, he showed special interest in anatomy and internal medicine.

Just when and how Meller's mind turned toward ophthalmology as a vocation is not known to me. The fact is that Meller's ophthalmic career started in 1898 when he became a resident at the Second University Eye Clinic or, as everybody then knew it, the Fuchs Clinic in Vienna.

Right from the beginning, he and ophthalmology got along well. He ascended the academic ladder with remarkable rapidity. In 1905, he had advanced to the position of first assistant; in 1912, to that of associate professor. In 1915, he was appointed to the Chair of Ophthalmology at the University of Innsbruck, from where he returned to Vienna in 1918 when, through one of the last decisions of the Austrian Emperor, he was appointed professor of ophthalmology and director of the First Eye Clinic at the University of Vienna.

After having reached ophthalmic maturity and fame in the heydays of the Austrian Empire and of the Viennese Medical School, Meller now had to shoulder the responsibility for carrying on under most adverse, most discouraging conditions, which—with brief intermissions—prevailed up to the time of his dismissal by the Ministry of Science and Education of the German Reich in 1944.

As early as 1939, one year after the "Anschluss," and again in 1942, Meller had submitted his resignation, but was prevailed upon by the Executive Faculty to continue at his post. His frankness in academic matters had led to a number of disagreements with the "Authorities in Berlin" which in a letter dated May 10, 1944, finally relieved him of all his academic duties "in the interest of the younger academic generation."

After 25 years of leadership under the most varied but never really favorable conditions, Meller retired to literary work and private practice in which he is still actively engaged.

Meller's scientific accomplishments are too well known to require more than brief mention here. There is no field in ophthalmology to which he has not made important contributions. His list of publications, 124 up to date, clearly reveals pathology as his main approach to ophthalmic problems, and as the recommended and actually practiced basis of his clinical thinking and acting.

Of his many fields of special attainments, his work on the tuberculous etiology of endogenous uveitis is probably most signifi-

cant. In Meller's own classification of ophthalmologists, he undoubtedly belongs to the small group that "keeps on working indefatigably in order to produce more and newer evidence in favor of the tuberculous etiology of endogenous uveitis."

In the United States, Meller is probably best known as the author of his textbook on *Ophthalmic Surgery,* the first edition of which was published in English in 1908. During a period of 40 years, seven editions of this text have been printed and avidly absorbed by ophthalmic readers all over the world. The success of this book, in my humble opinion, is due to Meller's mastery of the art of ophthalmic surgery as well as to his mastery of the art of clear, logical ophthalmic thinking, speaking, and writing. Of both of these arts he has given most generously. Three fourths of all the surgical patients of the clinics under Meller's direction have had the opportunity and benefit of his own, personal, surgical skill.

His mastery of the art of clear logical thinking accounts for his success as a teacher. His great gift of making the principles of ophthalmology attractive and fascinating to the undergraduate student is matched by a much-envied facility in presenting transcendental ophthalmology to very learned audiences.

During 44 years of academic activity, Meller has raised a large ophthalmic family, the American members of which, in the simple fashion of this country, will want to add "many happy returns" to the wishes of those who will be fortunate enough to attend the birthday celebration personally.

(Signed) Peter C. Kronfeld,
Chicago, Illinois.

BOOK REVIEWS

SURGERY OF THE EYE. By Meyer Wiener, M.D. New York, Grune & Stratton, 1949, second edition. 392 pages, 425 figures, index. Price, $12.00.

The first edition of Dr. Wiener's popular book on ophthalmic surgery and a second printing of it were quickly absorbed. The new publishers have performed a useful service in bringing out this second edition.

It has been revised and some parts have been rewritten by the author, who has brought up to date the advances in this art that have occurred in the last 10 years. This includes cataract sutures, goniotomy, and orbital implants. The author's method of corneal transplantation by means of a specially constructed punch is described and promoted as a tried and proven measure.

Old readers who are familiar with the first edition will recognize the arrangement of illustrations and text as old friends. Newcomers will find much of interest, value, and instruction. The views expressed, while generally universally held, are primarily based upon the experience of a great ophthalmic surgeon.

Derrick Vail.

CLINICAL ORTHOPTICS: DIAGNOSIS AND TREATMENT. By Mary Everist Kramer, Supervisor, The Orthoptic Department, The George Washington University Hospital, Washington, D.C. Edited by Ernest A. W. Sheppard, M.D., Professor of Ophthalmology, and Louise Wells Kramer, Certified Ophthalmic Technician. St. Louis, The C. V. Mosby Company, 1949, 475 pages, 147 illustrations, cloth bound. Price, $8.00.

The discussions of orthoptic training, strabismus, fusion, amblyopia ex anopsia, abnormal retinal correspondence, convergent and divergent strabismus, the vertical deviations, and the heterophorias are taken up in order. The author with the assistance of her co-writers presents an excellent resume of the anatomy, the visual pathways and oculomotor system, physiology, and optics for the use of an associate in the ophthalmic field.

At the end of each chapter are questions

relevant to the material presented and a list of references.

The different types of instruments including the major amblyoscopes and the other equipment available for making an examination of the ocular muscle balance are given and the mechanics illustrated.

The chapter on surgery by Dr. Ernest A. W. Sheppard emphasizes the importance of a complete diagnosis before surgery is outlined. The discussion of reading disabilities completes the presentation of orthoptics, as the hope of many parents of these children is that ocular training will improve reading ability. Miss Kramer discusses the complex problem and gives a list of references that will help the physician, as well as the parents, when confronted with reading problems in children.

                         Beulah Cushman.

LE MENINGO-ENDOCRANIOSI IN OFTAL-MOLOGIA. By Alfio Rubino. Bologna, 1949. 93 pages, 25 figures, bibliography.

In this monographic treatment of chronic arachnoiditis, the author indicates the importance of an understanding of the syndrome for many branches of medicine—neurology, endocrinology, and radiology, no less than ophthalmology..

A short review of the history of our knowledge of the lesion goes back to Morgagni. The author then discusses the etiology and pathogenesis and the relation to lesions in contiguous tissues. After a discussion of the general symptoms and radiologic signs, the eye manifestations and their significance are described and discussed in detail.

For example, the author points out the significance for topographic diagnosis of his "small chiasmatic syndrome" which consists of edema of the optic disc with passive hyperemia of the central retinal veins and signs of arterial and venous hypertension combined with a bitemporal upper quadrant hemi-anopia for color. In another chapter the relationship of the lesions to classic opticochiasmatic arachnoiditis is discussed at length. There is possibly a relationship to the Laurence-Moon-Biedl syndrome and to Leber's optic atrophy. In the concluding chapter some therapeutic suggestions are made.

                         F. H. Haessler.

TRANSACTIONS OF THE OPHTHALMOLOGICAL SOCIETY OF NEW ZEALAND (supplement to the New Zealand Medical Journal. Wellington, New Zealand, British Medical Association (New Zealand branch), 1948. Pamphlet form, paper covers, 74 pages.

Herein are published the papers presented at the second conference of the Ophthalmological Society, held at Dunedin, February, 1948. In addition to other papers mentioned below, the report is outstanding by reason of the presidential address, by Rowland P. Wilson, on "Some conjunctival affections." Dr. Wilson is well known for his 19 years of work in Egypt, the reports of which used to appear in the annual transactions of the Giza Institute of Egypt. His presidential address before the New Zealand society is chiefly occupied by an excellent review of the present status of knowledge concerning trachoma, although it deals also with various aspects of bacterial conjunctivitis, follicular conjunctivitis, spring catarrh, and allergic conjunctivitis. (Trachoma is approximately absent from New Zealand, except perhaps among the Maoris of the North Island.)

It is emphasized that what has been historically referred to as "military ophthalmia" or "ophthalmia egyptica," on account of its great incidence among the French and British armies during the Napoleonic campaign of 1798-99 in Egypt, was not an uncomplicated trachoma but a combination of trachoma with various forms of acute bacterial conjunctivitis, the greater part of the affected soldiers being blinded by acute

gonococcal conjunctivitis. Actually, not more than one percent of the blindness in Egypt is due to trachoma, although at least 95 percent of the indigenous population of Egypt is infected by that disease. "Trachoma is of low infectivity and only flourishes in the presence of bad hygienic conditions, carelessness, and apathy." "Unfortunately one of the principal obstacles in the way of further progress in the investigation of the disease is the fact that there is really no satisfactory experimental animal other than man."

Wilson's address is accompanied by 27 splendid illustrations, beautifully reproduced, most of them photomicrographs, and dealing with trachoma, folliculosis, and spring catarrh.

The other papers included in the annual report are: by J. B. Hamilton of Tasmania on the prognosis of sarcoma of the choroid (geneological trees); by W. A. Fairclough on cataract in dystrophia myotonica; by Graeme Talbot on pterygium; by W. C. Burns on herpes ophthalmicus associated with chicken-pox; by C. A. Pittar on late results of successful operation for detached retina; by W. J. Hope-Robertson on the prevention of industrial eye accidents; by W. H. Simpson on penetrating wounds of the eye; by W. A. Fairclough on contact lenses; by L. S. Talbot on congenital dislocation of the lens; and by J. S. Munro on dislocation of the crystalline lens.

The New Zealand Society has 40 members, comprising practically all the ophthalmologists in the country.

W. H. Crisp.

HISTOLOGY AND HISTOPATHOLOGY OF THE EYE AND ITS ADNEXA. By I. G. Sommers, M.D., Los Angeles, California. New York, Grune & Stratton, 1949. Clothbound, 764 pages. Price, $12.00.

The book is divided into three parts. The first 53 pages are devoted to very brief discussions of the normal histology, embryology, and senescence of the eye.

The second part entitled "General pathology in relation to the eye" should stimulate the interest in ocular histopathology of the beginner who often finds this subject dry unless it is correlated with more familiar clinical and pathologic knowledge.

The third part deals with the specific histopathology of the ocular tissues. It contains a wealth of informative material but suffers acutely from the paucity of illustrations. Greater brevity in stating the essential pathologic findings of each condition in lieu of pages of flowing descriptions without highlights, would greatly facilitate, particularly for the beginner, the creation, at least, of mental pictures.

It is also disappointing that the author did not avail himself of more modern terminology and classifications, as for instance in the discussions of tumors and the glaucomas.

The book is difficult to read because of the innumerable "Germanisms" in expressions and grammar, which not only mar the elegance of style but also detract from the clarity of statements, making them not infrequently ambiguous.

The most valuable part of the book, at least in this reviewer's opinion, is the short digest of source material, and the pertinent bibliography which follows each chapter. Although of necessity incomplete, it should promote collateral reading and acquaint the reader, without confusing him, with various divergent opinions expressed in the literature.

Bertha A. Klien.

ABSTRACT DEPARTMENT

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Fischer, Franz. **Embryonic properties of lens fibers.** Klin. Monatsbl. f. Augenh. 114:202-205, 1949.

In larvae of salamandra maculosa in which the lens had been removed 70 to 120 days before histologic examination, the author found that primary lens fibers can grow unusually long and are only inhibited in this growth by the anterior wall of the lenticular vesicle. The epithelial wall of this vesicle and the pressure within it are the definitive factors in the normal development of the lens fibers. The developing fibers have the property of imitating the form of a lens without the influence of an external factor. (3 figures, references.)

Max Hirschfelder.

Vetter, Joachim. **Peculiar pigmentation in optic nerves and surrounding tissues of the globe in animals.** Klin. Monatsbl. f. Augenh. 114:214-218, 1949.

The pigmentation of the region within and around the lamina cribrosa is very variable in different groups of animals as well as within the same group. The author examined the eyes of forty mammals and describes especially the pigmentation in camels (very fine pigmentation within the lamina mesh), in hyenas (coarse pigment) and in wapitis which show an unusual amount of pigment within the optic nerve along its sheats. This pigment is not related to the one found in the pigment layer of the retina. (3 figures, references.)

Max Hirschfelder.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Zollinger, R. **The occurrence of mast cells in iris and ciliary body.** Ophthalmologica 117:249-252, April-May, 1949.

True mast cells occur in pathologic sections of the uvea of chronically inflammed human eyes. In small numbers mast cells can be found in many ocular conditions and in similar numbers in the aqueous.

Peter C. Kronfeld.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Goldmann, H. **Do the aqueous veins contain aqueous?** Ophthalmologica 117: 240-243, April-May, 1949.

Goldmann reports accurate fluorescein determinations made in blood and aqueous by means of an optical method with an accuracy of ±5.5 percent. With this method he found the fluorescein concentration of the plasma to be at least a hundred times greater than that of the aqueous during the first hour following the intravenous injection of fluorescein. The absence of fluorescence under these conditions proves conclusively that the aqueous veins do not contain blood plasma.

Peter C. Kronfeld.

Michiels, J. **Experimental study on the formation of the aqueous humor.** Ophthalmologica Supplement No. 34, 1949.

The static and dynamic chemistry of the aqueous is reviewed rather thoroughly. No clear concept of the function of the blood-aqueous barrier can be derived from the experimental data which are now available. The author has studied the appearance in and disappearance from the aqueous of gum arabic which he injected intravenously into rabbits in a solution of the same osmotic pressure and viscosity as that of blood. Between 50 and 100 cc. of the gum solution were injected at the rate of about 2 cc. per minute. Gum arabic entered the aqueous in measurable quantities, together with an abnormal amount of blood protein. Just as in studies by other authors, the intravenous injection of gum arabic was found to alter the permeability of the blood-aqueous barrier. It is unlikely that the gum itself exerted any chemical or toxic effect on the capillary wall. The colloidal state of the blood was changed very profoundly by the addition of the gum. Probably this changed physical status affected the capillary wall. The gum disappeared from the aqueous slowly and without having been broken down into smaller molecules since the rabbit does not possess any enzymes that break down gum arabic. No important conclu-

sions concerning the elaboration of normal aqueous can be drawn from work of this kind.　　Peter C. Kronfeld.

Schenk, Fritz. **Pharmacological effects upon the ocular tension of the rabbit.** Ophthalmologica 118:42-65, July, 1949.

The effects upon the ocular tension of the drugs most commonly used in ophthalmology were studied on rabbits under urethane anesthesia. Fairly consistent fluctuations were observed after the instillation of atropine, hyoscyamine and scopolamine. An initial rise of from 1.5 to 4.5 mm. was followed by a drop of from 6.5 to 8 mm. The original level was reached after 3 to 4 hours. In 2 out of 26 rabbits the drop in tension was followed or superseded by a marked secondary rise. The instillation of cocaine caused fluctuations similar to those observed after atropine. Indifferent results were obtained after the intravenous injection of acetylcholine, methylene blue, caffeine and histidine. Ergotamine caused a slight drop in tension. In general, the administration of a large variety of drugs produced either no appreciable effects or a slight to moderate drop in tension. Whatever the experimental procedure is, the normal eye of the rabbit is more apt to respond with a drop than with a rise in tension. In a small number of rabbits the response is very different from that of the overwhelming majority. This exceptional behavior may be an expression of vasomotor or vegetative lability.

Peter C. Kronfeld.

4
PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Beach, S. J. **"Myopia cures."** Tr. Am. Ophth. Soc. 46:284-294, 1948.

The author discusses some evidence consistent with the unorthodox theory that improvement in vision in nearsighted persons which follows sight train-

ing exercises may in some instances be due to a genuine reduction of the myopia. The feature of sight training courses that keeps the devotees faithful is the flashes of distinct vision they elicit. As it frequently is monocular and shifts from one eye to the other it cannot be ascribed to improved interpretation of blurred images on the cerebral level. It seems to be a development of the squinting used by myopes. Use of akinesis of the orbicularis and retrobulbar akinesis of the extraocular muscles might give a clue to whether pressure is exerted by the orbicularis or the extrinsic musculature.

David Harrington.

Blum, J. D. **The tolerance for contact lenses.** Ophthalmologica 117:214-217, April-May, 1949.

A questionnaire was sent to fifty consecutive patients who had received molded plastic contact lenses and 86 percent reported that they are wearing their lenses for an average of nine hours every day.   Peter C. Kronfeld.

Dufour, R. **Plastic contact lenses. Preliminary report.** Ophthalmologica 117: 207-211, April-May, 1949.

This report from the University Eye Clinic of Lausanne deals with the results obtained with plastic molded contact lenses in 60 patients with varying ocular conditions. The lenses are constructed to admit a capillary layer of tear fluid between cornea and contact lens, either through an area of clearance nasally and below or through multiple channels in the scleral portion of the lens. Sixty percent of the patients are satisfied with the lenses and wear them regularly. In several cases of qualified success or failure, the fitting process has not been completed. One retinal detachment occurred coincidentally during the fitting process. The author's conclusions and experiences

do not differ significantly from those of the American ophthalmologists.

Peter C. Kronfeld.

Handmann, M. **Myopia after inflammatory diseases in the anterior part of the bulbus.** Klin. Monatsbl. f. Augenh. 114:224-233, 1949.

Factors of inheritance are the main cause in myopia. However, there are instances of myopia which cannot be ascribed to inheritance. The author describes the case histories of 14 patients who had unilateral myopia as a late result of dendritic, parenchymatous and eczematous keratitis. Amblyopia was frequently associated with the nearsightedness which developed over the course of many years. The author believes that inflammatory processes of the cornea may influence the metabolism, growth and tissue stability of the sclera as a whole. (References.)   Max Hirschfelder.

Knuesel, O. **Further experiences with contact lenses.** Ophthalmologica 117:212-213, April-May, 1949.

The author stresses the nonspherical surface of most human eyes. He measures the curvature of the sclera in several meridians and constructs the contact lens on the basis of these measurements. Accurate fitting of the scleral portions is the most important factor in the success of a contact lens. Corneal edema is usually due to one or two tight areas or a very tight fit of the entire scleral portion. The composition of the contact lens solution is of no significance. One patient is equally comfortable with well water or apple cider.   Peter C. Kronfeld.

Lancaster, W. B. **Some secondary subjective effects produced by prisms.** Tr. Am. Ophth. Soc. 46:262-283, 1948.

The various optical distortions produced by prisms can be explained on the

basis of the obliquity of incidence of the rays in two significant planes, the base-apex plane 'and a horizontal plane. The author's explanation of the obliquity is offered as a new contribution to the subject. When a prism is cut at right angles to the base and to the sides, the cross section is a triangle of minimum base and minimum apical angle. When it is cut obliquely, but still at right angle to the base, the triangular cross section has a longer base, a larger apical angle and more power to cause deviation.

David Harrington.

5

DIAGNOSIS AND THERAPY

Alden, H. S., Jones, J. W., and Rankin, J. Roentgen-ray treatment of the eye. Arch. Derm. and Syph. 59:430-434, April, 1949.

For 15 years the authors have used roentgen rays on 300 patients with corneal ulcer. A method is described whereby the cornea can be prepared and 160r per minute applied to it. The average dose used is 70 to 80r at weekly intervals for five treatments. Tissues that receive less than 300r usually recover while tissues that receive 1500r or more do not recover from damage caused by the rays. Of 159 patients treated before 1943 the average dose was 252r. Over 60 percent of these have been examined with the slit lamp and show no changes in the lense. One patient who had received other X-ray therapy for a resistent blepharitis had some slight lenticular opacities.

H. C. Weinberg.

Amsler, M., and Verrey, F. Injections of pencillin and adrenalin into the anterior chamber. Ophthalmologica 117: 243-246, April-May, 1949.

Penicillin, 300 to 400 units dissolved in 0.2 cc. of 2-percent procaine, plus a small amount of adrenalin is injected into the anterior chamber immediately after most of the contents have been withdrawn by means of a hypodermic needle and syringe in cases of serpentic ulcer, endogenous acute and chronic uveitis, perforating injuries, and intraocular foreign bodies. Results were on the whole good, at times almost miraculous, and other times nil. Injected into the anterior chamber, epinephrine is a powerful mydriatic.

Peter C. Kronfeld.

Badtke, G. Treatment of the eye with supersonic stimuli. Klin. Monatsbl. f. Augenh. 114:193-196, 1949.

Space and time difference of a wave have the physical effect of a massage of cells or cell groups. Local rise in temperature and stimulus of diffusion and penetration of fluids follow supersonic treatment. Therapeutic doses are too weak to damage the tissues by rupture and hemorrhage. The therapeutic dosage ranges up to 3.0 Watt per $\frac{1}{2}$ cm.^{2} Two stubborn cases of vitreous opacities after intraocular hemorrhage showed improvement after treatment with the ultrasonator and an incompletely absorbed chalazion responded to treatment. Experiments with rabbits eyes failed to reveal any damage to the tissues.

Max Hirschfelder.

Balcet, C. The use of novocaine in oil in ophthalmic practice. Rassegna ital. d'ottal. 18:44-47, Jan.-Feb., 1949.

Two-percent novocaine in almond oil has great advantages over the use of the aqueous solutions. The results of injection are practically uniform in effect. Anesthesia of the skin begins almost immediately and persists for 24 to 36 hours. Akinesia of the orbicularis appears within two minutes and lasts for six to eight days. The edema is slight and remains for only 24 to 36 hours. There are no subjective or objective disturbances and no tendency to produce ptosis or ectropion.

Retrobulbar injection of the oily solution results in more prolonged anesthesia and was used in cataract extractions and filtering operations for glaucoma. There is a striking difference in the action of the oleous solution on motor nerve fibers and sensory. The former are more profoundly and longer effected.   Eugene M. Blake. ·

Dupont, M. **The signs of syphilis or hereditary syphilis.** Ann. d'ocul. 182:295-300, April, 1949.

The clinical signs of acquired and congenital syphilis are compared with those of tuberculosis to facilitate more accurate ophthalmologic differential diagnosis. A familiarity with the extraocular evidences of syphilis is often of great value in differentiating ocular syphilis and tuberculosis.   Chas. A. Bahn.

Gát, L. **The technique of evisceration.** Ophthalmologica 117:343-346, June, 1949.

The evisceration of the globe has not been more widely accepted because of the danger of sympathetic ophthalmia and the slow and rather painful convalescence. The author removes the cornea completely by means of scissors and the ocular contents by means of a curette. The cavity is packed for two to five minutes to obtain complete hemostasis and is then thoroughly inspected for remnants of uveal tissue. After the internal surface of the sclera has been found to be perfectly clean and dry the cavity is filled with two or three grams of ultraseptyl, a sulfonamide, and the anterior opening is closed with interrupted sutures. Chemosis usually lasts less than four days.   Peter C. Kronfeld.

Goldmann, H. **Biomicroscopic findings in the chamber angle and in the eyeground.** Ophthalmologica 117:253-258, April-May, 1949.

The author describes and demonstrates in beautiful drawings some unusual

gonioscopic findings. His contact lens can be used to a great advantage in the study of fundus lesions. The important question whether small lesions are located in the outer retinal layers or in the lamina vitrea can be decided by slit lamp examination through Goldmann's contact lens.   Peter C. Kronfeld.

Morano, M., and Franchi, E. **Plesioroentgen therapy of ocular diseases.** Ophthalmologica 118:30-41, July, 1949.

The term plesio-roentgen therapy implies a special form of X-ray therapy. It is essentially a low voltage contact method in the development of which Chaoul has played an important part. The X-ray tube which is used in this work is designed by and named after him. In this paper beneficial results from this form of radiation are reported in tuberculous uveitis, localized, solitary chorioretinitis, deep keratitis and in some corneal ulcers. The doses were calculated to produce a series of biological effects which cause an increase of the vital power of the affected ocular tissues with following accelerations of the natural recovery process. Special care was taken to get a localized X-ray effect within the diseased tissue and a minimum of undesirable stray effect.   Peter C. Kronfeld.

6

OCULAR MOTILITY

Fink, W. H. **The surgical anatomy of the superior oblique muscle.** Tr. Am. Ophth. Soc. 46:154-184, 1948.

The superior oblique muscle, the trochlea, the reflected tendon and the insertion and such adjacent structures as the septum orbitale, the levator muscle, the superior rectus muscle, the nerves and blood vessels, and the various fascial membranes are described from the viewpoint of both the anatomist and the surgeon. Surgical procedures are limited to the re-

flected tendon and its insertion. Approaches to this area are discussed.

David Harrington.

Key, S. N., **Orthoptics without instruments.** Texas State J. Med. 45:146-148, March, 1949.

Two methods are described as supplemental to, or in place of the usual orthoptic training, a red filter which can be reduced in density, and bar framing exercises. Donald T. Hughson.

Pascal, J. I. **A static and dynamic muscle scheme.** Opthalmologica 117:217-221, April-May, 1949.

To facilitate the study of ocular muscle disorders, Pascal has devised a scheme in which the extraocular muscles are placed at the midpoints of the sides of a hexagon which is thought to be located in front of each eye. Proceeding clockwise from the 9-o'clock position, the arrangement of the muscles of the right eye on its hexagon is as follows: lateral rectus, superior rectus, inferior oblique, medial rectus, superior oblique, inferior rectus. The arrangement of the muscles of the left eye within its hexagon is the exact mirror image of that of the right eye. Such a scheme illustrates a great many physiologic as well as pathologic phenomena of ocular motility. Peter C. Kronfeld.

7
CONJUNCTIVA, CORNEA, SCLERA

Castroviejo, R. **Keratoplasty for the treatment of keratoconus.** Tr. Am. Ophth. Soc. 46:127-153, 1948.

From a thorough review of the literature on the surgical treatment of keratoconus and his own experience, the author concludes that the partial penetrating type of keratoplasty is the treatment of choice for advanced keratoconus. The preoperative study, technical details and minutiae which must be observed at the

time of operation, methods of suturing the graft and postoperative care are described, and the prevention of anterior synechia and their treatment when they occur, retransplantation after clouding of the graft, and use of radiation in the prevention of vascularization are discussed. (Photographs and drawings.)

David Harrington.

Heinsius, Ernest. **Involvement of the cornea in agranulocytosis.** Ophthalmologica 118:69-75, July, 1949.

The author reports a case of a severe, ulcerative, rapidly-progressive keratitis which for six days had been treated very inadequately at the patient's home. Most of the cornea was involved and a hypopyon filled more than the lower third of the chamber. During the first five days in the hospital the treatment consisted of atropine instillations, yellow oxide of mercury and optochine locally, and milk injections intramuscularly. Under this regime the corneal process became worse. Five days later penicillin treatment was started locally and systemically, and two days later a conjunctival flap was placed over the cornea. The corneal process began to regress but the patient's general condition was unsatisfactory and agranulocytosis was found which responded well to blood transfusions. The patient made a slow recovery. At the time of discharge the affected eye could count fingers at a short distance. The agranulocytosis might have been brought on by some analgesic such as amidopyrine, which the patient received early, but the author suggests that the patient had agranulocytosis from the beginning and that the corneal ulcer was just one of its manifestations.

Peter C. Kronfeld.

Jirman, J. **Physiologic treatment of certain corneal lesions.** Ann. d'ocul. 182:449-454, June, 1949.

Corneal healing depends largely upon the diffusion and osmosis of its nutritive substances. In the treatment of corneal burns and neuroparalytic keratitis the author had used amino acids, including a 2-percent glycocol solution and hemolized blood serum locally with intramuscular injections of 2 to 4 cc. histadine. He also uses antibiotics and irrigates with Ringer's solution. Six severe cases of corneal burns from acetone, potassium hydrate, hot iron, lime and methylene blue were treated by this method, and three of neuroparalytic keratitis. The results recorded were surprisingly favorable. There was very little loss of vision.
Chas. A. Bahn.

Paufique, M. and Etienne, R. **The conjunctival-ganglion syndrome of Parinaud.** Ann. d'ocul. 182:455-460, June, 1949.

The case reported was the result of infection with blastomyces in a 32-year-old woman. The intradermal reaction of a lysate of Rodo turula was strongly positive and she had an eosinophilia of 15 percent. Potassium iodide was administered by mouth, but did not prevent gland suppuration. Chas. A. Bahn.

Stein, A. **The therapy of serpentic ulcer.** Ophthalmologica 117:227-230, April-May, 1949.

Maintenance of a high local concentration of antibiotics is essential in the treatment of serpentic ulcers. The author reports favorable results with penicillin baths applied to the cornea for as long as six hours by means of a rubber eye cup with adjustable rim. The penicillin concentration of the bath varies from 2,000 to 4,000 Oxford units per cc. of fluid. In severe cases these baths are administered day and night with only short rest periods every six hours. A similar eye cup is used for iontophoresis. In Switzerland serpentic ulcers are ap-

parently still fairly common and are caused by pneumococci or staphylococci.
Peter C. Kronfeld.

Varley, R., and Kletz, T. **A case of Kaposi's varicelliform eruption (systemic herpes simplex) with dendritic ulceration of the cornea.** Brit. J. Derm. and Syph. 61:166-169, May, 1949.

A five-year-old girl with multiple umbilicated vesicular lesions over the face developed a typical dendritic ulcer of the cornea four days after admission. Kaposi's varicelliform eruption and dendritic keratitis are discussed as different phases of sensitization to the virus of herpes simplex. H. C. Weinberg.

8
UVEA, SYMPATHETIC DISEASE, AQUEOUS

Remky, Hans. **The diagnostic significance of chorioditis in retinitis albuminurica.** Klin. Monatsbl. f. Augenh. 114: 233-238, 1949.

Disseminated pigmented chorioditis-like spots developed in three patients with advanced albuminuric retinopathy. The eyegrounds resembled each other, even though the clinical diagnosis was malignant nephrosclerosis in one and secondary contracted kidney and endangiitis obliterans in the other two. The fundus findings are described in the literature as chorioditis albuminurica and are caused by endangiitic and necrotic vascular processes in the choroid. The finding points to a most severe vascular disease and usually means a poor general prognosis. (References.) Max Hirschfelder.

9
GLAUCOMA AND OCULAR TENSION

Christensen, L., and Swan, K. C. **Adrenergic blocking agents in the treatment of glaucoma.** Tr. Am. Acad. Ophth. pp. 489-498, May-June, 1949.

Two new drugs of the adrenergic blocking group are analyzed and their results reported in 18 consecutive cases of acute glaucoma which did not respond to other treatment. These drugs are Dibenamine N-N-dibenzyl-B-chlorethylamine hydrochloride), and SKF #194 (N-B-chlorethyl - N - benzyl - B - phenyl - isopropylamine hydrochloride). Dibenamine, a tissue irritant, is injected intravenously in doses of 4 to 5 mg. per kilogram of body weight. Because of its possible effect on the cardiovascular system, especially in hypertensive patients, bed rest for 36 hours is desirable after its use. Dibenamine causes miosis by relaxing the iris dilator. The immediate decrease of ocular tension ranged from 11 to 40 mm. This action is not altered by mydriatic or cycloplegic drugs. In several patients, repeated doses of Dibenamine were administered at intervals of several days. The hypotensive action of the drug decreased with subsequent use. It is not yet known whether supplementary local treatment influences the hypotensive effect of Dibenamine. SKF #194, is closely related to Dibenamine physiologically. In animals' eyes it is more effective than Dibenamine, but it has not yet been used in human eyes.

Chas. A. Bahn.

Esente, I. The Bloomfield-Lambert test on normal, glaucomatous, and hypertensive individuals. Boll. d'ocul. 28:77-90, Feb., 1949.

In the Bloomfield-Lambert lability test, pressure of 60 to 70 mm. Hg is applied for one minute and simultaneously one hand is immersed in ice-cold water. If the intraocular pressure exceeds 30 mm. Hg or if there is an increase of more than 9 mm. in the original tension, the test is positive for glaucoma. To evaluate the test clinically and to elucidate its mechanism the authors examined normal and glaucomatous patients without and with previous administration of cortico-

diencephalic depressor drugs, and persons with generalized arterial hypertension. In 20 normal persons, the test provoked increases in tension no greater than 7 mm. Hg accompanied by increase of the retinal arterial diastolic pressure to values which sometimes exceeded the normal by 20 mm. Hg. Administration of barbiturates did not markedly influence the results although a slight decrease of tension and intravascular retinal pressure was often observed. In 13 patients with glaucoma, barbiturates had little influence on the tension. In three patients with acute glaucoma, the test provoked an increase of intraocular pressure of 2 to 4 mm.; the diastolic arterial pressure in the retina of two of these patients increased slightly and decreased in one. This in spite of a 20 mm. increase of the brachial arterial pressure. In one patient with chronic simple glaucoma, the test was followed by a 5 mm. decrease of tension while the pressure in the brachial artery remained unchanged. In three eyes successfully operated on for acute glaucoma and with tension below 30 mm. Hg the test provoked tension increases of less than 9 mm. Hg and increase of the retinal arterial pressure of 6 to 12 mm. Hg. In the normal eyes of two patients with unilateral juvenile glaucoma and with tension below 25 mm. Hg, the test raised the tension by 10 mm.

Twenty-two persons suffering from general arterial hypertension were tested. In 12 of these patients, a decrease of the brachial artery pressure and an increase of both the tension and the arterial diastolic pressure was found; usually the test provoked an increase of all values. In a group of patients with exophthalmic goiter there was dissociation of the values measured. The Bloomfield-Lambert test increased the tension and reduced the intraocular arterial pressure.

Esente believes that both interpretations of the Bloomfield-Lambert test are

justified, that of Bloomfield and Lambert who consider it a measure of a local reaction to general pressure changes, and that of Magitot for whom it is a typical example of thalamic irritation. The clinical value of the test is not diminished by its complicated and not fully understood mechanism.   K. W. Ascher.

François, J. **The aqueous veins after iridencleisis.** Ann. d'ocul. 182:169-176, March, 1949.

The aqueous veins of Ascher which go to form the laminary veins of Goldman definitely contain aqueous and act as valves, especially if the ocular tension is increased. Iris inclusion operations on 61 eyes are reported. Aqueous veins were present in 52 percent as compared with 96 percent of normal eyes. Forty-three eyes with iris incarceration were studied. Aqueous veins were observed in 12 of 19 eyes with filtering cicatrix and in 6 of 24 eyes with closed angles. Of 18 eyes with flat cicatrix, 9 had open angles and of these 8 had aqueous veins and of the 9 with closed angles 5 had aqueous veins.
                        Chas. A. Bahn.

Inciardi, J. A. **Aids in the diagnosis of glaucoma.** New York St. J. Med. 49:836-838, April 1, 1949.

Inciardi says that it rests largely upon the general practitioner whether we shall have a small or a large number of persons blind from glaucoma. A large percentage of patients are likely to be seen first by him. There are approximately 200,000 blind persons in the country of which 20,000 are blind from glaucoma. Inciardi describes the symptoms of glaucoma and points out that unbearable pain after occlusion of the central vein means glaucoma and that secondary glaucoma has probably intervened if an eye with cataract suddenly becomes painful. The possibility of increased intraocular pressure is to be con-

sidered if an ocular injury is followed by congestion, pain, blurred vision, or steamy cornea, or if an eye with uveitis develops increased redness, pain, visual disability and steamy cornea.
                    Theodore M. Shapira.

Posner, A., and Schlossman, A. **Role of inheritance in glaucoma.** Arch. Ophth. 41:125-150, Feb., 1949.

Although the importance of heredity in the pathogenesis of glaucoma is often stressed, only about 90 pedigrees of families with glaucoma have been reported. The authors found that of 373 unselected cases of glaucoma in private practice, 51, or 13.7 percent, showed familial tendencies. In most families the disease follows a similar course in the various affected members. The pedigrees of 27 families are given; all but one showed dominant heredity. The genetic approach may be an aid in the early recognition of glaucoma and in the study of the preclinical and mild phases of the disease.
                        John C. Long.

Ullman, E. V., and Mossman, F. D. **Glaucoma and orally administered belladonna.** Northwest Med. 48:245-246, April, 1949.

Six cases of glaucoma clearly induced or aggravated by the internal use of a belladonna drug are reported. Five of the six eyes had narrow filtration angles. Of all prescriptions filled in local pharmacies 10 percent of those not by ophthalmologists contained belladonna in some form. The seriousness of this often-overlooked factor in glaucoma is emphasized.
                        Orwyn H. Ellis.

Verrey, F. **The behavior of the ocular tension after puncture of the anterior chamber.** Ophthalmologica 117:246-248, April-May, 1949.

At the University Eye Clinic of Zurich

the staff has been interested in the use of the anterior chamber puncture as a diagnostic procedure for a number of years. In a thesis by Strassman these studies will be reported in detail. About 2,500 punctures have been performed on patients. With very few exceptions the effects on the ocular tension are brief. In inflammatory disease the author has never observed an appreciable hypertensive reaction; on the contrary, most of the cases of chronic uveitis of long standing respond with hypotension for twenty-four hours. In hypertensive non-inflammatory disease with increased tension the hypertensive reaction after puncture varies a great deal. The authors could not confirm Kronfeld's view of the value of the anterior chamber puncture as a diagnostic test for certain glaucomas. In one of their patients acute glaucoma was precipitated, but the eye responded promptly to eserine In two cases of noninflammatory glaucoma the tension was normalized for several days by the puncture. In the hypertensive inflammatory ocular conditions the immediate reaction to the puncture varies much more than in any of the other groups. In one case of cyclitis with heterochromia the puncture precipitated an acute attack which was terminated by an iridectomy. In about ten cases of this inflammatory hypertensive type the ocular tension was normalized by puncture for several days to several months. The authors believe that paracentesis is not a method of treatment for simple glaucoma or for secondary hypertension except in a few unusual cases but it can render the service of a preoperative or postoperative temporary decompression operation. Complications are rare (2 in 2,500 cases). Puncture is definitely contraindicated in hemorrhagic absolute glaucoma. Slight and brief fluctuations of ocular tension may be observed in the other eye.   Peter C. Kronfeld.

Verrey, F. **The transconjunctival cyclodiathermy after Weekers.** Ophthalmologica 117:281, April-May, 1949.

The University Eye Clinic of Zürich, where Vogt in 1935 first advocated cyclodiathermic punctures, has apparently given up this operation during the last few years and has adopted the transconjunctival nonperforating technique of Weekers. A flat electrode, 0.8 mm. in diameter, is applied to the sclera through the conjunctiva, 7 mm. from the limbus. Over the entire circumference of the globe 18 to 20 coagulations are made in one sitting. A pyrometric eletrode is used which permits accurate measurement of the amount of heat applied. The current is turned on and gradually increased so as to reach a temperature of 90° C. in 3 to 5 seconds. This temperature is maintained for from 10 to 15 seconds. At the end of the operation the ocular tension is always markedly increased. This rise of tension can be alleviated either by a puncture of the anterior chamber or irrigation of the surface of the eye, between the coagulations, with a cool (35°C.) saline solution. The author has used this operation in 30 eyes of which 4 had infantile glaucoma, 2 juvenile, 8 acute or hemorrhagic, and 11 secondary glaucoma. The number of permanently successful operations is not stated.   Peter C. Kronfeld.

Weekers, L., and Weekers, R. **Non-perforating cyclodiathermy.** Ann. d'ocul. 182: 188-198, March, 1949.

The author considers iridencleisis the operation of choice in almost all primary glaucoma. With it tension was normalized in 96 percent of eyes with chronic glaucoma, in 93 percent with subacute, and in 85 percent with acute glaucoma. If tension persists after iridencleisis, nonperforating cyclodiathermy is considered preferable to cyclodialysis and other operations, because it is more effective,

simpler and less painful. Ten cases of such secondary cyclodiathermy are described.   Chas. A. Bahn.

Weekers, L. and Weekers, R. **The physiopathological foundation and the technique of the iris inclusion operation.** Ophthalmologica 117:305-324, June, 1949.

"Iridencleisis appears to be destined to occupy the first place among the anti-glaucomatous operations." On the basis of their own observations the authors do not consider the iridencleisis to be a filtering operation. A filtering scar, if it should develop after iridencleisis, is of only secondary importance. The paper consists of three parts: 1. the mechanism of the normalization of tension after iridencleisis, 2. the importance of the postoperative scar on the surface of the globe, and 3. the effect of the operation upon the function of the aqueous veins. In the hands of the authors the iris inclusion operation is successful in 96 percent of the chronic glaucomas, in 93 percent of the subacute, in 85 percent of the acute glaucomas, and in 70 percent of secondary. The criterion of success is an ocular tension below 25 mm. Hg (Schiøtz, 1924). Especially in the subacute and in the acute glaucomas the iridencleisis, if successful, causes the ocular tension to return to normal, that is, to the range between 17 and 24 mm. In the chronic glaucomas the postoperative tension varies within somewhat wider limits. If the distribution of postoperative tensions in glaucomatous eyes is compared with the distribution of ocular tension in normal eyes, almost identical curves are obtained. The diurnal variations of ocular tension were studied in two cases of bilateral chronic glaucoma several months after successful iridencleisis on one eye. The operated eyes still described typical diurnal variations though on a very much lower level than the unoperated eye. The

Seidel test has been almost invariably negative. No relationship could be found between the size of the scar and the ocular tension. In the cases with markedly bullous or cystic scars the tension was definitely lower. In these cases the authors admit the possibility of fistulization as a possible auxiliary but not indispensable factor. Averse to the theory of fistulization, the authors consider two other possibilities whereby a bullous scar could account for a lower ocular tension. The proximity of the bullous scar might modify the elasticity of the cornea and thereby introduce a "false" reading. The cystic cavity of the bleb with its watertight partitions might also represent a decompression chamber of greater or lesser elasticity and thereby influence the ocular tension. The important fact that very often the operative scars are flat in the presence of normal ocular tensions seems to exclude filtration altogether. The principal mode of action of iridencleisis is a different one.

Marked lowering of the ocular tension by the iridencleisis reduces the number of visible aqueous veins which are direct outlets of the trabecula and canal of Schlemm. The authors consider the latter as just an auxiliary system to the venous system of the anterior uvea which plays the preponderant role in the resorption of the aqueous. After a successful iridencleisis, this auxiliary system is not needed and it is for that reason that some of the aqueous veins disappear.

The technique of iridencleisis as practiced by the authors is described.
                    Peter C. Kronfeld.

Weinstein, Paul. **The treatment of glaucoma with furmethide and di-isopropylfluorophosphate.** Ophthalmologica 118:76-79, July, 1949.

During his recent trip to the United States, Weinstein observed the results

obtained with furmethide and DFP. On a group of glaucoma patients, in Budapest, he made and now reports observations similar to those reported by Uhler (Amer. J. of Ophth. 26:17, 1942) and by Leopold (Arch. of Ophth. 35:1, 1946).

Peter C. Kronfeld.

10
CRYSTALLINE LENS

Denig, Rudolph. **Early and late sequelae of the discision of congenital nuclear cataract and its variations.** Klin. Monatsbl. f. Augenh. 114:197-202, 1949.

The author discusses the dangers of discision in the treatment of congenital nuclear cataract and points to the damaging effect of lenticular remnants on the uveal tract. The frequent occurrence of late detachment of the retina after such discision is another result of the damage to the uveal tract and retina by lens protein. One of the author's patients developed a trophoneurotic damage of the corneal epithelium. Denig advocates optic iridectomy in suitable cases, or loop extraction. He prefers the slight loss of vitreous to the complications following a discision. (References.)

Max Hirschfelder.

Fanta, H. **Cataract formation after Elliot's trephining and Holth's iridencleisis.** Arch. f. Ophth. 148:643-657, 1948.

The formation of cataract, which was more frequent after Elliot's operation, can be more probably ascribed to postoperative iritis, rather than to postoperative hypotony.   Ernst Schmerl.

Harrington, D. O. **The mechanics of intracapsular cataract extraction.** Tr. Am. Ophth. Soc. 46:294-317, 1948.

The fundamental physical principles underlying the dislocation and intracapsular delivery of the lens is discussed. It can be demonstrated by slit lamp microscopy, by gonioscopic observation, dur-

ing actual intracapsular cataract extraction on the living eye, on animal eyes and on human cadaver eyes, that the rupture of the zonular lamella of the lens is accomplished primarily by the production by *external pressure of a wedge of vitreous* tissue which is made to insert itself between the equator of the lens and the ciliary processes. The deformity of the vitreous can be produced at whatever site is desired. The normal vitreous is a tissue and cannot be considered as a fluid in which pressure at one point is transmitted equally to all other parts. Certain safety factors in intracapsular cataract extraction may be reevaluated in the light of these basic principles.

David Harrington.

Jorio, A. **Two cases of cataract associated with skin diseases.** Rassegna ital. d'ottal. 18:17-33, Jan.-Feb., 1949.

The author discusses the various characteristics of syndermatic cataracts and reviews the literature on this rare condition. The first patient demonstrated the effects of the Rotmund-Werner syndrome, and in the second the syndrome of Sjögren was added to this. The latter association is the first reported in the literature. From the clinical examination and laboratory findings the writer considers the cause to be an endocrine dysfunction of the genital glands and other glands of the endocrine system may participate. (6 figures.) Eugene M. Blake.

Jaeger, A. **Collapse of the sclera after cataract surgery.** Klin. Monatsbl. f. Augenh. 114:148-151, 1949.

The sclera may sink in after lens extraction because of loss of an unusual amount of anterior aqueous with a deeply situated subluxated lens, or posterior aqueous with seclusion of the pupil or loss of vitreous. The condition corrects itself, if the loss is not too great. The

problem of proper closure of the wound is discussed. It is not difficult, if the collapse involves the region of the insertion of the muscles. In the region of the ciliary body it prevents the coaptation of the edges of the section. If one avoids too much tension in suturing the conjunctival flap, the incongruence will correct itself in a few days. Max Hirschfelder.

Knüsel, O. **Electric cataract.** Ophthalmologica 117:299, April-May, 1949.

The case of a thirteen-year-old boy who developed a cataract in his left eye one year and in his right eye six years after electric shock illustrates the greatly variable latent period of electric cataract. Peter C. Kronfeld.

Papolczy, F. **Statistical data of my cataract operations performed with a new suture of the sclera.** Brit. J. Ophth. 33:296-305, May, 1949.

A new suture is presented which has been used with good success in 325 cases. A 6-0 black nylon suture is placed through the conjunctiva and sclera parallel to the limbus and 1 mm. above it at 12 o'clock. Section is made with a knife and brought to the suture. A conjunctival flap is made with scissors and brought down over the cornea. A round pupil and intracapsular delivery are then accomplished and the wound closed with the single preplaced suture. Morris Kaplan.

Perera, Chas. A. **A simple appositional suture in operations for cataract.** Tr. Am. Ophth. Soc. 46:184-191, 1948.

A suture is described which is placed after keratome incision and before scissors enlargement of the wound. The exact approximation of the wound edges results in accurate closure, rapid reformation of the anterior chamber and only one iris prolapse in 100 cases. David Harrington.

Sedan, J., Levrat, M., and Paufique, L. **Petechiae test in diabetic cataract.** Ann. d'ocul. 182:177-187, March, 1949.

The test is made by applying a sphygmomanometer cuff to the upper arm which is inflated to the maximum arterial tension less 2 cm. and left for five minutes. If the test is positive, petechiae appear, and are recorded as +1 to +4 on the basis of their size and number. A positive test indicates a probable retinal vascular degeneration and probable unfavorable visual prognosis for cataract extraction. The petechiae on the arm are considered an index to probable hemorrhages in the retina. Twenty-nine cases are briefly discussed to illustrate the value of this test which the authors believe should be more widely used to determine the risks of cataract extraction in diabetics. Chas. A. Bahn.

11
RETINA AND VITREOUS

Blanchi, G. **Angioneurotic degeneration of the macula.** Rassegna ital. d'ottal. 18:34-43, Jan.-Feb., 1949.

The retinal alterations consisted of constriction of retinal vessels and of fine, and originally, limited pigmentation of the macular region. Early, active treatment with vasodilators and vitamin B resulted in but moderate improvement. Further studies of the circulatory system will probably confirm the opinion that there is an angioneurotic factor as in the three cases reported. Study of the endocrine functions, particularly of the hypophysis and the diencephalic centers, may prove the importance of this region in the regulation of the cerebral and retinal circulation. Eugene M. Blake.

Bruna, F. **Ocular complications in Werlhof's disease (essential thrombopenia).** Boll d'ocul. 28:41-56, Jan., 1949.

Few cases of eye involvement in Werl-

hof's disease have been described. Bruna observed a 16-year-old girl with lesions similar to retinitis proliferans in the region of the optic disc and with pigment rarefication in the macula of both eyes. Werlhof's disease was the probable cause. (References.)   K. W. Ascher.

Candian, B. **The fundus oculi of the newborn.** Rassegna ital. d'ottal. 18:3-16, Jan.-Feb., 1949.

The eyegrounds of 35 babies were examined in mydriasis within a few hours to three days after birth. Twenty-six showed pallor of the disc, in six it was of reddish hue and in three intermediate in color. Retinal hemorrhages were observed seven times, papilledema six times, and in only two was the refraction emmetropic. Hypermetropia of two to eight diopters was measured with the ophthalmoscope.

A table gives many details of each case examined and three excellent colored plates depict the peripheral palor of the fundus and of the disc and the various types of retinal hemorrhage. A good bibliography accompanies the article. (4 figures, references.) Eugene M. Blake.

Carreras Matas, B. **A conception of tapetoretinal degeneration.** Arch. Soc. oftal. hispano-am. 9:265-279, March, 1949.

A review of the literature and several personal observations led the author to believe that the mutation which deprives the cells of the sensory retinal epithelium and the pigment epithelium of essential elements, is the cause of tapetoretinal degenerations. The clinical implication of this theory leads to therapeutic attempts with drugs which stimulate the circulation of the choriocapillaris and provide abundant nutrition for the external layers of the retina, and with those which regulate the neurovegetative system and normalize the function of the glands of internal secretion. The intense vitamin

therapy and tissue therapy after Filatov may be tried. The retina should be protected from bright light, which may be within safe limits for normal eyes but is excessive for degenerate eyes.
        Ray K. Daily.

Costi, C. **Posterior detachment of the vitreous and rupture of the hyaloid.** Arch. Soc. oftal. hispano-am. 9:390-396, April, 1949.

In two patients, 44 and 24 years old, both emmetropic, and with history of trauma, anterior vitreous opacities indicated the presence of uveitis. The ophthalmoscopic appearance of the detachment and perforations in the hyaliod membrane are described in detail. The pathogenesis is discussed, and the author believes that a primary uveitis leads to a thickening of the hyaloid membrane, which, losing its elasticity, is easily torn, through slight trauma or effort. The degenerated and liquefied vitreous insinuates itself through the hole, in the same manner that it does in retinal ruptures. It is believed that improved exploration of the hyaloid membrane will reveal that ruptures in it are not as rare as is supposed. (3 figures.)   Ray K. Daily.

Czukrasz, Ida. **A Case of branch embolism of the central retinal artery.** Ophthalmologica 118:66-68, July, 1949.

A nurse, 26 years of age, presented herself in the eye clinic one hour after a spontaneous blackout of her left eye. The right eye was found to be normal, the left eye presented the picture of an embolism of the inferior papillary artery. The vision was reduced to light perception. Thorough examination revealed no other circulatory or cardiac abnormality. The patient was treated chiefly with a vasodilator of the acetylcholine group called stabilocholin which was used retrobulbarly and subcutaneously. She was also given several inhalations of amyl nitrite

and a paracentesis was done a few hours after the blackout. The vision improved gradually. Five days after the onset the patient was discharged from the clinic with a visual acuity of 5/8 and a moderate constriction of the upper half of the field.

Peter C. Kronfeld.

Delaney, A. J., and Rhoades, A. L. **Angioid streaks of the retina, report of a case.** U. S. Naval Med. Bull. 49:296-299, March-April, 1949.

A case of angioid streaks of the retina is presented, because of its rarity and its varied and apparently unrelated associated clinical findings. At the time the paper was written no evidence of pseudo-xanthoma elasticum appeared in the patient. Lesions in the mouth similar to pseudoxanthoma elasticum proved to be Fox-Fordyce disease. There was no X-ray evidence of bony change suggestive of Paget's disease, sometimes an associated finding.   Theodore M. Shapira.

Duke-Elder, Stewart. **The relation between peripheral retinal cysts and dialyses.** Brit. J. Ophth. 33:388-389, June, 1949.

The author reports a case of a retinal cyst in the extreme periphery. Six months later it had doubled in size and extensive dialysis of the retina was now present. Diathermy was performed with successful reattachment.   Orwyn H. Ellis.

Esente, Ivan. **The clinical and pathogenetic aspects of Purtschers's and Berlin's retinitis (commotio retinae).** Arch. di ottal. 52:195-217, July-Aug., 1948.

The author discusses these two forms of traumatic retinal disturbances. The former, retinal contusion following indirect trauma to the bulb, was described by Purtscher in 1910 and called "angiopathia retinae traumatica." The latter, called "commotio retinae" arises from di-

rect injury to the eyeball and was described by Berlin in 1874. Experiments carried out on rabbits and dogs under general anesthesia, showed an absence of the ocular signs typical of Purtscher's retinitis. These results are not sufficient to modify the author's theory that Purtscher's disease is an angioneurotic retinitis from indirect trauma.

Francis M. Crage.

Fajardo, R. M. **Congenital macular displasia associated with ocular anomalies.** An. Soc. mex. de oftal. 22:310-315, 1948.

The lesion was associated with persistence of the hyaloid artery and prepapillary membrane; the possibility of choroiditis about the seventh or eighth month of intrauterine life is suggested. (2 figures, references.)   W. H. Crisp.

Franceschetti, A., and Balavoine, C. **The prevention of retinal detachment by surgical therapy.** Ophthalmologica 117:259-263, April-May, 1949.

A question of when and how to subject retinal tears without detachment to surgical therapy has been discussed repeatedly at the meetings of the Swiss Ophthalmological Society. Weber recommended such surgical treatment in the presence of the following "unfavorable factors": detachment in the other eye, location of the tears in the upper quadrants, progressive degeneration of the retina, myopia, and hereditary tendencies. To these the authors add two other factors, namely the patient's age, and poor visibility of the fundus sector in which a detachment is most likely to occur. The authors have found bilateral progressive retinal degeneration more common in young people and they have been impressed by the occurrence of retinal detachment in those fundus sectors where the visibility was poorest because of dislocation of the lens in Marfan's syndrome.

Peter C. Kronfeld.

François, Jules. **Contribution to the study of tapeto-retinal degeneration.** Ophthalmologica 118:1-29, July, 1949.

The author reports a French family six members of which showed a bilateral degenerative disease of the central portion of the retina and choroid. In the early stages of the disease it resembled closely Stargardt's heredomacular degeneration. In the later stages a very marked choroidal sclerosis was added to the picture. The hereditary transmission followed the dominant mode. The author prefers the term tapeto-retinal degeneration for this disease to indicate that, just as in true pigmentary degeneration of the retina, the tapetum or its equivalent is involved in the very early stages of the disease.

To demonstrate the close relationship between true pigmentary degeneration of the retina and hereditary macular degeneration, the author reports another family in which one sister had a typical retinitis pigmentosa and one brother a macular disease of the Stargardt type.

Peter C. Kronfeld.

Hager, Hugo. **Thrombo-angiitis obliterans and the eye.** Klin. Monatsbl. f. Augenh. 114:238-247, 1949.

A patient with tobacco amblyopia presented a clinical picture of thrombo-angiitis obliterans of the extremities. The fundus showed temporal pallor of the disc, narrow arteries, tortuous veins and slight degeneration of the macula. It is suggested that in tobacco amblyopia the degenerative changes in the nerve and the retina are possibly not caused by toxin, but by thrombo-angiitis obliterans. In a second case of thrombo-angiitis obliterans the patient used tobacco excessively, had small aneurysms and partial obliteration of the vessels in part of the fundus. The vision was only slightly reduced. The author compares these findings with those usual in periphlebitis retinae and concludes that the latter has, contrary to the opinion of Marchesani, nothing to do with thrombo-angiitis obliterans. (4 figures, references.) Max Hirschfelder.

Huber, A. **Cerebral and retinal angiopathy.** Ophthalmologica 117:265, April-May, 1949.

In hypertensive cardiovascular disease of the benign as well as of the malignant type the parallelism between cerebral and retinal vascular changes is not very close. The likelihood of a cerebral vascular accident cannot be determined from the retinal findings. The parallelism between the renal and retinal vascular changes however is always very close. The author quotes in detail two cases of Buerger's disease with thrombo-angiitic obstructions of large cerebral arteries and pathognomonic eye findings. In both cases ophthalmoscopy suggested arterial occlusion as the main basis of the systemic disease. On the other hand, numerous cases are recorded in the literature in which, in the presence of advanced Buerger's disease, the eye grounds were practically normal. Peter C. Kronfeld.

Klien, B. A. **Histopathologic aspects of retrolental fibroplasia.** Arch. Ophth. 41: 553-561, May, 1949.

The author believes that retrolental fibroplasia is in some way connected with angioblastic overgrowth of the primary vitreous which may occur at any stage of gestation after formation of the primary vitreous has started. It is the stage in which the retina becomes involved that determines different and characteristic histologic pictures of retrolental fibroplasia. Ralph W. Danielson.

Moginier, A. **The treatment of retinitis pigmentosa with placental tissue and nicotinic acid.** Ophthalmologica 117:287-290, April-May, 1949.

Thirteen patients with retinitis pig-

mentosa received one or two subconjunctival inoculations of placental tissue and were followed for eight months. In eight the visual acuity and the visual field showed improvement. The dark adaptation remained unimproved. Four other patients were given daily intravenous injections and oral doses of 100 mg. of nicotinic acid for two weeks. The acuity improved in all of them. The visual field was only slightly influenced. Although one can not cure the advanced cases of retinitis pigmentosa, one may hope to keep early patients on a visual level which will permit them to lead a normal life.   Peter C. Kronfeld.

Neuenschwander, M. **Our experiences with placenta therapy of retinitis pigmentosa.** Ophthalmologica 117:290-292, April-May, 1949.

Fifty-seven patients with retinitis pigmentosa received placenta therapy after Filatov, in the form of either subconjunctival injections of placental blood serum or of subconjunctival implantation of placental tissue. The author reports "his six best cases" and draws the following conclusions. "Placenta therapy is not an infallible means of treatment, (but) there are cases (of retinitis pigmentosa) which are definitely improved by placenta therapy. . . . This improvement may last a whole year. . . . Although only a small percentage of cases can be improved, we believe that placenta therapy should be tried in every case of retinitis pigmentosa."   Peter C. Kronfeld.

Oxilia, E. **Tissue therapy in retinitis pigmentosa. Late results.** Ann. di ottal. e clin. ocul. 74:499-511, Sept., 1948.

From personal experience with 30 patients and from a review of the literature Oxilia concludes that if preserved and autoclaved tissue is used in exact accordance with Filatov's method the successes obtained are indisputable. The action does not depend on a colloidoclastic shock. The successes depend on the state of preservation of the vision, but are independent of the age of the patient. Best results are obtained early in the course of the disease, but even late, when destruction is great, some improvement may occur. Most successful are subconjunctival implantations of placenta, especially if accompanied by intramuscular injections of placental extract. Injections of cod liver oil are equally effective but are badly tolerated. Vision, visual fields, and light sense may all show improvement. No changes are observed in the ophthalmoscopic picture, but in some cases Oxilia noted a drop in the retinal arterial pressure. Rapidity and duration of therapeutic effects vary with the method employed and with the state of the visual functions. (References.)
          Harry K. Messenger.

Poos, F. **Ascending atrophy of the intraocular vascular system, retinal isobars and progressive concentric contraction of the visual field.** Klin. Monatbl. f. Augenh. 114:151-161, 1949.

The author attempts to correlate the factors which determine the characteristic concentric progression of certain defects in the visual field. The pressure within the retinal arteries decreases in all radii from the center of the retina toward the periphery and zones can be delimited by isobars. The center of these circles is not the papilla, but the macula. The embryonic development of the retinal vascular system, of which the arching and more strongly developed temporal arteries supply a larger retinal field, make this fact comprehensible. Concentric contraction of the visual field starts when the lowest peripheral pressure does not suffice to provide the proper blood supply in the capillary system, or when the increased or normal intraocular pressure exceeds the normal or decreased vascular pressure.

Hand in hand with the consequent peripheral retinal atrophy goes a progressive shrinkage of the vascular tree. These considerations explain the progressive and irreparable concentric contraction which is marked by isobars between the living and non-living retinal tissue. A special theory is developed for the pathologic physiology in retinitis pigmentosa. (References.) Max Hirschfelder.

Poos, F. **The origin of infarcts after vascular closure in brain and retina.** Klin. Monatsbl. f. Augenh. 114:247-251, 1949.

There are no true endarteries in the brain and retina and arterial and venous anastomoses do exist. The author explains the origin of the anemic infarct after arterial closure by a compression of the empty capillaries by intracranial or intraocular pressure. The normal balance between intracapillary pressure and the pressure of the surrounding region is disturbed when the capillary pressure sinks to almost zero after arterial infarct. The hemorrhagic infarct after closure of a vein does not lead to a collapse of the capillaries, whose pressure is actually elevated. This explains the lesser degree of functional disturbance after venous closure and the possibility of considerable recovery through collateral circulation. The term "compression infarct" characterizes the anemic infarct, while the term "congestion infarct" describes the hemorrhagic infarct. (References.)
Max Hirschfelder.

Puig Solanes, M. **Anticoagulating treatment of retinal vascular occlusion.** An. Soc. mex. de oftal. 22:237-262, 1948.

Rather weakly conclusive statistics lead the author to conclude that anticoagulant therapy is the fundamental treatment for obstruction of the retinal veins and is auxiliary but necessary in arterial occlusions. The results are felt to be on the average much better in obstruction of branches of the central vein than in that of the main trunk. (Statistical tables, 14 graphs, references.) W. H. Crisp.

Puig Solanes, M. **Retinal angioscopy in hypertensive patient operated upon by Smithwick's procedure.** (sympathectomy). An. Soc. mex. de oftal. 22:99-112, 1948.

In the first weeks after the operation one frequently sees narrowing of the retinal arterioles, with increase in the "edematous" papillo retinal lesions. In a few months an angiospasm and the "edematous" lesions may disappear, but with persistence of arterial contraction. The retinal vascular changes in these operated patients are independent of the effects upon arterial tension and the effects produced upon the general condition of the patient. The author supposes that similar modifications may be produced in other circulatory areas of the organism, especially the brain. (References.) W. H. Crisp.

Redslob, E. **Chorioretinal pigmentary degeneration with paradoxical evolution.** Ann. d'ocul. 182:443-448, June, 1949.

Tapeto-retinal degeneration is briefly described and a case is reported. A 51-year-old woman with defective night vision and a concentrically contracted field since childhood had noticed failing central vision since 1938. Central vision is 8/200 in both eyes. A central scotoma of 20 to 30 degrees is surrounded by a normal zone of 20 to 30 degrees and the periphery is blind. The retina and disc are ophthalmoscopically normal in the central zone. In the intermediate zone, the lesion resembles the constitutional type of pigmentary retinal degeneration with pigment migration into the inner retinal layers. In the periphery there is the salt and pepper fundus usually ascribed to congenital lues. Both congenital syphilis with negative serologic

reactions and a constitutional degenerative process must be considered.

Chas. A. Bahn.

Reese, A. B. **Persistence and hyperplasia of primary vitreous; retrolental fibroplasia—two entities.** Arch. Ophth. 41:527-552, May, 1949.

Reese presents an excellent discussion of this problem and contrasts the two conditions. Both have in common the persistence of the primary vitreous as the basic congenital lesion, but there is an important difference. In persistence and hyperplasia of the vitreous the primary vitreous remains in toto and, when the secondary vitreous forms, occupies its normal position in a funnel-shaped space behind the lens. There is merely a persistence of the primary vitreous and hyperplasia. In retrolental fibroplasia only a portion of the primary vitreous remains in the region of its base but it is adherent to a portion of the inner layer of the optic cup. As the secondary vitreous forms, it tends to compress and isolate the primary vitreous. This occurs everywhere but in the region where adhesion has taken place, and there the retina becomes detached. In addition, there may be hemorrhage from the persistent vascular primary vitreous, leading to organization, contraction and further retinal detachment. Attempts at relief by surgery have been disappointing, but roentgen treatment of the angiomatous tissue early may be of value.

Ralph W. Danielson.

Reese, A. B., and Blodi, F. C. **Retrolenticular fibroplasia.** An. Soc. mex. de oftal. 22:208-216, 1948.

This is an excellent summary in Spanish of the history of the subject, emphasizing the importance of the condition as a cause of blindness in children of preschool age. (References.) W. H. Crisp.

Rychener, R. O. **Retinoblastoma in the adult.** Tr. Am. Ophth. Soc. 46:318-326, 1948.

The clinical and pathologic study of the fifth case of retinoblastoma in an adult is recorded (Illustrations.)

David Harrington.

Schulte, D. **Spontaneous reversal of the arterial flow in the retina.** Klin. Monatsbl. f. Augenh. 114:251-259, 1949.

After embolism of a large branch of the retinal artery the author observed centripetal flow of blood in some peripheral retinal arteries. The phenomenon is explained by the theory that the capillary net has anastomoses with healthy regions of the retina which raise the capillary pressure sufficiently to overcome the vastly decreased pressure in the arteries of the affected part. (3 figures, references.)

Max Hirschfelder.

Shelburne, S. A. **Retinal arteriovenous nicking; a long term study of the development of arteriovenous nicking in hypertensive patients.** Arch. Int. Med. 83:377-381, April, 1949.

The author presents drawings made from actual patients showing various degrees of retinal arteriovenous nicking, early, moderate, and definite.

A study of 15 cases over a long period proved that early arteriovenous nicking progresses to moderate or definite arteriovenous nicking over a period of years and that the categoric classification previously reported actually represents degrees of the same lesion. These cases show in some measure the time required for progression from first degree of the lesion to the others and the many years required for the formation in hypertensive patients of the fully developed lesion which is called definite arteriovenous nicking.

Theodore M. Shapira.

Vila Ortiz, J. M., Maximo Soto, C., Staffieri, J. J., and Rose, Juan. **Diabetes**

and the ocular fundus. Arch. Soc. oftal. hispano-am. 9:245-264, March, 1949.

A review of the literature is followed by a tabulated report of the author's own investigations to determine the pathogenesis of the diabetic changes in the fundus. In 50 diabetic patients with ocular complications the arterial presure, renal function, proteinemia, cholesterinemia, calcemia, vascular fragility, and changes in the hemostatic mechanisms were noted and related to the ocular changes, but no correlation could be determined between the degree of these abnormalities and the gravity of the fundus changes. Only one patient had a hypercholesterolemia and the fundus picture was that of retinal sclerosis. In all who had a normal fundus the renal function was normal.

Ray K. Daily.

Vogelius, Henning. **The increasing frequency of diabetic retinopathy.** Acta ophth. 27:99-111, 1949.

The material which was the basis for this investigation was too small to permit of definite conclusions, and the author uses published data to support his statement that there is an increase in the incidence of retinopathy, which he attributes to inadequate insulin therapy and to the introduction of a free diet for diabetics.

Ray K. Daily.

Weber, E. **Retinal tears without detachment.** Ophthalmologica 117:263-264, April-May, 1949.

The author restates his findings that retinal holes without detachment can be found in two out of every thousand office patients. A typical case is described in detail. Peter C. Kronfeld.

12

OPTIC NERVE AND CHIASM

Benedict, M. L. **Etiology and treatment of optic neuritis.** Texas St. J. Med. 45: 126-130, March, 1949.

The subject of optic neuritis is covered completely and comprehensively. A cause which is frequently overlooked is plumbism. The other diseases simulating optic neuritis are mentioned. Over 50 percent of retrobulbar neuritis and a large percentage of optic neuritis is due to multiple sclerosis. Foreign protein therapy, particularly intravenous typhoid vaccine is the treatment of choice in acute cases and vasodilators are used in chronic toxic optic neuritis.

Donald T. Hughson.

Di Luca, G. **Optic nerve atrophy from methyl alcohol poisoning.** Boll. d'ocul. 28:17-31, Jan., 1949.

Two patients were observed with atrophy of the optic nerves due to methyl alcohol and one to quinine poisoning. The differential diagnosis and pathogenesis are discussed. Ten visual field diagrams and a differential diagnostic table make the data perspicuous. (References.) K. W. Ascher.

François, P. **Hyaline verrucosities of the papilla.** Ann. d'ocul. 182:249-278, April, 1949.

Hyaline is a polymorphous compound, more dense than colloid but chemically similar, which is deposited in the tissues as the result of local metabolic abnormalities. There are 198 reports of hyaline verrucosity in the papilla in the literature. The lesion may occur as a congenital anomaly; or as a postnatal, slowly-progressive process which may follow mechanical pressure or chemical irritation. Central and peripheral vision may be reduced. One to five or more verrucosities may be located in the papilla or in the optic nerve behind the eyeball. Several forms are mentioned. They occur in the phakomatoses and in Bournaville's disease, in ocular diseases such as retinal pigmentary degeneration, primary and secondary glaucoma, malignant uveal tumors, degenerative uveitis, retinal de-

tachment, and in brain tumors and some vascular diseases. They are essentially a degenerative processs involving primarily neuroglia. One of the six cases reported was secondary to a cerebral abscess which produced a lateral hemianopsia. All of the cases reported had field defects. Campimetric examinations should be made with a 1/1000 target on a Bjerrum Screen. (92 references.)   Chas. A. Bahn.

Klauder, J. V. **Penicillin treatment of syphilitic primary optic atrophy.** Am. J. Syph., Gonor. and Ven. Dis. 33:234-242, May, 1949.

This is an interim report on the treatment of 56 patients with syphilitic primary optic atrophy, begun in April, 1944. The syphilis was acquired in 53 and congenital in three. The results were variable but 32 patients showed no increase in the optic atrophy. No correlation could be made between the spinal fluid response during penicillin treatment and the progress of the optic atrophy. Patients who have had treatment before the penicillin therapy seem to retain the little vision they have. (3 tables.)

H. C. Weinberg.

Tornquist, Ragnar. **Hyaline bodies (Drusen) as the cause of atrophy of the optic disc.** Acta ophth. 27:1-9,1949.

Three patients developed reduced visual acuity and contraction of the visual fields during a few months. The visual defects were not complete, but numerous islands of perception within the defective field were preserved. In all three cases the discs were slightly pale, and top shaped in form and contained hyaline bodies. (6 visual fields.)   Ray K. Daily.

13
NEURO-OPHTHALMOLOGY

Agundis, Teoledo, Jr. **Romberg's facial trophoneurosis.** An. Soc. mex. de oftal. 22:153-166, 1948.

Two cases of this extremely rare disease, a progressive facial hemiatrophy, first described by Romberg in 1846, are reported. It occurs between the ages of 18 and 30 years, without previous abnormality and is initiated by such sensory disturbances as pain, tenderness and hyperesthesia in areas innervated by one or more branches of the trigeminal nerve. In the affected half of the face gradual atrophy of skin, muscles, and bony framework develops. The orbit and accessory nasal sinuses may be involved. The cause is unknown and no treatment is effective. (6 figures, references.)   W. H. Crisp.

Camisacca, Lionello. **The opticokinetic post-nystagmus in cranial traumas.** Riv. oto-neuro-oftal. 23:284-297, July-Aug., 1948.

In 19 patients who had sustained a trauma of the head, and in 19 normal persons as control, the test for opticokinetic nystagmus was positive in a few cases and in these cases the oscillations were isolated and not well marked. The writer's findings were not in accord with those obtained by Merloo of Holland who found oscillations that lasted up to one half minute. (References.)

Melchiore Lombardo.

Grasso Canizzo, E. **Unusual case of partial third nerve paralysis during a staphylococcic septicemia.** Boll. d'ocul. 28:110-116, Feb., 1949.

This rare condition was due to staphylococcus albus infection and was cured in a few weeks by administration of penicillin and of sulfathiazol. (References.)

K. W. Ascher.

Lauber, H. **Scintillating scotoma.** Klin. Monatsbl. f. Augenh. 114:168-171, 1949.

Lauber describes scintillating scotomas which he himself experienced during the past six years, at first only twice annually, but lately every 6 to 10 weeks. One attack

was followed by a loss of consciousness and another attack was combined with alexia. The author ascribes the phenomena to ophthalmic migraine caused by vascular spasms in the field of the vertebral and basilar arteries. (References.)

Max Hirschfelder.

Rubino, A., and Esente, I. **The eye and the diencephalon. (VII) The glycemic curve from addition of glucose and "photoglycemic" reflex in patients affected by pigmentary degeneration of the retina.** Riv. oto-neuro-oftal. 23:244-249, July-Aug., 1948.

In eight patients a glycemic curve was obtained which could be referred to the diencephalic glyco-regulator centers. The photoglycemic reflex was normal.

Melchiore Lombardo.

Tornquist, Ragnar. **An anomaly of the retinal vessels (so called aneurysma cirsoides) sometimes combined with symptoms from the central nervous system.** Acta ophth. 27:11-17, 1949.

Tornquist reports a case of a racemose aneurysm, in the left fundus of a 31-year-old woman, who had persistent headache and a slight right-sided hemiparesis which were tentatively ascribed to meningitis. The left eyeground presented a picture of typical racemose aneurysm, with a number of aneurysmal dilatations of the arteries near the disc, and there were a few retinal pigment spots. There were no visual disturbances and other examinations were essentially negative. The literature is reviewed. (1 figure.)

Ray K. Daily.

Wilson, W. C. **Inequality of the pupils in head injury; a clinicopathologic study.** Arch. Neurol. and Psychiat. 61:385-401, April, 1949.

In a series of 451 cases of anisocoria there were 192 clinical cases and 259 clinicopathologic. The number of cases of anisocoria with normally reacting pupils was inversely proportional to the severity of the lesions. In the majority of the cases the condition was associated with hematomas from 0.3 to 1.5 cm. in thickness. The hematoma was homolateral with the dilated pupil in the majority of the cases. By observations of the functional state of the unequal pupils it is possible to estimate the severity, thickness and laterality of the lesion.

In 166 cases (36 percent of the total number) there was an altered reaction to light with impingement on the oculomotor nerve. In the remaining 285 cases (64 percent) there was a brisk, reaction to light and no dysfunction of the extraocular muscles; autopsy, when performed, showed no evidence of impingement on the oculomotor nerve. The majority of the cresyl violet preparations of the premotor cortex showed no change, or only increased perineural and perivascular spaces with pale-staining cellular elements, therefore correlation was not great between the clinical evidence indicating interrupted physiologic continuity and the degree of demonstrable pathologic change.

Theodore M. Shapira.

14

EYEBALL, ORBIT, SINUSES

Chavira, R. A. **Clinical notes concerning fractures of the orbit.** An. Soc. mex. de oftal. 22:175-190, 1948.

Fourteen clinical cases are summarized with details of ophthalmologic and neurologic symptoms. (Reference.)

W. H. Crisp.

Giggleberger, H. **Cholesteatoma of the orbit.** Klin. Monatsbl. f. Augenh. 114:206-211, 1949.

Two cases of exophthalmus are described. X ray revealed hyperostosis of the bony wall of the orbit as well as rarefaction of bone. The cause was cho-

lesteatoma, one confined to the orbit, the other one broken through into the cranial cavity. Dermoids may give the same clinical appearance. Early surgical removal is advised to avoid a breakthrough of the tumor into the frontal sinus and the cranial cavity. (3 X-ray figures, references.)   Max Hirschfelder.

Goodyear, H. M. **Ophthalmic conditions referable to diseases of the paranasal sinuses.** Arch. Otolaryng. 48:202-208, Aug., 1948.

Goodyear presents his observations in cases of retrobulbar neuritis in patients with normal ethmoid and sphenoid sinuses. In these cases vision frequently returns to normal after the opening of the sphenoid sinus and posterior ethmoid cells on the side of the optic lesion.

In the past 15 years, he has observed that the injection of 27-percent iodized oil into the sphenoid will produce the same spectacular result as is obtained by surgical intervention. In acute swelling and edema about the eye after an acute infection of the frontal sinus, chemotherapy and external drainage is advised. Recurring corneal ulcers demand a careful survey of the paranasal antrums. Acute suppurative ethmoiditis in an infant is frequently mistaken for dacryocystitis. Patients with tumors in the paranasal sinuses often go to the ophthalmologist first because of disturbed vision and pain of the eye and frequent double vision.
                              Theodore M. Shapira.

Pfeiffer, R. L., and Nicholl, R. J. **Dermoids and epidermoids of the orbit.** Tr. Am. Ophth. Soc. 46:218-243, 1948.

Case histories, physical findings, photographs, X-ray pictures and treatment of nine cases of dermoid of the orbit are presented. The incidence of dermoids and epidermoids is discussed and the similarity between the growths is stressed.

Elimination of the term epidermoid is advocated. The roentgenographic characteristic of these lesions is an area of diminished density with smooth regular margins of increased density. Proper roentgenography is essential for diagnosis. The plan of treatment rests upon the defect revealed. David Harrington.

Semadeni, B. **Tuberculous panophthalmitis.** Ophthalmologica 117:273, April-May, 1949.

A young man, released from a German concentration camp was admitted to a sanitarium at Davos with localized infiltrates in the right lung and at the hilus. Diffuse peritonitis and tuberculous meningitis were suspected. A few weeks after admission the patient developed an acute iridocyclitis in his left eye. Within a few days the iris became studded with yellow nodules. The disease took the course of tuberculous panophthalmitis. The patient died of tuberculous meningitis about three weeks after the onset of the iridocyclitis. The pathologic findings were typical.
                              Peter C. Kronfeld.

Wüst, K. **Treatment of imminent optic nerve atrophy due to retrobulbar hematoma and surgical access to the retrobulbar space.** Klin. Monatsbl. f. Augenh. 114:140-144, 1949.

The author describes a case of retrobulbar hematoma with bilateral amaurosis after traumatic compression of the thorax. The retrobulbar space was entered through the maxillary sinus with removal of the floor of the orbit. This approach is ideally suited for such hematomas which may occur in disease (scurvy, hemophilia, venous stasis) or may be due to trauma. The author's patient recovered completely. Proptosis and amaurosis disappeared at once. (References.)
                              Max Hirschfelder.

15

EYELIDS, LACRIMAL APPARATUS

Berke, R. N. An operation for ptosis utilizing the superior rectus muscle. Tr. Am. Acad. Ophth. pp. 499-518, May-June, 1949.

The author has modified the Motais operation. Through a conjunctival incision the superior rectus tendon is divided into three longitudinal tongues on each of which a suture is placed. The ends are inserted into the lid margin and tied. A buried chromic catgut suture is passed through the stump of the superior rectus tendon and through the superior rectus in its new position. A third set of four sutures is placed through the superior rectus in its altered position and then through the skin. A weakened superior rectus may be used, a smooth curve of the upper. lid is obtained, entropion is prevented, and the operation may be used on very young children but normal winking is interfered with, and lagophthalmus is present during sleep. The author performed his operation on 20 patients without failure and recommends it only where resection of the levator is contraindicated. (18 figures.) Chas. A. Bahn.

Berke, R. N. Congenital ptosis: a classification of two hundred cases. Arch. Ophth. 41:188-197, Feb., 1949.

A statistical study has been made of 200 consecutive cases of congenital ptosis seen at the Institute of Ophthalmology during the past fifteen years. There was a normal superior rectus muscle in 147, weakness of the homolateral superior rectus alone or combined with weakness of the homolateral inferior oblique in 34, the jaw-winking phenomenon of Marcus Gunn in 12, and ptosis associated with plepharophimosis in 7. The ptosis was unilateral in 145 and bilateral in 55, simple in 147 and complicated by hori-

zontal or vertical anomalies in 52. In 107 the levator muscle was active enough to justify resection of the muscle. In the others there was no such function and some modification of the Motais-Parinaud operation or the frontalis type of procedure was indicated. John C. Long.

Castresana y Guinea, Angel. Palpebral filaria. Arch. Soc. oftal. hispano-am. 9:293-305, March, 1949.

The literature is extensively reviewed and a case is reported. The presence of a filaria in the lower lid of a woman who became infected with the parasite in Guinea was recognized by its movements. It was pinched in a fold of skin with a forceps and surrounded with injected novocain. It became immobile and was then removed through an incision.

Ray K. Daily.

16

TUMORS

Forrest, A. W. Intraorbital tumors. Arch. Ophth. 41:198-232, Feb., 1949.

In a series of 222 cases of intraorbital tumor from the Registry of Ophthalmic Pathology which were studied histologically and clinically, 184 tumors were primary in the orbit; 93 were of mesenchymal origin, 48 related to the nervous system, 25 mixed tumors of the lacrimal gland and 18 were dermoids. Forty-four, or 24 percent, of the primary tumors were malignant. The 38 secondary tumors were 24 carcinomas, 6 neuroblastomas, 6 malignant melanomas, 1 retinoblastoma and 1 adenoma. Lipomas and dermoids were often anteriorly situated, and sarcomas, meningiomas, neurofibromas and gliomas were more frequently posterior and caused exophthalmos. Mixed tumors and hemangiomas were about equally divided between the two locations. Malignant mesodermal tumors, gliomas of the optic

nerve, hemangiomas and metastatic neuroblastomas occurred predominantly in youth and the tumors of the hematopoietic system and secondary carcinomas in more advanced age.   John C. Long.

Kambara, G. K. **Choroidal metastasis of a testicular chorionic epithelioma.** Arch. Ophth. 41: 587-598, May, 1949.

A case of a testicular chorionic epithelioma with metastases to the choroid of the right eye and in the brain, breast, stomach, intestine, liver, adrenal gland, subcutis, heart, lungs and pancreas is presented. Only three others in men and three cases of metastases to the choroid in women from chorionic epithelioma of the uterus have been reported.

Ralph W. Danielson.

O'Day, K. **Leiomyoma of the iris.** Brit. J. Ophth. 33:283-290, May, 1949.

Tumors of the iris are rare and all too often the oculist approaches the problem with a mind biased toward malignancy so that eyes are too often removed needlessly. A case of a benign leiomyoma of the iris is reported. These tumors can often be removed completely by an iridectomy and diagnostic biopsy is urged. Clinically these tumors appear as gray, vascular, sessile or pedunculated tumors, with little, if any pigment. They may be slow growing with periods of activity and may give rise to hyphema or even to cataract accomplicata and probably originate in an embryonal defect. (8 figures.)

Morris Kaplan.

Oravisto, Terttu. **Neurofibromatosis in the region of the eye.** Acta ophth. 27:89-98, 1949.

The literature is reviewed, and two cases reported in detail, including histologic data. The patients were four-year-old girls. One had a mass in the upper lid, and the other in the lower lid with thick-

ening of the adjacent tissues. One patient had congenital hydrophthalmos in one eye, and optic atrophy in the other. The other had no other ocular abnormalities. (2 figures.)   Ray K. Daily.

Pasca, G. **Two cases of chloroma orbitae; its hematocytoblastic origin and its treatment with ethylurethan and penicillin.** Boll. d'ocul. 28:101-109, Feb., 1949.

In two cases of chloroma of the orbit in children, aged 4 and 5 years, hemocytoblasts were found in the circulating blood as well as in the tumors. This seems to confirm the new hypothesis that chloroma is a form of hemocytoblastosis. In the girl, the disease involved both eyes while it was unilateral in the boy. The therapy mentioned in the title did not bring any improvement. (References.)

K. W. Ascher.

Silva, Daniel. **Errors of diagnosis in infantile intraocular tumors.** An. Soc. mex. de oftal. 22:217-236, 1948.

The author reports three cases. The chief cause of error is the appearance of a supposed tumor mass ("cat eye") diagnosed as glioma. In the author's first case the existence of marked photophobia was erroneously interpreted in spite of Terry's insistence upon the characteristic photophobic facies of children with retrolenticular fibroplasia, who automatically raise their hands to cover their eyes in the presence of light. In the second case too much importance was attached to hemorrhages, in spite of Reese's advice as to the frequent relation between fibroplasia and angiomatous processes. Excessive weight may be attached to the absence of prematurity at birth. The third case, in which the eye was not enucleated for glioma until invasion of the optic nerve was far advanced, emphasizes the necessity for using every possible means of diagnosis, including transillumination

under general anesthesia if necessary, and even enucleation and microscopic study of one eye. (9 figures, references.)

W. H. Crisp.

Soria. **Radium therapy in malignant epibulbar tumors.** Arch. Soc. oftal. hispano-am. 9:405-414, April, 1949.

On the basis of his experience with 17 patients, treated since 1929, Soria urges the application of radium-therapy for epibulbar malignant tumors which have not extended into the eyeball. He describes a method of application which consists in fixing with conjunctival sutures a tube 22 mm. in length and 2 mm. in diameter over the site of the tumor; over the tube is placed a lead shield 1 mm. in thickness, also fixed to the conjunctiva with sutures, through small perforations on its edges. The tube contains 5 mgm. of radium, and is left in place for 72 hours, with the patient in bed, and both eyes bandaged. The results were good in all but one patient. The side reactions of the irradiation were mild conjunctivitis, which healed in a few weeks, vascularization of the adjacent conjunctiva, which was obliterated by the application of a diathermy electrode, edema of the lids which disappeared spontaneously, and, in the eyes which were treated without the lead shield, a localized madarosis, the occurrence of which was eliminated by the shielding with lead. (2 figures, 4 photomicrographs.)

Ray K. Daily.

Souders, B. F. **Juxtapapillary hemangioendothelioma of the retina; report of a case.** Arch. Ophth. 41:178-182, Feb., 1949.

A case of von Hippel's angiomatosis retinae in a man, aged 40 years, is reported. The tumor, immediately adjacent to the optic nerve head, gave the preoperative impression of a malignant tumor of the optic nerve and the eye was enucleated. A detailed pathologic re-

port and photomicrographs are included.

John C. Long.

17
INJURIES

Chavira, R. A. **Traumatic syndrome of the eye.** An. Soc. mex. de oftal. 22:113-130, 1948.

This is an 18-page thorough enumeration of various visual and other ocular effects arising from contusion of the eyeball. (References.)

W. H. Crisp.

Granstrom, K. O. **Extraction of non-magnetic intraocular foreign bodies.** Acta ophth. 27:47-58, 1949.

Fifteen extractions of non-magnetic foreign bodies are briefly described. In three the foreign body was situated in the anterior chamber, and the extraction was not difficult. Extraction of foreign bodies in the angle of the anterior chamber is greatly facilitated by X-ray control on the operating table and a T incision at the limbus. The precise location of the 12 foreign bodies in the vitreous or ocular wall was determined with a portable X-ray apparatus, and repeated X-ray photographs by the Larsson method, in which a point of a needle is imbedded in the exposed sclera over the previously determined site of the foreign body. The needle is moved and the roentgenogram repeated until the needle is shown exactly over the foreign body. A scleral flap, instead of radial incision, gives better access to the foreign body. In 3 of the 12 the author was successful.

Ray K. Daily.

Hill, J. C. **Visual manifestations of head injuries.** Canad. M.A.J. 60:464-468, May, 1949.

Most ocular abnormalities following head injuries are, 1. injury to the globe, 2. derangement of ocular motility, and 3.

lesions of visual pathways. This paper deals with lesions of visual pathways that occurred in World War II veterans seen at Christie Street Hospital Eye Clinic. Fifty-two cases of head injuries with ocular involvement were studied. In 25 cases disturbance of the optic nerve resulted in varying degrees of loss of visual acuity and optic atrophy. Fracture of the optic foramen was found in only four cases and only two lesions affecting the optic tracts were observed. In 25 cases the injury affected the optic radiation and visual cortex. There was marked loss of field with slight loss of visual acuity.

Theodore M. Shapira.

Stein, A. **The treatment of burns.** Ophthalmologica 117:232-237, April-May, 1949.

In the later stages of conjunctival and corneal burns, the author considers ischemic processes to be the predominant injurious factor. In order to alleviate this ischemia, he recommends the use of priscol in the form of constant eye baths. Twenty to 40 drops of the 10-percent priscol solution are added to 8 to 9 cc. of either artificial tears or blood plasma. This mixture is kept in contact with the cornea and conjunctiva by means of the rubber eye cup described in previous communications. A new feature has been added to this eye cup in the form of a heating device which keeps the solution at body temperature. The author reports good results in 10 cases of acid, lime and lye burns of the anterior surface of the eye. Peter C. Kronfeld.

Weber, E. **Simple procedure for the extraction of intracorneal wood splinters.** Ophthalmologica 117:238-239, April-May, 1949.

A splinter of wood penetrated the cornea more or less perpendicularly and no graspable portion protruded externally. For the extraction of such foreign bodies Weber recommends the following procedure. By careful dissection with a small Graefe knife, a small portion of the external end of the splinter is exposed. The tip of this Graefe knife is now introduced into the exposed portion, thereby securing the foreign body. With the aid of another Graefe knife introduced from the other side, the foreign body is extracted.

Peter C. Kronfeld.

Witmer, R. **The extraction of nonmagnetic intraocular foreign bodies.** Ophthalmologica 117:277, April-May, 1949.

The exact roentgenographic method of localization of intraocular foreign bodies by Goldmann and Bangerter (Ophthalmologica 101:139 and 215, 1941) has proved to be very helpful. The method is most suitable for foreign bodies which are situated close to the wall of the eyeball. After gross localization by means of lateral and antero-posterior X-ray examination, the scleral area closest to the foreign body is exposed surgically. A metal ring, 3 mm. in diameter, is attached to the sclera by means of fine barbs. A piece of dental film is placed right next to the ring and another X-ray picture is taken. The position of the ring is changed until the foreign body seems to be located in the center of the ring. Then the sclera is opened, and the choroid and retina carefully incised. The foreign body then either presents itself or can be found by feeling around "in the dark" with a small forceps. The remarkable thing about the report is that with this method of localization the final results of extractions on nonmagnetic foreign bodies are almost as good as those of magnetic foreign bodies.

Peter C. Kronfeld.

18

SYSTEMIC DISEASE AND PARASITES

Alpers, B. J., Foster, F. M., and Herbut, P. A. **Retinal, cerebral and systemic**

arteriosclerosis: a histopathologic study. Arch. Neurol. and Psychiat. 60:440-456, Nov., 1948.

The authors studied the retinal and cerebral vessels of 100 adults on whom autopsy was performed. Their findings are not in agreement with the general clinical impression that retinal arteriosclerosis is a sign of cerebral arteriosclerosis. Retinal arteriosclerosis merely indicates a 6 to 1 probability of cerebral arteriosclerosis, and absence of retinal arteriosclerosis does not exclude the presence of cerebral arteriorsclerosis.

R. Grunfeld.

Brand, I. **The ocular tension in myotonic dystrophy.** Orvosi Hetilap 12:376-380, 1949.

In a patient with myotonic dystrophy the tension of both eyes was strikingly low, especially on the side opposite the more atrophic testicle. The injection of antephysan resulted in a paradoxical response, namely increase of ocular tension. Hypotony is probably a frequent symptom in myotony. Gyula Lugossy.

Busacca, Archimede. **The green iridescent color of the intravitreal cysticercus.** Ophthalmologica 117:347-348, June, 1949.

Examination with the binocular ophthalmoscope of a typical intravitreal cysticercus revealed the iridescence of the cyst to be due to the presence of crystals in its walls. Peter C. Kronfeld.

Cass, E. E. **A case of ocular myiasis.** Brit. J. Ophth. 33:385-386, June, 1949.

Flies may lay their eggs in the conjunctival sac and some are dangerous as their maggots may burrow beneath the conjunctiva and even penetrate the globe. The case of a man who thought dust blew into his eye is presented. Severe pain with edema developed and eleven maggots were subsequently removed. The man

insisted that the maggots must have been in the cement mixture or the tap-water which was near and claims compensation.

Orwyn H. Ellis.

Dinger, G. **Observations in the fundus oculi in cases of pulmonary tuberculosis.** Klin. Monatsbl. f. Augenh. 114:105-107, 1949.

Almost 14 percent of 284 patients with pulmonary tuberculosis had fundus lesions. Nearly all patients had good central vision. The lesions were, for the most part, peripheral healed chorioretinitic scars. There were no patients with fresh lesions. (References.)

Max Hirschfelder.

Djacos, C. **The ocular symptoms of pellagra.** Ann. d'ocul. 182:279-294, April, 1949.

The author reports 41 cases of ocular lesion in an epidemic of pellagra. This disease results from a deficiency primarily of nicotinic acid, but also of other components of the B2 group. The most frequent ocular lesion was bilateral conjunctival edema with slight hyperemia. Corneal lesions were epithelial or interstitial. The former were characterized by a large number of fine, punctate epithelial opacities and depressions. The interstitial form usually involved the lower part of the cornea, and consisted of several deep nodules which had a tendency to ulcerate. Transient, faint, tongue-shaped opacities were observed in the lens. Night blindness was not an important symptom, nor were there retinal hemorrhages, papilledema, or neuritis. These lesions have been mentioned in the literature.

Chas. A. Bahn.

Doggart, J. H. **Diseases of the eye in relation to dental surgery.** Brit. J. Ophth. 33:338-347, June, 1949.

Developmental defects, trauma, and skeletal and endocrine diseases are

briefly reviewed because they offer many striking instances of associated dental and ocular disturbance. Eyes and teeth share susceptibility to a number of toxic hazards. The widespread theory of focal sepsis with teeth as the chief cause of ocular infection is vigorously attacked and ruthless dental extractions decried. Closer cooperation between the oculist and dental surgeons is urged.

Orwyn H. Ellis.

Fontana, Giuseppe. **Ophthalmoscopic examination of children with tuberculous meningitis and miliary tuberculosis, treated by streptomycin.** Arch. di ottal. 52:182-188, July-Aug., 1948.

Twenty patients, ranging in age from 9 months to 17 years, were observed ophthalmoscopically, some during treatment, with streptomycin, and others with streptomycin combined with a sulphonamide and vitamins A and D. Twelve had tuberculosis meningitis and eight had miliary tuberculosis in addition to the meningitis. In four there were no abnormal eye findings, in nine there was papilledema and in seven there was vascular stasis in the nerve head. In two of the last group miliary tubercles of choroid and iris tubercles were also present. In the nine with edema, marked regression of the edema was noted in 20 days, and two had normal papillae in 90 days. Those with vascular stasis in the papilla showed a greater resistance to treatment and persisted longer than others. This showed a direct relationship to the severity of the meningeal process. Miliary tubercles of the choroid indicated a general miliary tuberculosis. The manifestations of the nerve head and the choroid offered considerable information of value in the diagnosis and prognosis of these forms of tuberculosis.

Francis M. Crage.

Godtfredsen, E. **Pathogenesis of concurrent eye and joint diseases.** Brit. J. Ophth. 33:261-270, May, 1949.

An increasing awareness of an association between certain joint diseases both acute and chronic and eye symptoms along with increasing interest in allergies brings this report of study in Denmark. The list of acute joint diseases includes rheumatic fever, gonorrheal arthritis, simple urethritic polyarthritis (Reiter's disease) and uratic arthritis while the chronic diseases are Still's disease and ankylopoietic spondyloarthritis. In the first group eye symptoms were found in 2 to 80 percent, and in the second in 2 to 50 percent. These are in the main three groups of eye diseases namely: endogenous conjunctivitis, scleritis and episcleritis; iritis and iridocyclitis, and the sicca syndrome.

It is felt that most of the joint symptoms are an allergo-toxic reaction to a coccus, usually hemolytic streptococcus, or to a virus. It is supposed that the eye symptoms are a similar allergo-toxic phenomenon. This is borne out to some extent by histologic study. Concurrent disease in the heart, the skin and cavities lined with mucous membrane may also be significant.   Morris Kaplan.

González Aguilar, E. **The thesaurismoses.** An. Soc. mex. de oftal. 22:192-199, 1948.

These diseases are characterized by abnormal deposits of various substances in tissue cells such as Gierke's, Schuller-Christian's, Gaucher's, and Niemann-Pick's. (References.)   W. H. Crisp.

Magitot, A. **Congenital syphilis.** Ann. d'ocul. 182:306-312, April, 1949.

The changes of treatment and examination in syphilis during the past generation are reviewed. Retinal pigmentary degeneration and Leber's Disease are now known to have no relationship to congenital syphilis. Infection usually does not take place before the fifth month of intrauterine life because the embryo is not nourished directly by the mother's blood

until that time. Fewer fetal malformations are directly due to congenital syphilis than was thought. If the infection is virulent, the child is usually born dead and in approximately 30 percent, prematurely. Luetic infections tend to become less virulent with time. The positive Bordet-Wassermann test shows that maternal antibodies have been transmitted to the embryo, and disappears with the antibodies. Infection of the second generation is possible, but very rare. The symptoms may begin at birth or later. Iritis, choroiditis and cutaneomucous gummas are later manifestations. Dental changes, rickets, a tendency toward some infectious disease and endocrine anomalies are among the frequent evidences of congenital lues in youth. Medication should be continued until the patient is serologically negative. Trivalent arsenic and oil and soluble bismuth preparations are preferred to mercury in the treatment of the ocular symptoms of congenital syphilis. The use of penicillin is experimental.

Chas. A. Bahn.

Rosen, Emanuel. **The significance of ocular complications following vaccination.** Brit. J. Ophth. 33:358-368, June, 1949.

The literature on ocular complications following vaccination and also on post-vaccinial encephalitis is reviewed and six case reports are presented. Ocular complications developing within a specific period after vaccination are part of a post-vaccinial ocular syndrome which may consist of interstitial keratitis, central serous retinopathy and cranial nerve involvement. Cases illustrating activation of previously existing conditions are presented. The pathologic picture of post-vaccinial encephalitis and the encephalitis of the acute exanthemata are identical. The author points out many characteristics of this condition which may ultimately be explained on an allergic basis.

Orwyn H. Ellis.

Smith, Mary D. **Diabetic neuropathy with Argyll Robertson pupils: report of two cases.** Glasgow Med. J. 30:181-184, May, 1949.

The neurologic complications of diabetes mellitus are reviewed. In one series of 3,000 diabetics two had this complication and in another series of 19,000 only 10 had Argyll Robertson pupils. The first patient with severe diabetes had small irregular pupils that did not react to light but did react in accommodation. The iris was atrophic and there were lens opacities and retinal exudates and hemorrhages. The deep tendon reflexes were absent in the legs and diminished in the arms. Under treatment for diabetes the superficial and deep reflexes in the legs returned to normal. The pupillary reflexes did not change. The other patient displayed similar manifestations. The causes for the appearance of neurological changes in diabetes are reviewed.

H. C. Weinberg.

Wilson, W. A. **Temporal arteritis with report of a case.** Ann. West. Med. and Surg. 3:177-179, May, 1949.

Arteritis complicated an otherwise normal cataract extraction and recurring hemorrhages and secondary glaucoma followed. An inflammation of the adventitia of the vessel spreads to the media where focal necrosis and giant cell reaction occur. The intima becomes thickened but is not otherwise affected.

Orwyn H. Ellis.

19

CONGENITAL DEFORMITIES, HEREDITY

Briggs, A. H., and McLean, D. W. **An unusual congenital defect.** Brit. J. Ophth. 33:381-384, June, 1949.

A mass present in the anterior chamber and adherent to the posterior corneal surface in one quadrant and apparently of mesodermal origin, was seen at birth. Vessels were present on its anterior sur-

face. There was an anomalous distribution of the vessels of the optic disc. The condition was unchanged at six years of age and no useful vision was found.

Orwyn H. Ellis.

Cuendet, J. F., and Della Porta, V. Hereditary nystagmus. Ophthalmogica 117:199-201, April-May, 1949.

The report deals with a family of 106 members, 22 of whom were affected with typical congenital (hereditary) nystagmus. The mode of transmission was dominant and sex-linked.

Peter C. Kronfeld.

Franceschetti, A., and Maeder, G. Cataract associated with skin lesions of the poikiloderma and scleroderma type. Ophthalmologica 117:196-198, April-May, 1949.

On the basis of a review of the literature, the authors give a detailed description of the two hereditary diseases indicated in the title. The association of cataract with skin lesions of the type of poikiloderma atrophicans vasculare is known as Rothmund's disease. The skin lesions develop during the first year of life, often in the form of one eruption, and are characterized by patchy hyper- and hypopigmentation, telangiectasis and atrophy, preceded in places by true vesicles. Nails and hair are also affected. The skin lesions reach a standstill in early childhood. Cataracts of the endocrine type make their appearance between the ages of two to six years. Hypoplasia of the ovaries or testes is the characteristic endocrine manifestation of this disease. The affected individuals are of normal height and mentality. The disease is hereditary, the mode of transmission probably recessive. Franceschetti and Maeder have found 20 cases of this disease in the literature.

Scleroderma associated with cataracts is known as Werner's syndrome. Here again the basic anomaly appears to be genital hypoplasia, of a higher degree, however, than in Rothmund's disease. The skin lesions are progressive and recurrent. The disease is also hereditary, and more common in men than in women. The authors have found 42 cases of this disease in the literature.

Peter C. Kronfeld.

François, J. Familial dermochondrocorneal dystrophy. Ann. d'ocul. 182:409-442, June, 1949.

The author reports the first two cases of this rare dystrophic syndrome in siblings. In an otherwise normal boy, aged 11 years, and his 12-year-old sister, the several constitutional degenerative processes became manifest after birth. They had numerous bilateral, symmetrical, subepithelial corneal opacities of different sizes and shapes, deformities of the epiphyses of the metacarpal and tarsal bones, and numerous xanthomas on the fingers, nose, and ears. The differentiation from several types of corneal, osteochondral and lipid genetic abnormalities is briefly discussed. The disease in these siblings resembled dysostosis multiplex.

Chas. A. Bahn.

Heatley, Juan. Congenital familial miosis. An. Soc. mex. de oftal. 22:141-148, 1948.

A family tree of 5 generations and 30 individuals is presented. Nine were investigated, trustworthy data were obtained on 10, and the condition of 11 was unknown. Seven subjects had congenital miosis which was associated with microcornea in three, 11 had myopia, and three had increased tension. The defect was not pure hereditary and congenital miosis, but a series of four changes which seemed irregularly mixed, transmitted dominantly, and, except the tension, present from childhood. (References.)

W. H. Crisp.

Paraipan, C. **Bilateral anophthalmos.** Ann. d'ocul. 182:214-215, March, 1949.

The author examined an otherwise normal new-born girl with no traceable hereditary tendency to ocular defects who had microblephary and almost complete absence of both eyeballs. This rarity is ascribed to maldevelopment of the optic vesicle.   Chas. A. Bahn.

Straub, Wolfgang. **Congenital anterior synechia of the pars retinae of the iris.** Klin. Monatsbl. f. Augenh. 114:211-213, 1949.

A patient exhibited a brown tubular strand of tissue which originated behind the iris, penetrated the anterior chamber and was inserted in a gray area in the endothelium of the cornea. It is believed that this was caused by a damage of the corneal endothelium during early intra-uterine life resulting in an adhesion between the pars retinae of the iris and the endothelium corneae at a time when the cavity of the optic vesicle was still open. (1 figure, references.)

Max Hirschfelder.

20
HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Aug, J. C. **An early photograph of von Helmholtz with explanatory letter.** Arch. Ophth. 41:570-571, May, 1949.

An interesting letter written by Prof. Ernst von Brücke a few months before his death accompanies the photograph.

Ralph W. Danielson.

Fanta, H. **Causes of blindness in the young.** Klin. Monatsbl. f. Augenh. 114:219-224, 1949.

Among the 90 pupils of the Vienna School for the Blind there were 15 with partial and 75 with total blindness. Nearly one half of the partially blind had congenital cataract and most of them had

been operated on. Of the total blindness 20 percent resulted from injury, 14 from retinal degeneration, 9 from cataract, 9 from atrophy of the optic nerve, 7 from brain tumor and 5 from glaucoma. The blindness due to ophthalmia neonatorum was only 3 percent. Max Hirschfelder.

Hruby, K. **Urgent conditions in the eye.** Wien. klin. Wchnschr. 61:337-341, June 3, 1949.

This lecture was given to a group of general practitioners to point up the conditions in the eye which threaten vision. Symptoms seemingly unimportant to the patient, such as contraction of the field and slowly progressive loss of vision, beginning lid epithelioma, and lagophthalmos must be recognized as serious by the physician who first sees them. Vaccination blepharitis, diphtheria and gonorrhea are extremely serious. The practitioner should learn to differentiate ciliary from conjunctival injection and recognize the significance of each. Hruby describes the first-aid measures the general practitioner should employ in acute iritis and in chemical and perforating injuries. He discusses in detail the early recognition of glaucoma and the importance of not mistaking it for senile cataract. He points out how important early operation is in retinal detachment. Finally, amblyopia ex anopsia may lead to loss of vision and glasses should therefore be prescribed early after congenital cataract operation and in strabismus. Myopia and hyperopia in the child need correction only if they are very severe.   B. T. Haessler.

Kuhn, H. S. **A manual on toxic hazards.** Tr. Am. Acad. Ophth. pp. 595-596, May-June, 1949.

This manual, which has recently been published, is the result of two years' effort by the Joint Committee on Industrial Ophthalmology, and was made possible by the National Society for the Preven-

tion of Blindness. The first section deals with tests, protective means and similar data pertaining to industrial ophthalmology. In the second section, a preliminary report of ocular toxic chemicals is presented in detail. The scientific and trade names are given as well as the symptoms and chemical effects. In the third section a description of the accepted emergency first aid procedures in treatment of chemical eye injuries is reported in detail. This manual should be in the office of every ophthalmologist.   Chas. A. Bahn.

del Mazo y Ascona, J. G. **The protection of the blind in Spain.** Arch. Soc. oftal. hispano-am. 9:353-358, April, 1949.

The social and welfare organization for the blind in Spain is described.

Ray K. Daily.

Podesta, H. **Goethe and Kirschmann's "reversed spectrum."** Arch. f. Ophth. 148:787-794, 1948.

The paper presents some of Goethe's studies of the reversed spectrum in which the complementary colors appear in the place of the usual ones.

Ernst Schmerl.

Sullivan, R. R. **The navy eye-correction, eye-protection program.** Tr. Am. Acad. Ophth. pp. 615-620, May-June, 1949.

The fundamentals of eye-correction and eye-protection are briefly presented and a number of suggestions offered.

Chas. A. Bahn.

Trueman, R. H. **A survey of state fee schedules for industrial eye care.** Tr. Am. Acad. Ophth. pp. 605-614, May-June, 1949.

The author graphically compares and contrasts the ophthalmic surgical fees allowed by different states for patients under their care.   . Chas A. Bahn.

Uribe Troncoso, Manuel. **The fiftieth anniversary of Anales de Oftalmologia.** An. Soc. mex. de oftal. 22:205-207, 1948.

Uribe Troncoso, in association with Daniel M. Vélez, established the Anales in July, 1898, to promote the development of ophthalmology in Mexico. It was the only periodical publication in the Castilian language devoted to ophthalmology. The printing was at first undertaken by a department of the Mexican government and other expenses were borne by the founders. Then it was the official organ of the Mexican Ophthalmological Society and still is. Five or six years later Menacho of Barcelona, Spain, and Santos Fernández of Cuba started in the Spanish (Castilian) language the Archivos de Oftalmologia Hispano-Americanos and proposed combining the two journals under an editorial office in Barcelona. This invitation was rejected. After fourteen years the Mexican revolution of 1910 caused suspension of the Anales, and in 1916 Uribe Troncoso left Mexico and settled in New York. After the years of social depression the Anales was continued in Mexico by Daniel Vélez.

W. H. Crisp.

NEWS ITEMS

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

DEATHS

Dr. Ira Bradford Chadwick, Coffeyville, Kansas, died June 16, 1949, aged 79 years.

Dr. John M. Robinson, Goshen, New York, died June 24, 1949, aged 79 years.

Dr. Milton J. Stern, Lexington, Kentucky, died June 12, 1949, aged 59 years.

ANNOUNCEMENTS

AOS TRANSACTIONS

The 1949 Transactions of the American Ophthalmological Society, published in book form, may be purchased by advance subscription. Containing the scientific papers given at the annual meeting and the theses for membership, this volume may be ordered from the editor:

Dr. Wilfred E. Fry
1930 Chestnut Street
Philadelphia 3, Pennsylvania

The price is $12.00, and all orders must be received by December 1, 1949.

GILL GRADUATE COURSE

The 23rd annual spring graduate course of the Gill Memorial Eye, Ear, and Throat Hospital, Roanoke, Virginia, will be held April 3 to 8, 1950. The course is open only to qualified practitioners who are giving full time to their specialty. The hospital reserves the right to reject any application.

On the guest faculty will be the following: Dr. F. W. Stocker, Durham, North Carolina; Dr. Conrad Berens, New York; Dr. Fred Wilson, Chicago; Dr. C. W. Mayo, Rochester, Minnesota; Dr. Edmund B. Spaeth, Philadelphia; Dr. Arthur J. Bedell, Albany, New York; Dr. James J. Regan, Boston; Dr. W. Gayle Crutchfield, Charlottesville, Virginia; Dr. Stuart Cullen, Iowa City, Iowa; Dr. Richard G. Scobee, St. Louis; Dr. Daniel S. Cunning, New York; Dr. Alson E. Braley, New York; Dr. Karl M. Houser, Philadelphia; Dr. Hugo L. Bair, Rochester, Minnesota; Dr. Gabriel Tucker, Philadelphia; Dr. Edward M. Walzl, Baltimore; Sir Alexander Fleming, London; Dr. J. Barrett Brown, St. Louis; Dr. Walter B. Hoover, Boston; Dr. Oscar O. Hansen-Pruss, Durham, North Carolina.

HISTOPATHOLOGY COURSE

The schedule of the three-month course in "Histopathology of the Eye," given by Dr. Brittain F. Payne and associates at the New York Eye and Ear Infirmary has been rearranged to last one week in January, 1950.

The course will be given in the afternoons of the second week in January, and will consist of the same number of hours of instruction and material as previously allotted. The dates are from January 9th to 14th, and further information may be obtained by writing the Post-Graduate Division of the New York University College of Medicine.

WILLS HOSPITAL CONFERENCE

The annual clinical conference of the Wills Eye Hospital will be held in Philadelphia on Friday and Saturday, March 17 and 18, 1950.

Dr. Francis Heed Adler will deliver the annual Arthur J. Bedell Lecture on the evening of March 17th.

MEXICAN MEETING

From November 6th to 12th, the Association to Eradicate Blindness in Mexico will have its fourth biannual meeting. Further information may be obtained by writing the secretary, Dr. Ramón Olivera López, Gomez Farias 19, Mexico, D.F.

RESERVATIONS FOR FLORIDA MEETING

The National Society for the Prevention of Blindness will hold a five-day conference in conjunction with the interim session of the Pan-American Association of Ophthalmology, March 26 to 30, 1950, at the Floridian Hotel, Miami Beach, Florida. The theme of the meeting will be "The Americas Unite to Save Sight," and among the subjects to be discussed are: Current blindness prevention programs in countries of the Western Hemisphere; Trachoma; Industrial ophthalmology; Eye problems of school children; Medical and social management of the glaucomas.

Persons directly or indirectly concerned with eye health and safety will find this conference of interest. Details concerning the program may be obtained by writing directly to the National Society for the Prevention of Blindness, 1790 Broadway, New York 19.

Reservations should be made in the near future with the Floridian Hotel, 540 West Avenue, Miami Beach, Florida.

GRANTS-IN-AID OFFERED

The National Council to Combat Blindness, which was established for the purpose of financing and stimulating ophthalmological research, is now offering grants-in-aid to scientific investigators. Applications to be considered for the first group of awards should be in the office of the council by February 15, 1950. Application forms may be obtained by ad-

dressing: Secretary, National Council to Combat Blindness, Inc., 1186 Broadway, New York 1, New York.

SOCIETIES

ORTHOPTIC TECHNICIANS PROGRAM

On October 10th and 11th, at Chicago, the American Association of Orthoptic Technicians held its eighth annual meeting. On the program were:

"Anomalous retinal correspondence: Its essence and its significance in diagnosis and treatment," Dr. Hermann M. Burian, Boston; "Orthoptics in relation to preoperative training," Mrs. Elsie Laughlin, Iowa City, Iowa; "Physiology of vision," Miss Ann Stromberg, Boston; "Standards for vision," Miss Ruth McNab, Detroit; "Treatment of amblyopia," Miss Martha Peterson, Columbus, Ohio; "Types of occlusion and results," Miss Ruth Fisher, Denver; "Differentiation of Phi phenomenon and parallax and use of Phi phenomenon in determination of retinal correspondence," Miss Dorothy Franklin, Beverly Hills, California (with a discussion by Dr. S. Rodman Irvine, Beverly Hills); "Orthoptics in relation to postoperative training," Miss Frances Fowler, Seattle; "Orthoptic suggestions," Miss Eva DeMars, Philadelphia; "Stimulus-response mechanisms in binocular coördination," Dr. Edwin F. Tait, Norristown, Pennsylvania (with a discussion by Miss Electra Healy, Chicago); "Anomalous correspondence," Miss Marjorie Enos, New York (with a discussion by Dr. Michel Loutfallah, Santa Barbara, California); "The accommodative effort syndrome," Dr. Robert Hill, Portland, Oregon (with a discussion by Mrs. Louise Wells Kramer, Washington, D.C.).

PENIDO BURNIER OFFICERS

The Medical Association of the Institute Penido Burnier, Campinas, Brazil, has elected the following officers for 1949-1950; President, Dr. Penido Burnier Filho; 1st secretary, Dr. Alfonso Ferreira Filho; 2nd secretary, Dr. Alfredo Martinelli; historian and treasurer, Dr. Leôncio de Souza Queiroz; directors, Dr. Guedes de Melo Filho, Dr. F. J. Monteiro Sales, and Dr. José Martins Rocha.

CENTRAL ILLINOIS SOCIETY

The next meeting of the Central Illinois Society of Ophthalmology and Otolaryngology will be held at the Abraham Lincoln Hotel in Springfield, Illinois, on November 18th, 19th, and 20th. Dr. William L. Benedict of the Mayo Clinic will give lectures on: "Cataracts and systemic diseases," "General diseases: Ocular manifestations," and "Tumors of the eye and orbit."

Dr. H. P. House, associate professor of otolaryngology at the University of Southern California, will speak on: "Indications and end results of fenestration surgery," "Management of otitis media," and "Management of the continually stuffy nose."

Dr. Walter E. Owen, Peoria, Illinois, a member of the society will speak on: "Drug therapy in respiratory allergy." Dr. Herbert M. Kobes, director of the University of Illinois, Division of Services for Crippled Children, will speak on the "State of Illinois coöperates with the ophthalmologist and otolaryngologist."

HAWAII SOCIETY PROGRAM

The Hawaii Eye, Ear, Nose and Throat Society held its opening fall meeting at Tripler General Hospital, Honolulu, Territory of Hawaii, on September 15th.

A paper on "An evaluation of methods of treatment in 155 cases of pterygium" was presented by Lieut. Col. John H. King, Jr. (MC), chief of EENT section, Surgical Service, Tripler General Hospital. His talk was illustrated by descriptive slides on cases of pterygium and on various operations performed during the past 12 months. The presentation was discussed by Dr. Forrest J. Pinkerton, Dr. Ogden D. Pinkerton, Dr. H. F. Moffat, and Dr. Philip M. Corboy. Maj. Aubrey K. Brown (MC), assistant chief of EENT section, presented a case report on "Esophageal stenosis." His paper was discussed by Dr. John P. Frazer, Dr. L. Q. Pang, and Dr. Clarence J. Kusunoki.

TORONTO REFRESHER COURSE

The Faculty of Medicine of the University of Toronto offers a combined refresher course in ophthalmology and otolaryngology from January 9 to January 14, 1950.

The otolaryngological subjects will be presented during the first three days of the course and the ophthalmological subjects during the last three days. Lectures and surgical clinics in both subjects will be given by outstanding guest speakers as well as by members of the Faculty.

Guest speakers in otolaryngology will be: Dr. W. J. McNally, Montreal, and Dr. Henry Orton, Newark, New Jersey; in ophthalmology: Dr. P. C. Kronfeld, Chicago, and Dr. J. A. MacMillan, Montreal.

The course will be given for a minimum of 10 students and a maximum of 20 students. The fee for all or any part of the course will be $100.00, payable to the chief accountant, Simcoe Hall, University of Toronto. Application should be made to the Dean of the Faculty of Medicine, not later than November 30, 1949.

GLASGOW AUTUMN TERM

During October a series of meetings are being held in the Department of Ophthalmology, University of Glasgow. On October 5th, Dr. George Leaf presented a paper on "Biochemical aspects of methanol poisoning," and on October 12th, Dr. W. O. G. Taylor spoke on "Control of clotting in ophthalmology." "Tobacco amblyopia," is the subject Dr. R. Leishman presents on October 19th. Dr. A. Wright Thomson will speak on "Cyrate atrophy of the choroid" on October 26th. At each meeting, discussion will follow the presentation of the main paper.

CONTENTS

THE DIAGNOSIS AND TREATMENT OF OCULAR ALLERGY*

ALAN C. WOODS, M.D.

Baltimore, Maryland

The proper diagnosis and treatment of ocular allergy require a clear concept by both the ophthalmologist and the allergist of the relation of hypersensitivity to inflammations of the external eye and uveal tract, of the specific allergens most frequently responsible for the hypersensitive state, and of the methods for detecting and treating such hypersensitivity. Much of our knowledge on these points is fragmentary and there are great gaps where little or nothing is known. In this paper, the effort is made to outline the broad principles of ocular allergy as we now understand them and to describe the methods of diagnosis and treatment usually accepted at the present time.

Allergic reactions in the eye are dependent upon an underlying hypersensitivity to a specific antigen and contact of this antigen with the sensitized cells. The underlying hypersensitivity may be either of the anaphylactic and pollen type or of the bacterial type.

The anaphylactic and pollen types of hypersensitivity are caused exclusively by proteins or by the combination of nonprotein substances (such as drugs or metals) with the native protein of the host, thus forming a new compound which acts as a foreign protein. In the anaphylactic and pollen types of hypersensitivity the reactions of the sensitized cells to contact with the specific antigen is an immediate one, is characterized by an urticarial weal, a contraction of smooth muscle, and increased capillary permeability. It is believed due to the liberation of histamine or a histaminelike substance. The anaphylactic reaction does not in itself cause actual damage to the cells. However, after repeated local anaphylactic reactions an Arthus phenomenon may occur. This is the occurrence of local necrosis and is due not to a direct toxic action on the cells, but to thrombosis and rupture of the nutrient vessels.

The hypersensitivity of infection is also known as bacterial hypersensitivity or the tuberculin type of hypersensitivity. It is produced only by the parenteral contact of the tissue with the living or dead bacterial body or filterable viruses. It cannot be produced by the soluble proteins of the organisms, but once the hypersensitivity is produced by the bacterial body, reactions can be elicited by the soluble specific proteins. When tissues with the bacterial type of hypersensitivity come into contact with the specific bacterial antigen or its soluble products, the allergic reaction is delayed, coming on in 24 to 48 hours. The reaction in bacterial allergy causes actual damage to the cells, in severe cases actual death and necrosis. The cause of this cell damage is not clear—it is variously believed that the antigen-antibody union produces a toxin which damages the cells, or that the cell damage is the result of some enzymelike action.

CLINICAL ALLERGIC REACTIONS

The various clinical allergic reactions in the eye may be classified as follows.

A. CONJUNCTIVA

Four types of allergic reactions are recognized in the lids and conjunctiva:

1. *A sudden, edematous type of reaction,* affecting primarily the conjunctiva alone, characterized by a glassy edema of the conjunctival fold, marked congestion of the palpebral and bulbar conjunctiva with profuse lacrimation, sudden in its onset, and sudden in its disappearance.

The classic example of this type is the conjunctivitis associated with hay fever and asthma. This is a typical pollen-type hypersensitivity. The mucous membrane of the eye participates in the general hypersensitivity of the mucous membranes of the upper respiratory tract and like them reacts with a sudden inflammatory edema when in contact with the specific sensitizing substance, the air-suspended allergens. There is usually chemosis of the palpebral and bulbar conjunctiva, profuse lacrimation, and a nonpurulent secretion without bacteria. The reaction usually subsides quickly after the instillation of epinephrine hydrochloride.

2. *Eczematous, edematous type of blepharoconjunctivitis.* The lids are swollen with a firm edema, the margins are inflamed, the skin of the lids has a characteristic, dry, eczematous feeling, the palpebral conjunctiva is congested; there is usually a slight chemosis. There is profuse lacrimation. The most frequently observed example of this type of allergic reaction is that due to drug sensitivity, atropine, butyn, and other alkaloids. As already stated, the drug, *per se,* is not believed to be the offending allergen, but a combination of the drug with the native protein, forming a new specific allergen which is foreign to the host.

3. *Chronic or recurrent irritative conjunctivitis.* Often this is associated with a slight marginal blepharitis. Subjectively, the most pronounced symptoms are a sensation of dryness and itching. Objectively, there is usually a slight or moderate congestion of the palpebral conjunctiva, often with small patches of dry folliculosis and no chemosis. A low-grade irritative marginal blepharitis, usually without crusts of any cutaneous reaction, may be present. The allergens responsible for the underlying sensitivity may be bacterial, notably staphylococcus toxin, or the various epidermals, inhalants, animal dusts, and so forth.

4. *Vernal catarrh.* The clinical picture is almost characteristic, with seasonal occurrence, lacrimation, itching, conjunctival congestion, with large follicles over the palpebral, and occasionally on the bulbar conjunctiva. In the latter stages, these assume the appearance of large "cobblestone" follicles with irregular distribution.

The evidence in favor of an underlying allergy as the predisposing cause is the seasonal occurrences of the attacks, the tendency of the disease to attack the young, the comparative absence of bacteria in the secretions, the usual abundance of eosinophiles in the discharge, the specific hypersensitivity to various allergens so often demonstrated, and the general allergic diathesis of many of the patients.

B. CORNEA

Two types of superficial keratitis are believed to be allergic in origin—phlyctenular keratoconjunctivitis and recurrent marginal ulcers. It is quite possible that various other forms of superficial keratitis may be on an allergic basis, or their course influenced by a concomitant hypersensitivity of the corneal epithelium to bacteria or filterable viruses.* However, as a rule, such relationship is so tenuous or hypothetical that from the practical standpoint it is of little concern.

It is also undeniably true that the course of certain forms of deep keratitis (notably tuberculous keratitis and the nummular keratitis sometimes seen in chronic brucellosis) is profoundly influenced by the degree of specific local sensitivity present in the

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* Such as recurrent corneal erosion after minor corneal trauma and infection.

cornea. The problem here, however, is identical to that of similar endogenous infections of the uveal tract and the same principles which influence them would govern corneal lesions. These will be discussed later.

1. Phlyctenules. The well-known clinical picture requires little comment. The onset is usually acute, small millet-seed nodules froming on the cornea and occasionally on the adjacent conjunctiva, usually at or near the limbus, the phlyctenules being surrounded by a zone of local inflammation. A grayish crater soon forms at the apex, absorption is rapid, and the small ulcer so formed epithelizes over rapidly, usually leaving little trace. They frequently occur in small showers, and recurrences are common.

The allergic basis of phlyctenules appears clearly established. Phlyctenules in both man and experimental animals have been produced by the instillation of tuberculin in the conjunctival sac, and by the instillation of other specific sensitizing allergens. Tuberculoprotein is the allergen commonly incriminated, and, in children suffering with phlyctenulosis, a high degree of tuberculin hypersensitivity can usually be demonstrated, and likewise a history of exposure to open tuberculosis. Various other allergens have from time to time been incriminated. The diagnosis offers no difficulty.

2. Marginal ulcers. These begin as small infiltrates, near the limbus. they rapidly break down and form small pinhead ulcers, often in a crescent around the limbus. There is associated hyperemia. The tendency is to rapid healing without deep penetration. Itching and irritation are marked. Recurrences are common. They occur frequently in elderly people and may follow a catarrhal conjunctivitis. Low-grade foci of infection, in the sinuses, tonsils, and so forth, are frequently found.

The evidence that these ulcers are allergic is largely circumstantial and not altogether conclusive. Cultures of the ulcers are usually sterile. The patients usually show evidence of bacterial hypersensitivity and the presence of remote foci of infection. A concomitant or preceding low-grade conjunctivitis is the rule oftener than not. The fact that they occur characteristically near the limbus has given rise to the supposition that the intoxicating bacterial allergens may reach the sensitized corneal epithelium at the limbus from the adjacent vascular bed. The patients usually do well on specific desensitization and recurrences can, as a rule, be controlled. On these grounds, and the inability to find any other concrete cause to explain them, this type of marginal ulcer is usually regarded as an example of bacterial allergy.

C. UVEAL TRACT

Allergic reactions of the uveal tract may be classified as follows: (1) Inflammations related to a hypersensitivity from absorption of the native organ specific proteins of the eye, uveal pigment and lens protein (sympathetic ophthalmia and endophthalmitis phacoanaphylactica) ; (2) nongranulomatous uveitis due *per se* to a bacterial hypersensitivity; (3) granulomatous uveitis due to the direct invasion of the ocular tissues by specific living pathogens, in which the course and character of the lesion is influenced by tissue hypersensitivity.

1. a. Sympathetic ophthalmia. The assumption of an allergic phase in sympathetic ophthalmia is based upon an abnormal reaction to uveal pigment, developed by the body cells either before the outbreak of the disease or early in its course.

The pigment of the uveal tract possesses the immunologic quality of organ specificity and lacks species specificity—in short, it is potentially able to act as a foreign protein in the homologous animal.

The abnormal reaction to uveal pigment may be demonstrated by injecting small amounts of uveal pigment in the skin. The results are epithelioid, and lymphocytic infiltration about the injected pigment and phagocytosis of the pigment occur—a picture comparable to the histologic picture of

sympathetic ophthalmia in the eye.

This hypersensitive reaction to pigment does not, however, appear to be the cause *per se* of the disease for it may be present in some individuals with posttraumatic and postoperative uveitis without sympathetic disease. It apparently sets the stage for the outbreak of the disease and determines its pathologic and histologic pattern.

Other, as yet unknown, and possibly quite nonspecific factors, may be responsible for the actual causation or outbreak of the disease, once the stage is set by the development of pigment hypersensitivity. The development of cutaneous hypersensitivity to uveal pigment after any traumatism or operative insult to the uveal tract of the eye is therefore a cause for alarm and increased vigilance.

1. b. Endophthalmitis phaco-anaphylactica. This is a term applied to an endogenous inflammation of the uveal tract, supposed to be dependent on the development of a hypersensitivity to lens protein, and the further absorption of lens protein by the sensitized tissues. It has been abundantly demonstrated that some of the proteins of the lens are organ specific and lack species specificity and are thus potentially capable of acting as foreign proteins. It is also recognized that an inflammatory reaction may follow the absorption of lens protein.

There has, however, been considerable question of the allergic or anaphylactic nature of this recognized clinical disorder, many observers pointing out the weak antigenic action of lens protein and attributing the delayed inflammation which follows its absorption to an inherent toxicity of the material, to a low-grade infection, or to both.

The weight of evidence, however, indicates there is an actual hypersensitivity to lens protein in individuals with this type of ocular reaction. The development of the hypersensititive state may be related to the synergistic actions of toxins absorbed from some remote focus of infection or an actual low-grade infection in the eye, such a factor enhancing the antigenic activity of the lens protein and producing the hypersensitive state. Further evidence that this is a clinical entity are the therapeutic results which follow proper desensitization procedures.

2. Nongranulomatous uveitis. The nongranulomatous uveitis resulting from a bacterial hypersensitivity is dependent upon a prior infection with the specific bacteria. The original infection may have been in the eye, in which case the ocular tissues are especially reactive; or it may have been a systemic infection, the eye participating in the general tissue reaction. Once this hypersensitive state has been established, an allergic inflammatory reaction may be elicited either by contact of the sensitized cells with the soluble bacterial protein, as in the case of ocular focal reactions produced by tuberculin, or by direct contact with the living or dead bacterial body, as in the case of the experimental "ophthalmic reaction."

Nongranulomatous uveitis in the anterior uvea is characterized by an acute onset, with marked ciliary congestion, photophobia, and lacrimation. The inflammatory changes in the iris are usually limited to loss of luster, blurring of the normal iris pattern, and dilatation of the capillaries. There is frequently a gelatinous or fibrinous exudate in the anterior chamber. The keratitic precipitates are usually small, pinpoint in type, and composed chiefly of lymphocytes. The course is stormy but usually brief, and the eyes recover with amazingly few residua. After repeated attacks, however, organic changes may take place in the eye, with synechia and organized exudates, and the eyes assume the picture of the granulomatous form of the disease. The destructive changes which occur after repeated attacks of nongranulomatous uveitis may possibly be interpreted as an Arthus phenomenon.

In the posterior uvea, the nongranulomatous uveitis is not so characteristic. In general, the eyes show only slight blurring of the vitreous; there are no discernible exu-

dates, but there is marked subretinal edema, blurring the elements of the fundus pattern.

Nongranulomatous uveitis is seen, in its' purest form, in the iritis and uveitis associated with rheumatoid arthritis or with old gonococcal infections. The supposition is that, at the time of a former bacteriemia, the eye has been invaded by the organisms. These bacteria have been destroyed by the normal bactericidal action of the ocular fluids but, as a result of the ocular invasion and parenteral contact of the tissues of the eye with the organism, there has been left behind a hypersensitivity of the uveal tract. Any later contact of this sensitized ocular tissue with the specific organism or its products, brought to the eye either by a later chance transient bacteriemia or by absorption of the bacterial products from a focus of infection, or, indeed, from a normal cutaneous or mucous membrane surface, results in a sudden, sharp, allergic reaction. The underlying sensitivity is probably of the bacterial type, although there may be an anaphylactic type of sensitivity to the hapten or polysaccharide fraction of the invading organisms.

3. Granulomatous uveitis. The underlying cause of granulomatous uveitis is an actual invasion of the uveal tract by the causative organisms in their living form. Granulomatous uveitis may be caused by tuberculosis, syphilis, brucellosis, sarcoidosis, toxoplasmosis, virus diseases, and quite probably by other as yet unidentified agents.

The clinical picture of granulomatous uveitis is quite different from that of nongranulomatous uveitis. The onset is usually insidious; the inflammatory reaction is not unduly severe. Organic changes occur in the iris with edema of the iris stroma, often localized thickening or felting of the iris, and frequently with actual nodules or tubercles. There is a marked tendency to the formation of posterior synechias and greasy exudates over the anterior capsule of the lens. The keratic precipitates are usually heavy, of the mutton-fat variety, and are composed chiefly of epithelioid cells. Small accumula-

tions of epithelioid cells may occur on the pupillary border or over the surface of the iris, the so-called Koeppe and Busacca nodules. In granulomatous disease of the posterio uvea, the characteristic picture is heavy vitreous opacities and actual exudates, with more or less associated subretinal edema.

The influence of a hypersensitivity in granulomatous uveitis is best illustrated by the tuberculous form of the disease, where the question has been extensively studied. While the injection of tuberculin and other fractions of the tubercle bacilli will produce pure allergic reactions in sensitized tissue, the progressive tuberculous lesions with cellular infiltration, tubercule formation, tissue necrosis, and caseation or encapsulation are produced only by the actual invasion of the tissues by the tubercle bacillus.

The acute inflammatory phases of the lesion with tissue destruction, caseation, and necrosis are dependent largely upon tissue hypersensitivity to tuberculoprotein. If there is no restraining immunity, the tubercle bacilli spread rapidly and first produce hard tubercles. Thereafter, tissue hypersensitivity to tuberculoprotein develops, and with this there is acute inflammation, and lastly, necrosis, and caseation. If the spread and multiplication of the bacilli is restrained by the forces of immunity, the development of tissue hypersensitivity is slight.

The character of a tuberculous lesion is therefore largely dependent upon the balance of immunity and tissue hypersensitivity present. The other factor is, of course, the number and virulence of the invading bacilli. With this last factor a constant, circumscribed, rapidly encapsulated lesion should be regarded as an indication of high immunity and low tissue hypersensitivity; while spreading, destructive lesions are dependent upon a low immunity and high tissue hypersensitivity. Lesions midway between these two extremes are dependent upon the varying balance of these two factors.

The therapeutic indications based on this

concept of the pathogenesis of tuberculous lesions are obvious. The invading bacilli may be attacked by the chemotherapeutic and antibiotic agents which have a specific action on the tubercle bacillus. All possible efforts should be made to achieve any possible enhancement of immunity and the fatal tissue hypersensitivity should be abolished. This latter can be done only be desensitization with tuberculin.

It is quite probable that allergy may play an equal role in other forms of granulomatous uveitis, although this is as yet unproved.

DIAGNOSIS OF OCULAR ALLERGY

The diagnosis of an allergic ocular disorder depends upon two basic points, the recognition of the probability of a hypersensitive state being concerned in the clinical picture and the proof of an underlying specific hypersensitivity.

The recognition of the probable existence of hypersensitive reactions begins with the history, which often suggests an underlying allergy, the realization that the clinical picture is similar or compatible with an allergic reaction, and the elimination of other manifest causes for the ocular disease—bacterial infection, metabolic disorders, degenerations, and so forth.

The proof of a specific hypersensitivity depends upon the demonstration of an increased cutaneous or ocular reactivity to nonbacterial or bacterial allergens.

The cutaneous reactivity is demonstrated by either the patch or the intracutaneous test. The latter is preferable in as much as it permits exact dosage, and an accurate determination of the degree of reactivity. The intracutaneous test consists in the injection of 0.05 cc. or 0.1 cc. of the various allergens, in varying concentration, in the superficial layers of the skin, raising a small bleb slightly less than the size of a dime. The tests are read at the end of 15 minutes for an immediate anaphylactic reaction, and at the end of 48

hours for the delayed tuberculin-type of reaction.

Increased ocular reactivity is determined by the ophthalmic test. This is, however, neither as simple, conclusive, nor as safe as it first appears, for the local reaction following the direct instillation of a specific allergen in the conjunctival sac may be of such severity that the eye may be permanently damaged. It is therefore doubtful if this diagnostic procedure is justified except in rare instances.

The technique of the ophthalmic test is as follows. An extremely dilute mixture of the allergen is first used (a 1:100 dilution of the dose causing a cutaneous reaction.) One drop is instilled in the conjunctival sac. The patient is instructed to keep his eyes gently closed to facilitate absorption. With the airborne allergens, where the hypersensitivity is of the anaphylactic or pollen type, the reaction is an immediate one, comes on within 15 minutes, and is usually limited to conjunctival erythema.

If the instillation of the weak dilution gives no reaction, the test may be repeated at the end of one-half hour, using a 10 times stronger dilution. Stronger dilutions than a 1:10 dilution of the strength producing a skin reaction should not be used.

If a positive reaction is obtained, manifested by conjunctival congestion, lacrimation, secretion, and so forth, the eye should be immediately and thoroughly washed out with saline and epinephrine hydrochloride should be instilled. With the bacterial allergens where the hypersensitivity is the delayed tuberculin type, any reaction is delayed and comes on only after 24 to 48 hours.

A positive reaction to bacterial antigens may be characterized not only by the erythema and edema, but even by phlyctenules and marginal corneal ulcers. If the test is negative, one is never sure that a sufficient concentration of the bacterial antigen was used, or if absorption took place. Thus negative tests are inconclusive, and positive tests may be disastrous. It is therefore more than

questionable if the direct introduction of bacterial antigens in a suspected hypersensitive conjunctival sac is ever warranted.

When one considers the vast number of protein compounds, air-borne allergens, drug compounds, and bacterial fractions to which an organism may become hypersensitive, the complexity of the diagnostic problem is at once evident. There are, however, certain broad clinical principles on ocular hypersensitivity which may be emphasized.

Primarily there is no evidence that food allergy plays any role in the production of any form of ocular allergy. Patients may be found hypersensitive to wheat, in whom the instillation of the most minute amount of wheat or flour in the conjunctival sac causes the most violent reaction. Such patients do not, however, as a rule develop ocular symptoms after the ingestion of bread, pastry, flour, and so forth. It is reasonably clear that actual contact of the sensitized conjunctiva with the specific allergen is necessary to cause an ocular reaction. This limits the field to the air-borne allergens, the organ-specific tissue extracts, and the bacterial antigens.

I. AIR-BORNE ALLERGENS

The most important air-borne allergens usually incriminated in allergic conjunctivitis are the spores, pollens, inhalants, including house dust and animal dander. In the routine testing of any patient, the tests may be extended to include usual groups of common foods. In actual practice, the various allergens are divided into groups, each containing from 5 to 24 component members. There are some 14 of these groups.

All these various allergens used for testing are standardized on their protein-nitrogen-base content and are diluted to the proper concentration for testing. The spores (Group I) are used in three concentrations: 1:1,000, 1:100, and 1:10. The rare tree pollens (Group II—ash, poplar, and so forth) and the rare grass pollens, (Group III—Bermuda grass, and so forth) are used

1:1,000, 1:100, and 1:10. The epidermals and inhalants (Group IV), of which there are 18 components (black flag, camel hair, cat hair, feathers, cow epidermal, dog hair, stock dust, goat epidermal, horse dander, kapok, orris root, rabbit hair, sheep wool, cotton seed [1:1,000], flaxseed [1:1,000], silk, rayon, tobacco), are used in concentrations 1:100 and 1:10. Groups 5 to 11 and 15 are all foods, vegetables, fruits, grains, dairy products, meats, fish, and common foods. These are all used 1:10 in intracutaneous testing. The nuts (Group 11) are used 1:100 and 1:10. All these allergens, spores, pollens, epidermals, and inhalants, various foods and nuts, are read for the immediate anaphylactic or pollen type of reaction.

II. ORGAN SPECIFIC TISSUE EXTRACTS

A. Uveal pigment. Uveal pigment is not available commercially. It is prepared as follows from fresh beef eyes obtained at a slaughter house. The eyes are scalded and clipped free of adventitious tissue. Under aseptic precautions the cornea is clipped away, the eye opened by a sagittal section, the lens expressed, the retina removed, and the uveal tract dissected out *in toto.*

The uveal tracts of several eyes are then ground in a sterile mortar with salt solution and broken glass until all the pigment has been ground from the tissue. This pigment-containing water is then decanted, precipitated with 50-percent ammonium sulphate, the pigment thrown down and removed by centrifugation. This is then washed six times in sterile distilled water and finally taken up in normal salt solution, 5.0 cc. of salt solution to each uvea. This gives a 0.5-percent pigment concentration. Tricresol (0.5 percent) is then added as a preservative.

The cutaneous sensitivity is determined by injecting 0.1 cc. of the pigment suspension intracutaneously. The site of injection is then read for erythema and induration at the end of 30 minutes and 1, 2, 24, and 48 hours. In a positive reaction there is often a visible

macroscopic cutaneous reaction at the end of one hour and 24 hours. The pigment is so slowly absorbed that this dermal reaction may be inconspicuous.

The diagnosis of a positive reaction is usually made by histologic study of the excised skin. At the end of two weeks the bit of skin containing the ·pigment is excised and sectioned for microscopic study. The microscopic appearance of a positive reaction is striking. The tissue is densely infiltrated with lymphocytes, epithelioid cells, and giant cells, and practically all the pigment is phagocytosed by the epithelioid and giant cells. In a negative reaction, the pigment is inertly distributed throughout the dermis, without cellular reaction or cellular invasion of the tissue.

B. Lens protein. Lens protein for testing and treatment is not available commercially. It is prepared as follows. Beef eyes are obtained from the slaughter house. Under aseptic conditions the lenses are extracted. The lenses are immediately taken up in one-hundredth normal NH_4OH, with 0.5-percent tricresol added, 20 cc. to each lens. These are then shaken 24 hours with broken glass, the gross particles removed by centrifugation and passed through a coarse (B) Berke-feld filter. A specimen of the filtrate is then dehydrated at 104° C. and the total solids are determined. The balance of the filtrate is then adjusted to 2-percent concentration of lens protein and 0.85-percent NaCl by adding distilled water and 10-percent NaCl solution.

The cutaneous sensitivity is determined by the injection of 0.1 cc. of the 2-percent solution intracutaneously. The test is read at 1 hour, at 24, and at 48 hours. Theoretically, the reaction should be an immediate one, but lens protein is such a weak antigen that the reaction is usually of the delayed type. As a control, 0.1 cc. of 0.5-percent tricresol in salt solution is used.

III. BACTERIAL ANTIGENS

When the infinite number of bacteria to which mankind is continually exposed is con-sidered, and the number of antigenically distinct strains which exist for many organisms, it is manifestly impossible to examine for hypersensitivity to all bacteria, or completely to exclude bacterial hypersensitivity in any given case. All that is practical is to examine for hypersensitivity to what appear to be the most important organisms, and when hypersensitivity is found, to determine, when indicated, the specific strain responsible for the sensitivity.

In inflammations of the external eye, where the hypersensitivity is certainly the result of contact with air-borne bacteria, the most important organisms are the staphylococcus, and to a less degree the streptococcus. In uveitis, the hypersensitivity is the result of contact of the uveal tract with organism in the blood stream. In the non-granulomatous disease, the most important organisms are the streptococcus, and to a less extent the gonococcus. In the granulomatous form the most important organisms are the Mycobacterium tuberculosis and Brucella. With these various organisms there are certain basic immunologic and bacterial concepts which should be remembered.

A. Staphylococci. The diagnosis of hypersensitivity to staphylococci or their products is determined by use of the staphylococcus toxin or toxoid. Staphylococcus toxin is prepared by growing a toxin-producing strain of staphyloccus in hormone bouillon for 10 days at 37°C. Tricresol (0.5 percent) is then added, the culture is centrifuged, and the supernatant fluid is filtered through a Berke-feld V filter. The toxoid is prepared by growing the staphylococci on semisolid agar under partial carbon-dioxide tension, and the filtrate is detoxified with formaldehyde.

The toxin and toxoid further differ in that the toxin contains no rabbit erythrocyte hemolysin or dermonecrotizing factor and is not lethal for young rabbits but is highly toxic for older rabbits. The toxoid contains these factors and is moderately toxic for rabbits of any age. Both filtrates produce, in horses, serums which are equally effective

in neutralizing the lethal effects of toxin in rabbits. The toxin is not usually available commercially, while the toxoid is so available. Both have equal therapeutic effects in man.

The cutaneous hypersensitivity is determined by the injection of 0.1 cc. of a 1:100 dilution of the toxin intracutaneously, and by the later injection of a similar amount of a 1:1,000 or 1:10 dilution, depending on whether the first injection gave a positive or a negative result. The reaction is of the delayed tuberculin type, coming on from 24 to 48 hours after the test injection. A reaction of 3 by 3 cm. to the 1:100 dilution is regarded as the usual reaction in a normal individual. Reactions greater than this, or similar reactions to a 1:1,000 dilution are regarded as indicative of hypersensitivity.

Individuals with this hypersensitivity appear peculiarly susceptible to contact with toxin-producing staphylococcus, the mechanism of local infection appearing to be an antigen-antibody reaction. Such hypersensitive individuals may be protected by repeated injections of the staphylococcus toxin (or toxoid), the injections being repeated with stronger dilutions until the individual is nonreactive. Whether this is a desensitization process or an active immunization is not clear—it is probably the former. The toxin prepared from any strong toxin-producing organism gives this protective reaction not only against toxin-producing strains, but also against the nontoxin-producing albus strains and against the pus-producing strains.

B. Streptococci. The situation as concerns the streptococci is far more complex and there is no individual strain or universal toxin which permits a quick and easy manner of determining streptococcus sensitivity. The streptococci are generally divided into the alpha, beta, and gamma types on the basis of their hemolysis. The alpha streptococci produce a greenish discoloration and partial hemolysis on blood agar plates. This group includes the Str. pyogenes, Str. viridans, some four or more other strains of a relative low-grade pathogenicity for man. The

beta produces clear hemolysis on blood agar plates and contains most of the human pathogens. The gamma group gives no hemolysis, and the streptococci of this group are rarely pathogenic for man.

The beta group is subdivided into various subgroups, A, B, C, D, E, F, G, H, and K, on the basis of different antigenic action. Each subgroup has a common polysaccharide, but the individual strains differ in their bacterial body proteins.

The "A" group is by far the most important and contains most of the streptococci pathogenic for man. The various strains in this group differ in acid-soluble proteins known as the "M" and "T" substances. The nature of this "M" and "T" substance determines the individual antigenic action. In the "A" group of the beta streptococci are now 42 known pathogens for man, all antigenically distinct.

The B, D, E, H, and K groups are only rarely pathogenic for man. The "F" group is the minute beta staphylococcus. There are a few pathogens in the "C" group, probably closely related antigenically. There also appear to be a few low-grade pathogens for man in the "G" group, probably related antigenically.

Thus the complexity of demonstrating a specific hypersensitivity to streptococci is apparent. Such a sensitivity must finally be determined by intracutaneous tests with the individual strains. In actual practice the following are the minimum number of test vaccines which should be used: Alpha streptococci, one strain; Beta streptococci—subgroup A, all 42 strains; subgroup C, one strain; subgroup F, one strain; subgroup G, one strain; Gamma streptococci, one strain. If desired, the study may be further extended by the use of additional strains of the Alpha, representatives of the subgroups B, D, E, H, and K of the Betas and by additional pathogens from the Gamma group.

The test vaccines are prepared as follows: Organisms of each strain are grown for 24 hours on trypticase soy broth, are killed.

washed to remove traces of the broth or any exotoxin, taken up in salt solution, a preservative added, and the density of the vaccine standardized to the desired concentration on a spectrophotometer.

In actual practice it has been found that the optimum concentration of a test vaccine for individual strains is a 1:10 dilution of T-50, or approximately T-5. In higher concentrations the protein content is so great that nonspecific reactions may be elicited. The patient is tested intracutaneously with 0.1 cc. of each of the 42 strains of the "A" group and one representative of the B, C, D, F, and G groups. The tests are read at the end of 48 hours.

As a short cut to determine sensitivity to the 42 individual "A" strains, four master mixtures are sometimes used. These master mixtures each contain 10 or 11 individual strains. The concentration is adjusted to a 1:10 dilution of T-50 and the patient tested intracutaneously with each master mixture. The mixture to which the patient gives the strongest reactions is noted, and the patient is then tested out similarly to each of the component members of this master mixture.

The weakness of using such master strains is that the combination of individual strains lowers the concentration of each strain to such a point it may be too low to elicit reactions. If the individual strains are used in higher concentrations to compensate for this dilution, the resulting protein content of the master mixture may be so high that nonspecific reactions result.

In the interpretation of results, it should be remembered that, since exposure and infection with streptococci is more or less frequent in all patients, undue consideration should not be given to weak reactions, and a test vaccine should not be used in too great concentrations.

C. Gonococcus vaccine

The antigenic structure of the gonococci is largely unknown. There are probably two main types with different but probably related antigenic properties. These two strains are supposed to occur respectively in acute infections (Type I) and in chronic infections (Type II). Between these two extremes may be a number of intermediates, containing antigenic fractions common to both main types. Further, there is some evidence that the nucleoproteins of the gonococcus resemble those of other Gram-negative cocci, and the polysaccharide fraction is related to the polysaccharide fraction of Type III pneumococci. Thus the complexity of the problem is evident, and the difficulty of establishing a specific hypersensitivity is likewise apparent.

In routine testing with vaccines prepared from gonococci, if Type I and Type II are available, the patient may be tested with each strain. Probably equally significant results are obtained by the use of any single strain. For diagnostic use the vaccines should be prepared in the concentration which gives the most specific readings. This concentration is usually about T-50. The vaccine is preserved with 0.5 tricresol. The test injections are made in the forearm, 0.1 cc. of vaccine being injected intracutaneously with a proper saline control containing 0.5-percent tricresol. The tests are read in 15 minutes for the immediate anaphylactic type reaction to the polysaccharide or hapten group and at the end of 24 and 48 hours for the delayed tuberculin type reaction to the bacterial body protein.

D. Organisms from a focus of infection

The probable relationship of remote foci of infection to endogenous ocular disease has long been recognized. The mechanism through which a focus of infection produces inflammatory changes in a remote tissue or organ has been a subject of considerable controversy. It is now generally assumed that the probable mechanism is through bacterial hypersensitivity, the remote tissue or organ becoming sensitized to the organisms from the focus of infection, and intoxication resulting from absorption of the soluble bacterial products from the focus.

The only means of demonstrating such a

hypersensitivity is by determining the bacterial flora of the infected focus, selecting such organisms as appear suspicious, and testing the patient's cutaneous sensitivity to these organisms.

Test vaccines should thus be prepared from suspicious organisms cultivated from a focus of infection. Organisms other than streptococci are probably best used in a T-50 concentration, and the streptococci in a 1:10 dilution of the T-50. The test dose is 0.1 cc. intracutaneously with proper controls. Lacking definite information of the antigenic action of such organisms, the tests should be read at the end of 15 minutes for an immediate reaction, and at the end of 48 hours for the delayed reaction.

E. Other organisms

The other common pathogens appear relatively unimportant in the production of a bacterial hypersensitivity of the eye, although their possible role in the production of allergic ocular reactions has not been adequately explored. A specific sensitivity for pneumococci is difficult to determine, since the specificity is determined by the polysaccharide fraction, and to date at least 70 or more antigenically distinct strains have been isolated. The delayed reaction to the protein fraction of the pneumococcus is not type specific.

There has been some circumstantial evidence produced incriminating the coliform bacilli in uveitis. It has been shown that the colon bacteria produce in culture media a toxic substance which has an irritative action on the uveal tract. There is, however, no evidence yet adduced of a hypersensitive state to the coliform organism in patients with uveitis, or the importance of such a hypothetical hypersensitivity.

There is little or no evidence that other bacteria or bacterial products, H. influenzae, and so forth, are concerned with endogenous ocular disease, although it is highly probable that many other heretofore unsuspected strains of bacteria, as well as filterable viruses, may ultimately be incriminated in

both nongranulomatous and granulomatous uveitis.

F. Tuberculin

Cutaneous hypersensitivity to tuberculin may be determined either by old tuberculin or by the Purified Protein Derivative (P.P.D.). The technique of the intracutaneous test (Mantoux) is as follows:

a. Old tuberculin. Three intracutaneous injections of O.T., with one saline control, are made.

Right forearm (upper) Control—0.1 cc. normal saline with preservative
(lower) 0.001 mg. O.T. (0.1 cc. O.T.—1:100,000 dilution)
Left forearm (upper) 0.01 mg. O.T. (0.1 cc. O.T. —1:10,000 dilution)
(lower) 0.1 mg. O.T. (0.1 cc. O.T. —1:1,000 dilution)

If there is no reaction to 0.1 mg. after 48 hours, 0.1 cc. of O.T. (1:100 dilution) is given. This represents an intracutaneous dose of 1.0 mg. If there is no reaction, the patient is considered insensitive to tuberculin. If the patient shows a strong reaction to the test dose of 0.001 mg., the test is repeated with 0.0001 mg. (0.1 cc. of dilution— 1:1,000,000) to determine the limit of extreme hypersensitivity.

b. Purified Protein Derivative. The P.P.D. comes in two vials. Vial No. 1 contains 0.0002 mg. P.P.D. to the cc.; vial No. 2 contains 0.05 mg. P.P.D. to the cc. The intracutaneous dose is 0.1 cc. of these two strengths, the equivalent of 0.004 mg. O.T. and 1.0 mg. O.T. respectively. If the patient reacts to strength No. 1, he is considered highly sensitive, if only to test No. 2, as slightly sensitive, if negative to vial No 2, as insensitive.

In the interpretation of the cutaneous reactivity to tuberculin the following fact must be borne in mind. If the cutaneous sensitivity is high, the ocular sensitivity must likewise be considered as high, since the ocular tissues participate in any generalized hypersensitivity. However, it has been clearly demonstrated experimentally that there can be active tuberculous disease in the eye with high ocular reactivity to P.P.D., while the

cutaneous sensitivity is low. The probable reason for this is that, in the absence of other tuberculous lesions, a tuberculous lesion within the scleral envelope is insufficient to influence the cutaneous reactivity to any appreciable degree. Another possible explanation would be that the increased vascularity in the eye, produced by the local lesion, may be responsible for the increased local reactivity. These two explanations are of academic interest rather than clinical importance.

G. BRUCELLA

The diagnosis of chronic brucellosis can be made only on an evaluation of a number of factors. These are the history, the present symptomatology, the exclusion of other etiologic factors, the presence of certain immunologic tests—the agglutination reaction, the complement fixation reaction to Brucella antigens, the opsonocytophagic index against living Brucella organisms, and the cutaneous reactivity to Brucella bacterial fractions. Table 1 from Huddleson gives a summary of the usual interpretation of these serologic reactions:

chronic brucellosis—nummular keratitis and recurrent uveitis—occur as a rule rather late in the chronic disease, and occur usually in individuals with a relatively high degree of cutaneous sensitivity. These patients appear to do phenomenally well under vaccine treatment which tends to lessen or abolish the sensitivity at the same time it immunizes.

The cutaneous sensitivity in brucellosis is determined by the intracutaneous injection of either brucellin or brucellergin, preferably the latter. Brucellin is the filtrate of a 20-day-old broth culture of one of the Brucella strains, Br. melitensis, Br. abortus, Br. suis, sterilized and preserved. Brucellergin is the protein nucleate fraction from all three strains. Theoretically, and indeed in practice, brucellergin gives more precise and specific reactions than brucellin.

In actual practice, 0.1 cc. of either brucellin or brucellergin is injected in the flexor surface of the forearm, with proper controls. The reaction is a delayed one of the tuberculin type and is read at the end of 24 and 48 hours. Positive reactions are erythema, edema, and induration from 2 to 10 cm. in

TABLE 1

SUMMARY OF USUAL INTERPRETATIONS OF SEROLOGIC REACTIONS TO BRUCELLA ANTIGENS*

Agglutination Test	Allergic Skin Test	Opsonocytophagic Power to Blood	Status Toward Brucella
—	—	Zero to 20 percent of cells, slight	Susceptible
—	+	Zero to 40 percent of cells, marked	Infected?
+	+	Zero to 40 percent of cells, marked	Infected
—	+	60 to 100 percent of cells, marked	Immune
+	+	60 to 100 percent of cells, marked	Immune

* From Huddleson.

The test for cutaneous sensitivity becomes positive relatively late in the disease, and may be present when the agglutination titer has fallen to zero. Once positive, the cutaneous reactivity may persist for years. The relation of sensitivity to the course and type of the lesions has never been worked out in brucellosis to the same extent it has been in tuberculosis. It is noteworthy, however, that the ocular symptoms associated with

size and may often persist for a period up to 5 to 7 days.

TREATMENT OF ALLERGY OF THE EXTERNAL EYE

The cardinal principles of treatment of external allergic disorders of the eye are (1) isolation, (2) specific desensitization, and (3) adjuvant therapy. If the specific allergen responsible for the hypersensitive re-

action is known, the first objective in treatment is isolation of the patient from the offending allergen. If this is impossible, then specific desensitization must be considered. Adjuvant treatment is the use of local palliative measures, washes to remove secretion and promote cleanliness, weak astringent collyria to control the tearing and prevent secondary infection, the use of various antihistamine preparations to give symptomatic relief in the anaphylactic type of reaction, and the use of beta irradiation to clear up the large follicles of vernal catarrh.

1. ISOLATION

The isolation of the patient from the offending allergen may be sufficient to give complete relief and so avoid the tedious and oft-repeated courses of desensitization. Once the specific compound, pollen, animal dust, feathers, cosmetics, or what not, has been identified, the condition is carefully and fully explained to the patient. It is amazing how often a simple readjustment of life may solve the problem.

Thus the patient sensitive to certain pollens takes his vacation during the local season and moves to another environment where the pollen is not present; a patient sensitive to feathers uses a glass floss or hair pillow, gets rid of the pet canary, and eats, sells, or gives away his chickens; the woman hypersensitive to a face powder or certain cosmetics changes her brand to one of the many free of orris root or such substances; the individual sensitive to cat or horse dander shuns cats and horses as he would the plague. These examples may be multiplied endlessly.

The essence of treatment here is accurate diagnosis—the detection of the offending allergen. With all the various pollens, dusts, epidermals, and so forth, it is evident that this is always difficult, and at times may be impossible. Yet the experienced allergist frequently shows the ingenuity of a Sherlock Holmes, and at times it appears almost

miraculous when the answer is produced. It must be remembered, however, that isolation therapy can be applied only to patients hypersensitive to the air-borne and epidermal allergens. Patients hypersensitive to bacterial allergens have no method of avoiding contact with the common pathogens.

2. SPECIFIC DESENSITIZATION

A. Nonbacterial allergens. Specific desensitization is a long and laborious procedure. Some people may be almost impossible to desensitize. Even when successfully accomplished there is a great tendency for the sensitivity to return, and the successfully desensitized patient must be kept under observation, repeatedly tested for a return of the sensitivity, and treatment instituted either annually, or on recurrence of the cutaneous reactions or symptoms.

Desensitization with the pollens, dusts, inhalants, foods, epidermals, and so forth is primarily the problem of the allergist. In view of the somewhat unsatifscatory results of such desensitization therapy in the treatment of external ocular allergy, the ophthalmologist and internist are probably wisest to advise desensitization only when the condition cannot be controlled by isolation and the adjuvant therapy of local washes, collyria, and antihistamine drugs.

If desensitization with the spores, pollens, inhalants, or even the foods is indicated, the general principle is to make up the desensitizing extract in a strength so that the initial dose (0.1 cc.) contains each of the various antigens to which the patient reacted, in a maximum of one hundredth or one thousandth the dose producing a cutaneous reaction.

Thus, for a patient reacting to 0.1 cc. of a 1:1,000 giant ragweed dilution, 1:100 Bermuda grass, and 1:10 orchard grass, the desensitizing treatment extract would contain these allergens in such strength that 0.1 cc. of the treatment vaccine would contain the equivalent contained in 0.1 cc. of a

1:100,000 dilution of giant ragweed, of a 1:10,000 dilution of Bermuda grass, and a 1:1,000 dilution of orchard grass. However, there is often no parallelism between the cutaneous and systemic reactivity of the patient to the allergens, and it is essential that there be no constitutional reaction to either the initial or to subsequent injections. Therefore, in the case of some individuals, the initial dose may be 1:10,000 or occasionally 1:100,000 of the test cutaneous dose.

The initial dose of the mixed allergens is 0.1 cc. The injections are given subcutaneously every four days and increased 0.1 cc. at each dose until a dose of 0.9 cc. is reached. A dilution 10 times the strength of the original preparation is then used, the initial dose again being 0.1 cc. and again is increased to 0.9 cc. when a 10 times stronger dilution is used. This is repeated until a concentration 100 times, and occasionally 1,000 times, the concentration of the original mixture is attained. After a dose of 0.9 cc. of the highest concentration is reached, this dose should be repeated first at weekly intervals, and then at biweekly intervals for an indefinite period, even years. Certainly this maintenance dose should be repeated as long as there is any suggestion of symptoms or activity; otherwise the sensitivity will almost certainly return.

B. Bacterial allergens. The question of desensitization with bacterial extracts and vaccines is quite different from desensitization with air-borne allergens. In bacterial hypersensitivity, isolation from the incriminated bacteria is usually impossible, and the physician has little else to offer the patient except desensitization and some adjuvant therapy. Desensitization in bacterial hypersensitivity should therefore be advised when palliative or adjuvant therapy is insufficient, when the severity of the ocular condition justifies such treatment, and when the promise of success is insufficiently great to make the effort worthwhile.

There are two allergic conditions of the external eye which fulfill these criteria. These are the dry irritative conjunctivitis associated with staphylococcus-toxin hypersensitivity and phlyctenulosis associated with tuberculin hypersensitivity. The use of other bacterial fractions or vaccines in other forms of allergic conjunctivitis or keratoconjunctivitis is of too uncertain outcome to warrant their use unless the disease is of unusual severity and all other possible methods of therapy have been exhausted.

STAPHYLOCOCCUS TOXIN. Desensitization with staphylococcus toxin is accomplished by the repeated intracutaneous injection of the toxin. In patients with an initial reaction not over 8 by 8 cm. to the 1:100 dilution, the 1:100 dilution is the first strength used. If the patient reacts definitely to the 1:1,000 dilution, or gives a greater than 8 by 8 cm. reaction to the 1:100 dilution, a weaker dilution (1:1,000) is used for the initial treatment. A dose of 0.1 cc. of the first dilution is given every four days until the patient no longer gives repeated reactions to this amount. The strength is then increased to the next stronger dilution—1:10 or 1:100 as the case may be, until again the patient no longer reacts to the injection.

Thus, the strength of the toxin is increased and treatment continued until the patient tolerates 0.1 cc. of a 1:10 dilution, or in exceptional cases to 0.1 cc. of the pure toxin without reaction. This is regarded as the final point of desensitization.

A patient may react violently to one injection, and later injections give only a minimal effect. After the point of desensitization is reached, a weekly dosage of 0.1 cc. of the 1:10 dilution should be given at weekly intervals for a period of at least six months to maintain desensitization and prevent the recurrence of the sensitivity which otherwise so often occurs.

PHLYCTENULES WITH TUBERCULIN. The treatment of phlyctenules with tuberculin is identical with the treatment of tuberculous uveitis with the same agent and is discussed below.

3. ADJUVANT THERAPY

A. Local washes and collyria. In allergic

reactions of the external eye there is frequently a good deal of lacrimal secretion and discharge. The object of washes is to cleanse the eye and prevent the matting of the lashes with the dried secretion. This is best accomplished by the use of bland washes, warm physiologic saline, or warmed 2-percent boric-acid solution. The dried crusts along the lids may be removed by gently swabbing the lid margins with a cotton swab moistened in the wash. If the crusts are adherent, they may be readily loosened by moistening the lid margins with a saturated solution of bicarbonate of soda. The secretion and congestion may be partially controlled by the use of an astringent collyrium containing also a small amount of epinephrine hydrochloride.

B. *Antihistamine therapy.* The toxic symptoms of the anaphylactic reaction are quite similar to those caused by histamine. The reaction is therefore usually considered due to the liberation of histamine or a histaminelike substance which acts directly on the fixed cells. The obvious direct therapy would therefore be the use of drugs which would either neutralize or prevent the toxic action of the histamine or histaminelike substance.

In 1937, drugs with such an antihistamine action were isolated in the Pasteur Institute in Paris, but they were too toxic for human use. Later derivatives were prepared which had a diminished toxic action. Since then, pharmacologists in France, Switzerland, and this country have improved and modified these early antihistaminic drugs with the result that there are now available at least eight such preparations—Benadryl, Pyribenzamine, Hydryllin, Histadyl, Thenylen, Theophain, Neo-Antergan, and Antistine. Most of these compounds have the same general chemical structure, the basic radical being either two phenyl rings, or a benzyl, an pyridyl, a thiodiphenyl, or a thiophenyl group.

Experimentally it has been found that these antihistaminic drugs prevent the action of histamine in contracting smooth muscle, inhibit the fatal effect of lethal doses of histamine in guinea pigs, diminish the pressor action of histamine on blood pressure, prevent or decrease the capillary permeability which normally follows the absorption of histamine, reduces the urticarial whealing which follows the intracutaneous injection of histamine, and are more active in preventing anaphylactic shock than are comparable doses of papaverin and epinephrine.

The antihistamines all have a definite anesthetic action; thus Antergan is 3.3., Benadryl 2.5., Antistine 1.5 times as effective as similar strengths of procaine.

Clinical investigations have shown that these antihistamines are of great value in the control of skin irritability, urticaria, the itching which accompanies dermatitis of various types, the skin eruptions which often follow sulfonamides, antibiotics, and organic extracts, and the nasal and ocular symptoms of hay fever and perennial rhinitis. The results in the treatment of bronchial asthma and asthmatic bronchitis have not been too favorable. Hydryllin (a combination of Benadryl and Amnophyllin) and Neo-Antergan have been the most effective in this regard.

There may be various unpleasant side effects with these drugs. Chief of these are drowsiness, dizziness, weakness, tremor, headache, nausea, diarrhea, anorexia, and so forth. It is notable, however, that different drugs react differently in different individuals, both as concerns therapeutic effect, and unpleasant side reactions. It is therefore possible, in any given case, to switch from one preparation to another, seeking the preparation that in the individual patient will give the maximum of therapy combined with the minimum of side effects.

The doses of these various antihistamines vary from 25 to 500 mg. daily for adults, the average effective dose being 50 mg., 3 to 4 times daily. The drugs can be applied topically, in solutions or ointments.

The manner whereby these antihistaminic drugs counteract the action of histamine is not fully understood. Certainly it does not appear to be a direct neutralization or detoxification of histamine, or a prevention of the

antigen-antibody union which leads to the liberation of histamine. Rather, it appears that the antihistaminic drugs are absorbed at the site of action of histamine and so prevent or diminish the absorption or action of histamine on the same cells. In other words, these drugs compete with histamine for position in the target cells, and by occupying these cells block off the absorption and resultant action of histamine.

The effect of the antihistamine drugs in the anaphylactic and pollen types of hypersensitivity has been fairly well established. Little or nothing is, as yet, known of any deterrent action these drugs may exert in allergic reactions resulting from bacterial type of hypersensitivity. It may well be that they may influence profoundly the basic allergic reaction of nongranulomatous uveitis, or depress the inflammatory, caseating reaction in granulomatous uveitis. There is, as yet neither experimental nor clinical evidence of this. There is, however, sufficient evidence to indicate the use of these compounds in external ocular allergy of the anaphylactic type.

In the first two types of allergic conjunctivitis—that is, the sudden, edematous type associated with hay fever, and the edematous type of blepharoconjunctivitis associated with drug allergy—the use of antihistamine drugs is clearly indicated. In the hay-fever type, the usual treatment is 50 mg. of Pyribenzamine, three times daily by mouth. The local symptoms are best controlled by an astringent collyrium containing epinephrine hydrochloride. In the greater number of cases both the nasal and ocular symptoms can be well controlled by such treatment.

In the eczematous blepharoconjunctivitis associated with drug reactions, the itching is often intolerable. In addition to the oral administration of antihistamine drugs, the local use of these compounds may be of value. The one most frequently used is Antistine, which comes prepared in a 0.5-percent solution for ophthalmic use. In a number of cases, this gives effective symptomatic relief when all other collyria fail. How much of the relief is due to the anesthetic action of the drugs is, however, difficult to say.

Since little is known of any effect the antihistamine drugs may exert in bacterial hypersensitivity, there is little indication to use the drugs in the conjunctivitis secondary to staphylococcus-toxin sensitivity. Nevertheless, the use of Antistine locally sometimes appears to control the itching and discomfort. It is quite probable that this action may be due to the anesthetic rather than the antihistamine action of the drug.

In the other manifestations of external ocular allergy—phlyctenules, marginal corneal ulcers, vernal catarrh—there appears to be no indication for the use of antihistamine drugs, although the use of Antistine to control the local itching and discomfort, which so often accompanies vernal catarrh, might be worthy of trial.

C. Beta irradiation in vernal catarrh. Excellent results are obtained in both the palpebral and bulbar forms of the vernal conjunctivitis by irradiation with the beta rays of radium. This form of irradiation is applied preferably with the radon beta applicator described first by Burnam. This is, however, obtainable only in large medical centers where there is a large concentration of radium.

In vernal conjunctivitis almost equally good results can be obtained by the use of the flat radium applicator described by Iliff, containing 50 mg. of radium. This is now available commercially. These applicators give off both the beta and the gamma rays. However, the skin erythema dose (H.E.D.) of the beta rays is 18 gram seconds, while the H.E.D. dose of gamma rays is 8 gram minutes. This differential permits the administration of the full therapeutic dosage of beta, 12 gram seconds, while only a minute amount of gamma is given.

The beta rays penetrate tissue only 2 to 3 mm. They have no effect in the irradiated tissues unless absorbed, their zone of action,

therefore, being limited to a depth of 2 to 3 mm. Their action is essentially an ionization or destructive action in the irradiated tissue. However, some tissues are more sensitive than others, especially rapidly proliferating tissues, embryonic tissue, proliferating capillary endothelium, germinal epithelium and certain neoplasms.

This form of irradiation therapy is especially efficacious against the follicles of vernal catarrh and more so against newly formed fresh follicles than against the older organized pavement-stone vegetations. In vernal catarrh, therefore, it is sometimes wiser to excise the older fibrous follicles before irradiation.

If the Iliff applicator is used, a mechanical holder for the applicator is needed on account of the long duration of treatment. While the applicator holds 50 mg., the effective output is only 30 millicuries. The length of exposure needed to obtain any given number of gram seconds is determined by the following formula:

$$\text{No. sec. exposure} = \frac{\text{No. gm. sec. treatment desired} \times 1,000}{\text{millicuries of radon}}$$

Thus, with an effective output of 30 millicuries, and a desired treatment of 12 gram seconds, 6 minutes and 40 seconds exposure is needed:

$$\frac{12 \times 1,000}{30} = 400 \text{ seconds.}$$

In actual practice, the patient is seated comfortably in a reclining chair with a head rest; the eye is anesthetized with 0.5-percent pontocaine solution; the lid to be treated is everted and held with a clamp or hook. The radium applicator, held in a mechanical holder, is then approached to the lid just short of contact, and a treatment of 6 minutes and 40 seconds given. Two areas in the same lid may be treated consecutively. Treatments are not given oftener than every two weeks to avoid any cumulative effect.

With the Burnam applicator, the treatment is much shorter. This applicator may hold as much as 500 millicuries of radon, all of which is effective. The time of exposure is calculated as above. Thus with 500 millicuries in the bulb, only 24 seconds' direct application would be the full therapeutic dose.

With the Burnam applicator, the follicles, of vernal catarrh are best treated by the "spray" method. In this method the applicator is held by hand about 1 to 3 mm. from the conjunctival surface, and moved slowly back and forth over the area to be treated. Since no one area thus receives the full irradiative effect, the exposure time may be safely increased 50 percent, or a total of 18 gram seconds given over the entire lid. Treatment should not be repeated oftener than every second week. In early cases, where the follicles consist of lymphoid cells, young fibroblasts, and blood vessels, 2 or 3 treatments may be sufficient to obtain an almost complete resolution. In more advanced cases where there is a good deal of fibrosis, more prolonged treatment may be needed.

TREATMENT OF ALLERGY OF THE INTERNAL EYE

The allergic reactions of the internal eye are dependent upon a hypersensitivity of the uveal tract either to one of the organ-specific ocular tissues, or to bacteria or bacterial fractions. The treatment of the allergic phase of the disease by desensitization would be in some instances (nongranulomatous uveitis, endophthalmitis phaco-anaphylactica) a direct attack on what is believed to be the actual cause of the disease, seeking to cure the disease and prevent recurrences by removing the cause.

In other instances (granulomatous uveitis, sympathetic ophthalmia) desensitization therapy would be directed only to the removal of the allergic factor which influences unfavorably the course of the disease. The actual cure of the disease would result

only from treatment with antibiotic or chemotherapeutic agents, or the control and destruction of the specific exciting organisms by the normal body defenses.

DESENSITIZATION WITH ORGAN-SPECIFIC TISSUE EXTRACTS

A. Uveal pigment. Parenteral injections of uveal pigment have been employed in the treatment of sympathetic ophthalmia with the idea of abolishing the phase which appears to set the stage for the outbreak of disease and to determine its histologic picture. The obvious criticism of such treatment is that the pigment in its present preparation is highly insoluble, is very slowly absorbed, and that the pigment sensitivity will probably fade spontaneously before it could be affected by parenteral injections. There is much truth to such criticism. Nevertheless, in the over-all picture, the cases of sympathetic ophthalmia so treated do appear to have done somewhat better than might have otherwise been expected, and to have stood later operations more successfully than would ordinarily have been hoped for.

In actual practice, the 0.5-percent standard suspension of uveal pigment is used. The injections are given at four-day intervals, intramuscularly in the buttocks or deltoid. The first injection is 0.5 cc., the second 1.0 cc., then 1.5 cc., 2.0 cc., 2.5 cc., 3.0 cc., 3.5 cc., and 4.0 cc. The 4-cc. dose is repeated at four-day intervals usually for a period of three months, or until the disease appears burned out.

Pigment therapy is accompanied by a marked increase in the opsonocytophagic index for pigment, and there are evidences of a high degree of phagocytosis of pigment in the diseased eyes (excised iris specimens). This may account for its apparent therapeutic action as well as desensitization.

B. Lens protein. Lens protein is a complex antigen, containing at least two organ-specific globulin fractions and one albumin fraction. It is an excessively weak antigen and, even in heterogenous species of animals, specific

antibodies are produced only with great difficulty. For that reason, in therapy with lens protein, the principle of synergistic action of antigens has been employed. This consists in combining the weak specific antigen with a stronger nonspecific antigen in order to enhance the antigenic action of the weak antigen.

In actual practice in order to desensitize a patient found hypersensitive to lens protein, a mixture of lens protein and staphylococcus toxin is used. To 9.9 cc. of the 2-percent lens protein is added 0.1 cc. of undiluted staphylococcus toxin. This gives a 1:100 concentration of toxin in the lens protein. The initial dose is 0.1 cc. given intracutaneously and this dose is repeated every four days, until the patient no longer shows a reaction.

At this point the patient is tested with 0.1 cc. of the 2-percent lens protein solution. If there is no reaction, desensitization is considered accomplished. If there is a reaction to the lens protein, the patient is then tested with a 1:100 dilution of staphylococcus toxin. If negative to this, he is tested with a 1:10 staphylococcus toxin, and finally to straight toxin, until a dose of toxin is found to which he does react.

A new lens protein-staphylococcus mixture is now made up, containing the reactive dose of toxin, and treatment is continued until the patient no longer shows any cutaneous reaction to an injection of lens protein alone. This is regarded as the point of desensitization. The staphylococcus toxin-lens protein is readily absorbed, and desensitization is usually quickly and readily accomplished within 3 to 6 weeks.

DESENSITIZATION WITH BACTERIAL ANTIGENS

The *principle* of desensitization with bacteria or bacterial extracts is (1) the determination, with the greatest possible exactness, of the specific organism responsible for the hypersensitivity; in the case of bacteria with many antigenically distinct strains, this

involves the further determination of the strains involved; (2) the preparation of the vaccine from the proper strains and also from the proper fractions of the antigenic mosaic; (3) the decision of the proper manner of administering the vaccines, intracutaneous, subcutaneous, intramuscular, or intravenous; (4) the careful observation of the patient during the period of treatment, in order that the dose may be kept below the point of reactivity and increased as the reactivity recedes.

The streptococci and gonococci are the important organisms concerned in nongranulomatous uveitis, and the Mycobacterium tuberculosis and Brucella organisms are the important ones in granulomatous uveitis. In syphilis there is no antigen available to determine hypersensitivity to the Treponema pallidum. There are doubtless many more other exciters of granulomatous and nongranulomatous uveitis, but they are either unknown, or there is no means of testing for hypersensitivity to them.

A. *Streptococcus vaccine.* The indications for the use of a streptococcus vaccine are (1) that the clinical condition be a nongranulomatous uveitis; (2) that there are clinical evidences of systemic nongranulomatous disease (rheumatoid arthritis, a chronic focus of infection, and so forth) or a history of a former nongranulomatous infection with some suggestive time relationship to the ocular disease; (3) that other obvious causes for the ocular disease are eliminated; (4) that the bacterial hypersensitivity demonstrated is specific and is greater than shown by normal controls, and not part of a general reaction to all bacterial antigens.

The route of administration of streptococcus vaccine is of great importance. Experimental work indicates that the subcutaneous administration of killed streptococci often tends to increase the tissue hypersensitivity, while the intravenous administration tends to desensitize.

Wainwright utilized this finding in the vaccine treatment of rheumatoid arthritis,

using the intravenous route for the administration of the streptococcus vaccine. This same principle has been followed in the desensitization for nongranulomatous ocular disease. On the basis of the results so far obtainable, all the "successes" have followed this method of administration, while no improvement has been observed after subcutaneous injections. The intravenous administration therefore appears the method of choice with streptococcus antigens.

Since the hypersensitivity produced by streptococci is dependent upon the acid-soluble proteins of the bacterial body, the vaccine must be prepared from the bacterial bodies themselves. The individual strains are grown in broth for 24 hours, the organisms killed by heat, the bacterial bodies thrown by centrifugation, washed in saline to get rid of any trace of broth or exotoxin, and are finally taken up in salt solution, the concentration adjusted to T-50 on the spectrophotometer, 0.5-percent tricresol added, and this stock suspension cultured for sterility.

The first treatment vaccine should contain the organisms in one-tenth the concentration to which the patient reacted intracutaneously. Since the test vaccine was a 1:10 dilution of the stock T-50 concentration, the "first strength" treatment vaccine should be the pooled 1:100 dilutions of the T-50 stock concentrations of the various strains to which the patient reacted. The second strength treatment vaccine is the pooled 1:10 dilutions of the same T-50 stock concentrations, while the third strength is the straight pooled T-50 stock concentrations of the same strains. After the vaccines are prepared 0.5-percent tricresol is added, and the vaccines are tested for sterility.

The first intravenous dose is 0.1 cc. of the "first strength" vaccine. If there is no general reaction (malaise, fever, leukocytosis, and so forth) the dose is repeated at four-day intervals, and increased 0.1 cc. at each injection until 0.9 cc. is reached. The second strength is then similarly administered. This is con-

tinued in a similar manner until the patient receives 0.9 cc. without reaction. The third strength vaccine is now given and the dose then repeated weekly as a maintenance dose.

After the early injections, the patient should be carefully observed, his temperature followed for 24 hours, and a leukocyte count done four hours after the injection. If the patient shows a reaction to the initial dose of 0.1 cc. of the first vaccine preparation, the preparation is then diluted 10 times, and 0.1 cc. *again similarly administered*. Thus there is determined an original dose below the patient's individual point of reactivity. This is then accepted as the proper starting dose, and the dosage thereafter is increased as outlined above. In the event of a general reaction, or focal reaction in the eye being observed during the course of desensitization, the dose is dropped to one-tenth or one one-hundredth the amount given before the general or focal reaction, and again increased from this point.

The question of how long such treatment should be continued is an interesting one. Since this form of therapy has been used in selected cases in the Wilmer Institute of The Johns Hopkins Hospital, several cases have been encountered which showed the same general picture. Prior to the administration of the streptococcus vaccine the patients had had repeated violent attacks of nongranulomatous uveitis. During vaccine therapy they were free from attacks. Within 3 to 6 months after stopping treatment, the attacks recurred, and the sensitivity to the specific streptococci returned. Further treatment was again followed by freedom from attacks. In actual practice, after the point of apparent desensitization has been reached, it would seem wise to continue the treatment at weekly intervals.

B. *Gonococcus vaccine.* The indications for the use of a gonococcus vaccine are that the patient have a recurrent nongranulomatous iritis, which from the history and associated findings appears to be of gonococcal origin, that he also shows a cutaneous hypersensitivity to gonococci, and that other methods of treatment have been inefficacious in controlling the inflammation or curtailing attacks.

The best route of administration, subcutaneous or intravenous, is unknown. In view of this uncertainty, the wisest course is to adopt the simplest method and administer the vaccine subcutaneously.

The vaccine for treatment should be prepared from the type to which the patient showed the greatest reaction. Commercial stock vaccines may be used if the patient shows an equal sensitivity to them. The original concentration of a prepared vaccine should be one tenth of that to which he showed a cutaneous reactivity. The original dose is 0.1 cc. The injection should be given every third or fourth day, and increased in the usual manner until a dose of 0.5 cc. of a T-500 concentration is reached. A small group of such cases treated in this manner have shown a favorable course. This is all that can be said.

C. *Other organisms.* If it is decided to use a vaccine prepared from an organism isolated from a focus of infection in the patient, the vaccine should be prepared as used or described for gonococcus vaccine.

D. *Tuberculin treatment.* Treatment with tuberculin is essentially desensitization therapy. Old tuberculin or one of its many variants is used. Denys' Bouillon Filtrate (D.B.F.), a glycerinated 1:10 dilution of O.T. has certain advantages. Bacillen emulsion is to be avoided on account of the irregularity of dosage that occurs in higher dilution.

For treatment, the D.B.F. is prepared in nine different strengths—No. 1 represents the undilated D.B.F.; No. 2, a 1:10 dilution; No. 3, a 1:100 dilution; No. 4, a 1:1,000 dilution; and so on to No. 9, which is a 1:100,000,000 dilution of the D.B.F., or 0.000,001 mg. to the cc. Thus, 0.1 cc. of the various dilutions represents the following dosages:

Dilution	Dosage
No. 1—straight D.B.F.	0.1 cc. = 100 mg.
No. 2—1:10	0.1 cc. = 10 mg.
No. 3—1:100	0.1 cc. = 1 mg.
No. 4—1:1,000	0.1 cc. = 0.1 mg.
No. 5—1:10,000	0.1 cc. = 0.01 mg.
No. 6—1:100,000	0.1 cc. = 0.001 mg.
No. 7—1:1,000,000	0.1 cc. = 0.0001 mg.
No. 8—1:10,000,000	0.1 cc. = 0.00001 mg.
No. 9—1:100,000,000	0.1 cc. = 0.000001 mg.

In actual practice, the initial dose is usually 0.1 cc. of No. 8. In the extremely sensitive, it is wiser to start with 0.1 cc. of No. 9, or occasionally with a No. 10 dilution. Injections of dilutions 9, 8, 7, 6, and 5 are given twice weekly or at four-day intervals. The initial dose each dilution is 0.1 cc. Subsequent doses are 0.2 cc., 0.3 cc., 0.4 cc., 0.6 cc., and 0.8 cc. When 0.8 cc. of a dilution is reached, the next higher dose is 0.1 cc. of the next higher concentration.

When 0.8 cc. of No. 4 dilution is reached, further injections are given at weekly intervals. The injections numbers 4, 3, and 2 are 0.1 cc., 0.2 cc., 0.3, 0.4 cc., 0.5 cc., 0.6 cc., 0.7 cc., 0.8 cc., 0.9 cc. When a dosage of 0.5 cc. of No. 2 or 50 mg. is reached, the dose is not increased further. This dosage should, however, be repeated at weekly intervals for a minimum period of two years as a maintenance dose to prevent the recurrence of the hypersensitivity which, without maintenance of treatment, is so prone to occur.

During tuberculin treatment the patient should be carefully watched both for local reactions at the site of the injection and focal reactions in the eye. In the case of a local reaction (erythema, induration) of the site of the injection, the dose should be dropped three levels, and increased again when no local reaction is observed. If there is a focal reaction—that is, a lighting up of the inflammatory process in the eye—the dose is dropped to one tenth of that which produced the focal reaction (the dose of the next weakest dilution), is repeated at this level, and is only increased when the focal reaction has subsided.

It should be emphasized that there is no such thing as an absolute dose of tuberculin for any one individual. The essential point of desensitization therapy with tuberculin is to keep the dose beneath the patient's point of reactivity, and to increase the dosage only as the point of reactivity recedes.

D. Brucella vaccine. The three known strains, Br. meletensis, Br. suis, and Br. abortus are certainly all closely related antigenically, all containing varying amounts of identical antigens. They are thus so closely related antigenically that a single vaccine can be used for treatment.

Various preparations have been suggested, the best known being the Brucellin of Huddleson and oxidized vaccine of Foshay.

Brucellin is the mixed clear filtrate of 20-day-old cultures of the known strains. It is administered intracutaneously with the idea of evoking general systemic allergic reactions, and it is considered that 3 to 4 such reactions are necessary to produce any therapeutic effect.

The usual procedure is first to test the patient with an intracutaneous dose of 0.1 cc. of Brucellin. If he does not show a systemic reaction to the dose in four hours, the first treatment dose of 0.5 cc. is given. If the patient does show a systemic reaction to 0.1 cc. this is held as the treatment dose as long as the patient reacts. After the reaction dose is determined, this is repeated at three-day intervals until the patient has had three or more systemic reactions.

Thereafter, the dose is spaced to 15-day intervals and so continued for six months, together with any other supportive treatment (antibiotics, sulfa compounds, and so forth) desired. Advocates of this treatment claim about 25 percent of the chronic cases are benefited. This would appear to be a high figure, and it is somewhat doubtful if the low incidence of improvement warrants the severe systemic reactions entailed.

Various other vaccines, bacterial extracts, and suspensions have been prepared for the

treatment of chronic brucellosis. In the effort to produce a vaccine with a maximal reduction of toxicity and a minimal loss of antigenicity, Foshay has prepared an oxidized Brucella vaccine.

This vaccine is prepared by growing a smooth abortus strain of established antigenicity on solid media or a fortified tryptose broth. The organisms are harvested, killed with formaldehyde, the turbidity adjusted to about T-1,000 in the spectrophotometer, and the organisms then oxidized by taking them up in 30-percent aqueous sodium nitrite, 5 ml. to each 3 ml. of packed bacterial sediment together with 5 ml. of 30-percent acetic acid; the mixture is stored in centrifuge tubes, carefully marked for original volume, and the organisms are thus oxidized 4 to 5 hours at room temperature. Acids and salts are then removed by repeated washings and centrifugation and the oxidized bacteria finally taken up to the original volume in 0.5-percent phenolized saline.

In treatment, four strengths of the vaccine are prepared: T-1, T-5, T-50, and T-500. The initial dose is 0.1 cc. of T-1. The patient is watched carefully for any evidence of systemic reactions. If none are observed, the doses are repeated every second day, and increased 0.1 cc. at each injection until a dose of 0.5 cc. is reached. The concentration of the vaccine is then increased to T-5, and 0.1 cc. is given. This is likewise increased 0.1 cc. at each dose until a dose of 0.9 cc. is reached. The concentration is then increased to T-50, the initial dose is again 0.1 cc., and

it is increased as before until a dose of 0.9 cc. is again reached.

If there have been no reactions, the concentration is increased to T-500 and 0.1 cc. again given. This is increased in like manner until a dose of 0.5 cc. is reached. This is continued twice weekly for two months when the blood should be examined for the opsono-cytophagic index.

In the treatment of patients with chronic ocular brucellosis, the vaccine is always administered with the idea of keeping the dose below the patient's point of reactivity and avoiding all local, focal, or systemic reactions. If there is any systemic or focal reaction at any level, the dose is immediately reduced to one-tenth the amount causing the reaction, and again cautiously given as usual. The treatment is continued until the opsono-cytophagic index shows marked phagocytosis in at least 90 percent of the cells. This development of a high opsonic index is almost invariably accompanied by a diminution in the cutaneous sensitivity.

It is interesting that frequently the patients volunteer the information of improvement in their general health and sense of well being while under treatment. It is not clear whether the local therapeutic effect in the eyes is due to the immunity acquired or produced by the vaccine treatment, or is the result of tissue desensitization. It is interesting, however, that the ocular symptoms have, as a rule, occurred in patients with high degree of cutaneous hypersensitivity.

The Johns Hopkins Hospital(5).

THE OPHTHALMOSCOPIC EVALUATION OF OPTIC ATROPHY*

ALFRED KANT, M.D.

Watertown, New York

A survey of the available literature on the diagnosis of optic atrophy brings forth the familiar triad of symptoms—pallor of the disc, reduced visual acuity, and defects in the visual field. Although, in many cases, these signs permit us to diagnose optic atrophy with a considerable amount of assurance, there remain a number of cases in which they are either not available to us, as in the case of children or others unable to coöperate, or are wholly untrustworthy, as in some cases of retinitis pigmentosa.

In some of these uncertain cases, in spite of all the classical signs and symptoms including the "peculiar waxy atrophy of the disc," subsequent pathologic study has revealed no evidence of atrophy in the nerve even after the use of the myelin-sheath stain.

Most ophthalmologists will admit that the present diagnostic criteria for optic atrophy are inadequate in many cases, with the result that we are frequently forced to play a delaying game, not through any lack of training or thoroughness on our part, but simply because no purely objective method exists for the diagnosis of optic atrophy. It is the purpose of this paper to present a possible method.

Since testing visual acuity and taking visual fields are, in large measure, subjective procedures, we can immediately discount their value. There remains, then, the ophthalmoscopic appearance of the disc. Walsh states that pallor of the discs alone is not evidence of optic atrophy. Adler has summarized the opinions of numerous observers in the following statement, "pallor of the disc may be due to one or all of the following

factors: low hemoglobin content of the blood, diminution in the number of capillaries on the disc, overgrowth of glial fibers and, finally, actual loss of the nerve fibers."

Of these factors, the number of capillaries on the disc facilitate ready and precise ophthalmoscopic evaluation. There are many scattered references throughout the literature pertaining to a loss of capillarity on the disc in optic atrophy but it remained for Kestenbaum, in 1946, to quantitate these small vessels and to point out their possible utility in the diagnosis of primary optic atrophy by what he calls the Kestenbaum capillary number test. To acquaint those not too familiar with this test the following portion of his book is quoted in its entirety:

"In order to set a numerical value on the degree of atrophy, the vessels which pass over the margin of the disc may be counted. One starts at the twelve o'clock point and counts all the vessels crossing the margin, counting separately the arteries, the veins and the small vessels. 'Small vessels' mean the vessels which cannot be recognized as arteries or veins. The number of vessels passing over the margin in normal eyes is fairly constant. Without dilatation of the pupil, usually 9 large vessels (4 or 5 veins and 4 or 5 arteries) and about 10 small vessels can be seen.

"Of course there are many exceptions in normal eyes. Sometimes the arteries and veins branch repeatedly on the disk, so that more than 9 large vessels pass over the disk's edge. In disks with irregular or inverse distribution of the vessels, the number test is also unreliable. In the large majority of cases, however, the arrangement of the vessels is regular enough to permit the use of this test.

"In primary optic atrophy, the number of arteries and veins remain unchanged, but the number of small vessels is diminished to 7, 6 or even less, down to only 3, so that an approximate numerical measure of the degree of pallor is possible. This test may be of value in the observation of the development of the disease." (See Diagram 1.)

This paper does not claim any originality but simply tests the validity of Kestenbaum's conclusions and seeks to extend their usefulness to apply to all cases of optic atrophy from whatever cause.

PROCEDURE

An attempt was made to study all cases of optic atrophy appearing at the out-patient department of the Massachusetts Eye and Ear Infirmary, as well as the house cases on the wards of the Massachusetts General
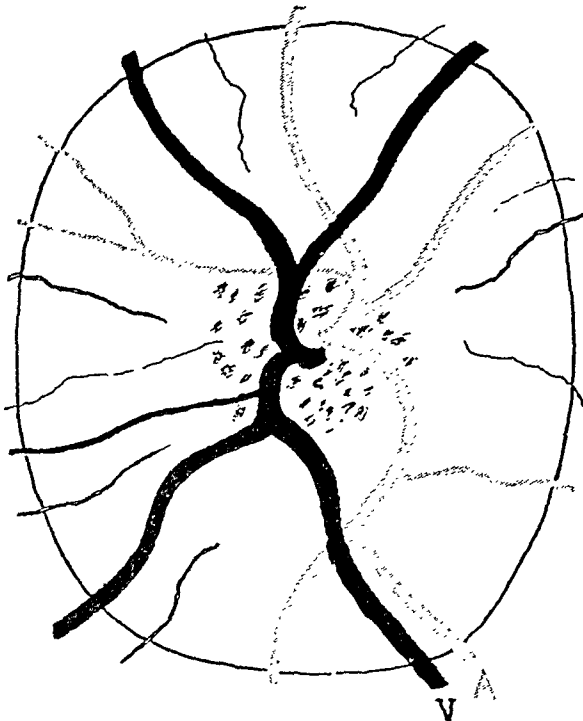
Diagram 1 (Kant). This drawing of the disc shows the "small vessels." Only those vessels which cannot be recognized as arteries or veins are counted.

Hospital for a period of nine months. Only those cases affording a clear view of the disc were utilized.

The small vessels on the disc were counted according to the method elaborated by Kestenbaum. To make the method as simple and practical as possible, an ordinary electric ophthalmoscope was used. The number of vessels counted was recorded and then refraction and fields were done under comparable conditions. A number of normal eyes were similarly studied and recorded.

The patients varied in age from the 1st to the 6th decade. Of the 65 patients examined, 20 were normal and 45 showed atrophy of some type, affording a total of 125 eyes of which 49 were normal and 76 atrophic.

Etiologic study of the atrophic cases showed:

Primary atrophy, cause unknown	7
Neurosyphilis	3
Nasopharyngeal carcinoma	1
Acromegaly	1
Glioma of chiasm	1
Rolandic meningioma	1
Suprasellar cyst	1
Orbital tumor (meningioma)	1
Retrobulbar neuritis, cause unknown	1
Multiple sclerosis	3
Toxic amblyopia	2
Optic neuritis	5
Vascular occlusion	3
Chorioretinitic disease	2
Fuchs's atrophy	1
Birth injury	1
Auto accident	3
Combined systemic disease	1
Glaucoma	7

Columns for visual acuity ranging from nil vision to 20/15 were laid out and the number of small vessels counted in each case was recorded under the appropriate visual acuity found. The tabulated results were averaged giving a mean number of small vessels under each visual acuity.

Similarly, columns representing the number of small vessels from 0 to 14 were laid out. The visual fields were analyzed by means of a polar planimeter for preserved area of field expressed in square centimeters. The results thus found were tabulated under the appropriate column of the number of vessels in each case. The totals were then averaged for each column. For this study, based upon a number of determinations, an approximately full field constituted between 19 to 22 square centimeters.

It was assumed that the number of small vessels on the disc reflected the overall functional integrity of the optic nerve. Practically, in order to evaluate the nerve, we usually consider two things: namely, the central vision, as shown by the visual acuity, and the peripheral vision, as shown by the area of preserved field.

If our assumption is correct—that the number of small vessels on the disc expresses the degree of functional integrity of the nerve or, conversely, indicates the de-

gree of total atrophy present—then the larger the visual field the greater should be the number of small vessels.

Similarly, the higher the visual acuity the greater should be the number of small vessels, provided decreases in visual acuity were part of an overall atrophy and not due to a selective atrophy involving the papillomacular bundle which could cause a drastic reduction in central vision without causing a commensurate loss in peripheral field.

Graph 1 shows the correlation between the number of small vessels and the area of preserved field expressed in square centimeters. The black dots represent the actual values found in the individual cases and the solid black line represents the mean value of area of field. It can readily be seen that a surprisingly direct relationship exists between these two factors.

Graph 2 shows the mean value of ·the number of small vessels counted plotted as a curve against visual acuity. The black dots represent actual values as found and the solid black line indicates the mean value of
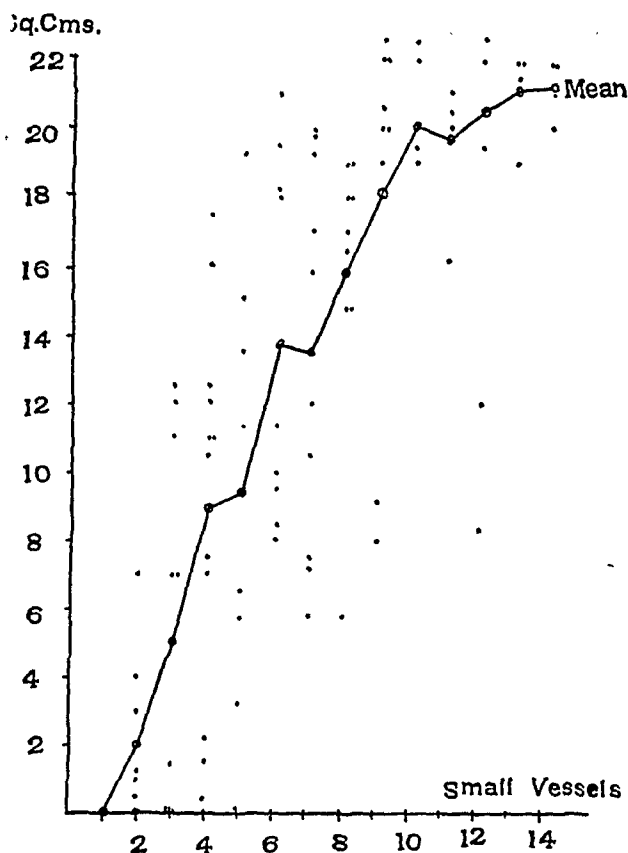
Graph 1 (Kant). Correlation of the size of the visual field to the number of small vessels. The abscissa shows the number of small vessels; the ordinate, the preserved area. A full field is 19 to 22 sq. cm.

| NO. | 4 | 2 | 5 | 6 | 2 | 3 | 3 | 5 | 4 | 13 | 10 | 11 | 24 | 15 | 18 |

Total ~ 125.
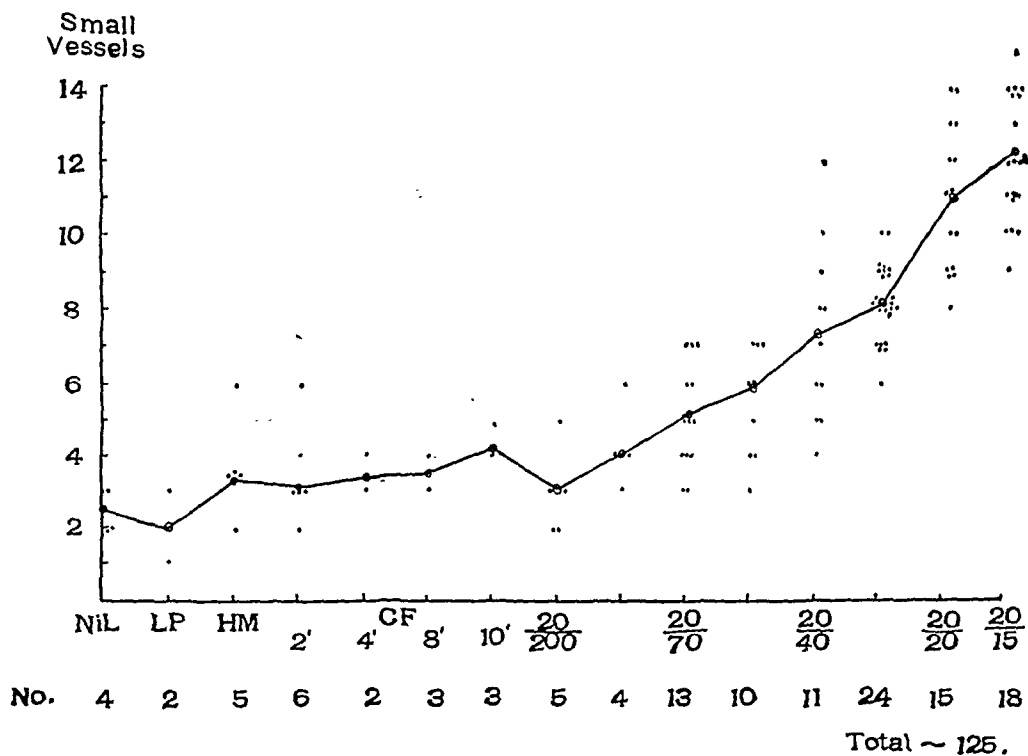
Graph 2 (Kant). Correlation of the visual acuity to the number of small vessels. The abscissa shows the visual acuity; the ordinate, the number of small vessels. Numbers under the acuity listings indicate the number of cases having that acuity.
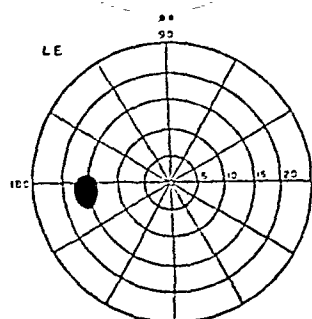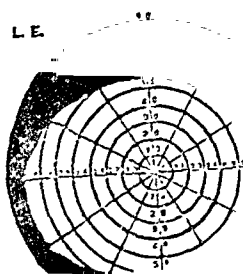
Chart 1. Visual fields for (above) 3/330 white and (below) 1/1,000 white. The patient, a man, aged 35 years, showed 13 small vessels in this eye and had a visual acuity of 20/15 and a field area of 21.5 sq. cm.
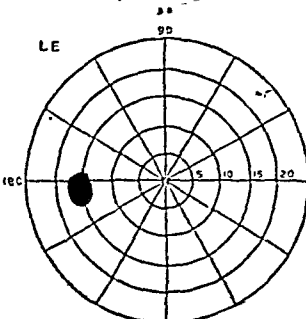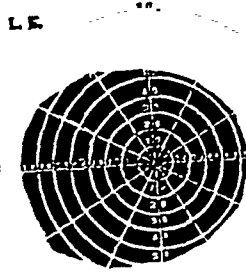
Chart 2. Field studies of the left eye of a boy, aged 10 years (above) for 3/330 while and (below) 1/1,000 white. Visual acuity in this eye was 20/20, the number of small vessels was 12, and the field area, 19.5 sq. cm.
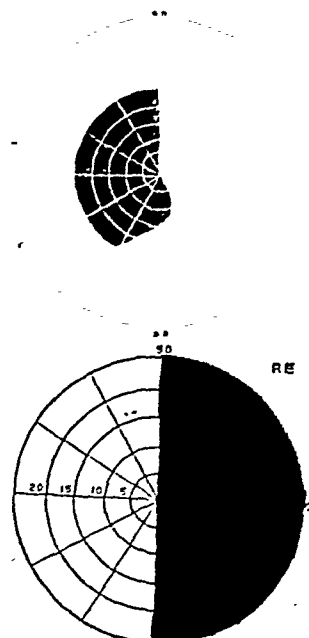
Chart 3. Field studies of the right eye of a boy, aged 16 years for (above) 3/330 white and (below) 1/1,000 and 10/1,000 white. The patient, who had diabetes insipidus, had a visual acuity in this eye of 20/40 + 3. The number of small vessels was five. Field area 5.8 sq. cm.
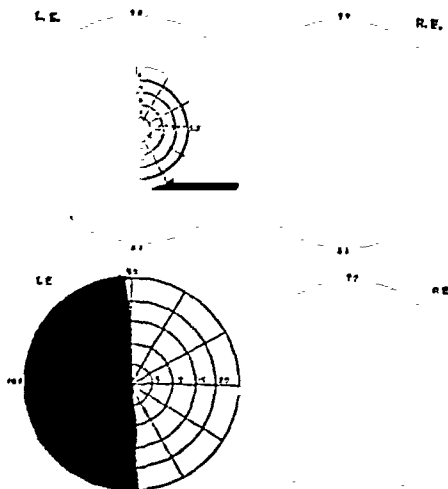
Chart 4. The patient was a woman, aged 30 years, who had 20/20—3 vision in the left eye, which showed eight vessels. The right eye was blind but showed three small vessels. (Above) Field studies for 3/330 white. (Below) Fields for 1/1,000 and 10/1,000 white. Area of field L.E., 7.2 sq. cm.

Charts 1 to 4 (Kant). The visual fields are numbered to correspond with the numbers of the Kodachromes which they illustrate.
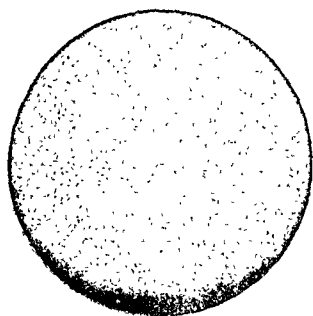
1. NORMAL BLOND.
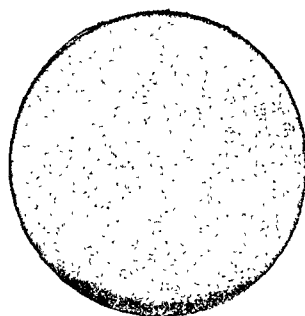
2. PHYSIOLOGIC PALLOR.
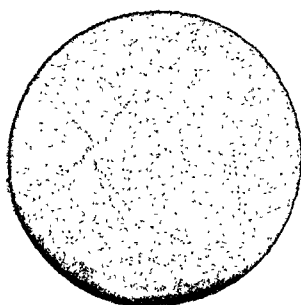
3. POSTTRAUMATIC.

O.S.
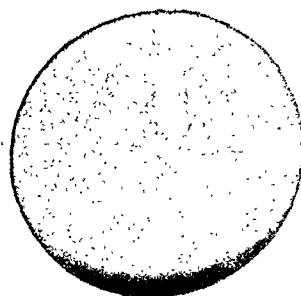
O.D.

4. GLIOMA OF CHIASM. RIGHT EYE (POSTSURGICAL).

FIGS. 1 TO 4 (KANT). KODACHROME ILLUSTRATIONS OF FUNDI. GIVING A SUBJECTIVE IMPRESSION OF THE DEGREE OF PALLOR OF THE DISC WHEN COMPARED TO THE SURROUNDING FUNDUS.

O.S   O.D.
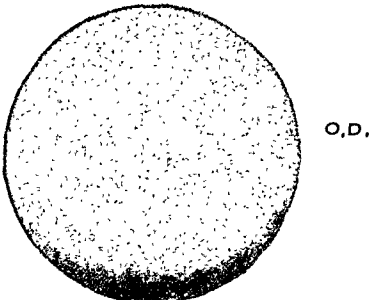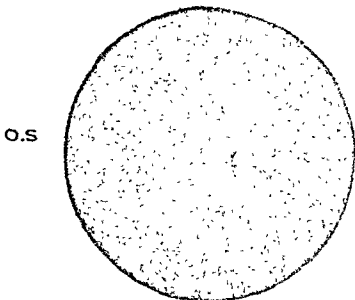
5. MENINGIOMA, ROLANDIC AREA, RIGHT EYE (POSTSURGICAL).
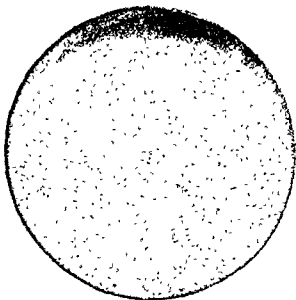
6. EMBOLISM CENTRAL ARTERY.
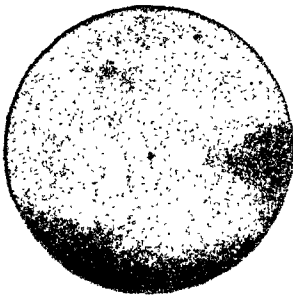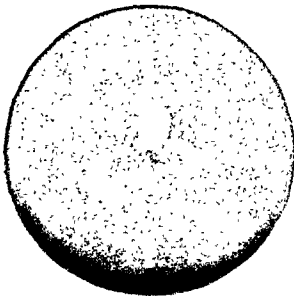
7. MULTIPLE SCLEROSIS.   8. SUPERIOR PAPILLARY OCCLUSION.

FIGS. 5 TO 8 (KANT). THESE KODACHROMES, AS WELL AS THOSE IN FIGURES 1 TO 4, ARE NOT SUFFICIENTLY CRITICAL TO SHOW THE SMALL VESSELS, IN MOST INSTANCES. SINGLE EYES ARE SHOWN IN ORDER TO ILLUSTRATE THE SCOPE OF APPLICATION OF THE NUMBER TEST
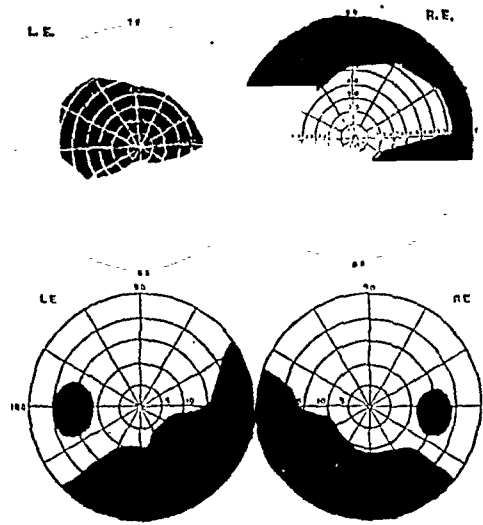
Chart 5. These field studies are for a woman, aged 40 years, for (above) 3/330 white and (below) 1/1,000 and 10/1,000 white. Vision in each eye was 20/30+. The left eye showed six small vessels and the area of the visual field was 9.5 sq. cm. The right eye showed seven small vessels and a visual field area of 10.5 sq. cm.
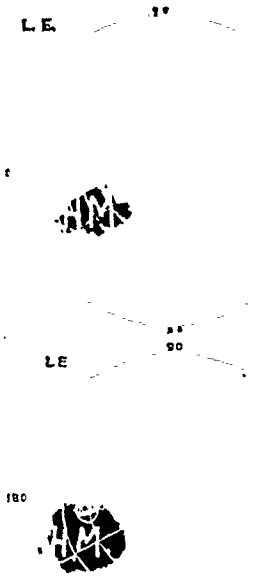
Chart 6. The visual acuity in the left eye of this patient, a man, aged 49 years, was hand movements temporally. The *number of small vessels* present was three.
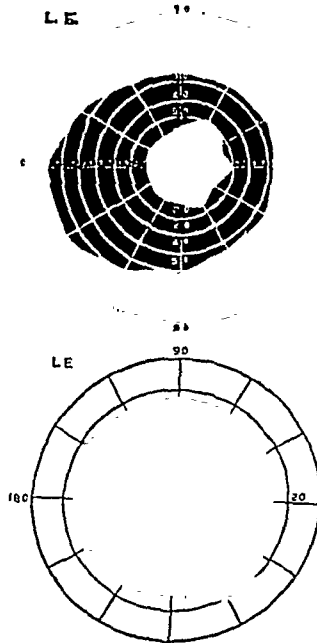
Chart 7. Visual field studies for the left eye of a man, aged 23 years, for (above) 5/330 white and (below) 10/1,000 white. Visual acuity in this eye was counting fingers at two feet; six small vessels were counted. Area of field, 18 sq. cm.
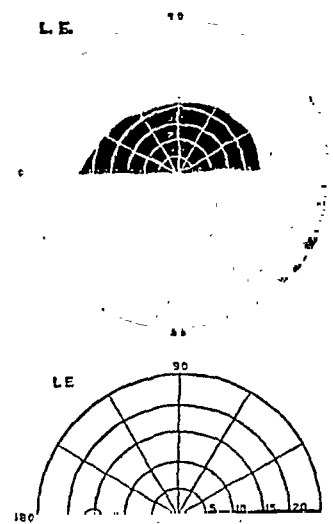
Chart 8. The left eye of this man, aged 56 years, had 20/20 vision, and the number of small vessels was eight. (Above) Field for 3/330 white. (Below) Field for 1/1,000, 3/1,000, and 10/1,000 white. The normal right eye of this patient showed 14 small vessels. Area of field L.E., 5.8 sq. cm.

Charts 5 to 8 (Kant). The visual fields are numbered to correspond with the numbers of the Kodachromes they illustrate.

these findings. The numbers under the acuity listings represent the number of cases observed under that acuity.

It can be seen that there is a surprising correlation between the number of small vessels and the visual acuity, especially between the range of 20/200 and 20/15, where an almost linear function exists. Between
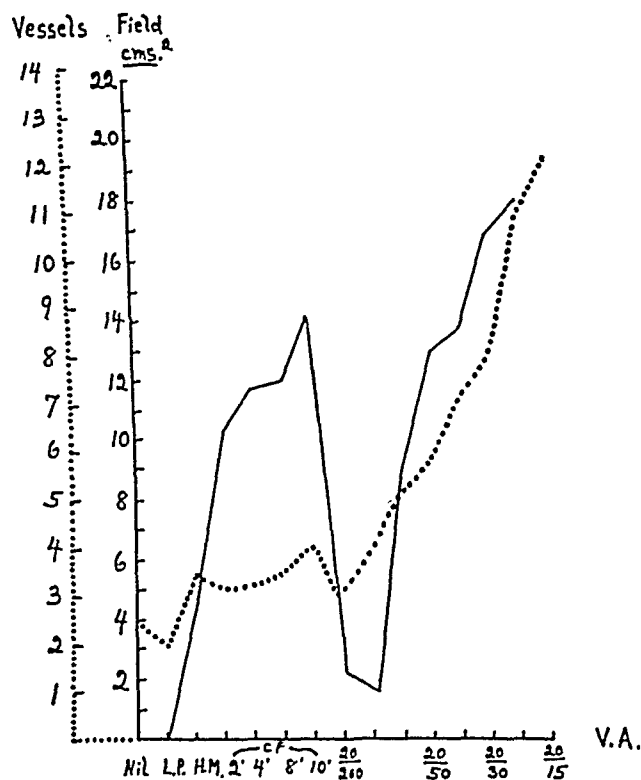
Graph 3 (Kant). Correlation of visual acuity, extent of visual field, and number of small vessels. The abscissa represents the visual acuity. The solid line of the ordinate shows the area of field; the dotted line, the number of small vessels.

20/200 and nil vision the curve is less regular.

There are several possible explanations for this segment of the curve:

1. There is the subjective element of error in counting which, however, does not seem too important in view of the fact that the remaining portion of the curve is based on the determinations of the same observer.

2. Only relatively few determinations in this range of the curve were available and it is possible that, if a greater number of cases had been studied, this section might have conformed more closely to the general curve.

3. If the fibers subserving central vision were damaged to a greater extent than the peripheral ones, the visual acuity would then be expected to be low, with preservation of a relatively large field. Since the number of small vessels expresses the degree of overall atrophy, there would be present a relatively greater number of vessels than would be expected for that acuity. In effect, this is exactly what happened in these cases in this portion of the curve as is shown in Graph 3.

Graph 3, in addition, shows that there is no reliable relationship between the visual acuity and the amount of field preserved except when the atrophy is general and overall.

In those cases, and there were quite a few, in which the number of small vessels found was at variance with the amount of visual acuity, which was either inordinately high or low for reasons already mentioned, the area of preserved field closely approximated the amount expected, the data in Graphs 1 and 2 being used for mean values. These points can be illustrated by reporting a few cases.

CASE REPORTS

Case 5. A man, aged 68 years, had chronic simple glaucoma of both eyes, with marked cupping and atrophy in the left eye and slight in the right eye.

	O.D.	O.S.
No. small vessels	8	6
Visual acuity		
actual	20/30	Fingers at 5 inches
expected	20/30	20/50+
Visual field		
actual	14.8 sq.cm.	13.6 sq.cm.
expected	15.8 sq.cm.	13.6 sq.cm.

Here the right eye shows an excellent agreement between the actual and expected values both as to acuity and area of field. The left eye shows an inordinate decrease in acuity compared to the number of small vessels on the disc. In this instance, apparently, the papillomacular fibers had been severely damaged with resultant poor acuity. The remaining overall, functional integrity of the nerve is shown, however, by the

preservation of exactly that amount of field expected for a nerve with this capillary index. In this case both the ophthalmoscopic appearance of the disc and the markedly reduced visual acuity would have suggested a greater degree of total atrophy.

Case 17. A woman, aged 60 years, had chronic simple glaucoma of both eyes, more advanced in the left eye.

	O.D.	O.S.
No. small vessels	7	2
Visual acuity		
actual	20/40	20/100
expected	20/40	Light perception
Visual field		
actual	18.0 sq.cm.	1.0 sq.cm.
expected	13.4 sq.cm	2.0 sq.cm.

Here again there is a good correlation in the right eye as regards acuity and fairly good as regards field. However, in the left eye there is considerable disparity between the actual and expected acuities. In this case, apparently, the macular fibers were relatively spared. The visual fields both actual and estimated agree very closely.

From these findings one is led to the conclusion that the number of small vessels on the disc quantitatively measures the degree of functional integrity of the optic nerve or, in other words, can be used as an indicator of the degree of overall atrophy present.

It may be of interest to consider the findings in an unquestioned case of retinitis pigmentosa which had all the classical signs and symptoms including the peculiar waxy pallor of the disc so characteristic of the disease.

Case 1. A woman, aged 26 years, had a diagnosed case of retinitis pigmentosa.

	O.U.
No. small vessels	13
Visual acuity	
actual	20/200
expected	20/15
Visual field	
actual	4° fixation (0.5 sq.cm.)
expected	21+ sq.cm.

CONCLUSION

Either the capillary index is no measure of optic atrophy in this case, or there is no optic atrophy present.

In this connection it is interesting to note that Verhoeff, in 1931, reported a case of retinitis pigmentosa that had been blind for 20 years in which the ganglion cells were well preserved and abundant and even the myelin-sheath stain failed to show any evidence of atrophy in the nerve. By citing this case, it is not meant to imply that atrophy does not occur sometimes in this condition. However, the striking disparity in this one case between the obvious waxy pallor and the capillary index of the disc was of sufficient interest to warrant mention.

COMMENT

The number of small vessels is not difficult to count. However, as some of these vessels are quite minute, a little practice will improve one's recognition of them and increase the accuracy and reproducibility of the count. Separate observers, on the first trial, have agreed to within 1 to 2 vessels on the same eye.

Care must be exercised to count only those vessels which cannot be recognized as being either arterial or venous. A darkened room is to be preferred. When the accommodation is active, cycloplegia facilitates the counting considerably.

A clean, well-focused ophthalmoscope with good illumination is essential. In my experience, red-free light was not superior to ordinary light in the final count although it did make the small vessels more striking in appearance.

Noteworthy in this series were two cases of marked physiologic pallor of the disc which had been previously diagnosed as atrophy by several members of the staff. These cases, subjected to the capillary number test, fell well within the range of normal, which impression was subsequently confirmed by refraction and quantitative perimetric studies on the Goldmann perimeter.

One case of partial vascular occlusion failed to show an appropriate correspondence between the number of small vessels and acuity and fields. As far as could be determined, it did not have any anomalous vascularization of the disc.

Although the number of cases in this study is admittedly small, the results from the Kestenbaum capillary number test in optic atrophy are sufficiently suggestive to warrant further study and consideration. The capillary test can serve as an interesting adjunct and check on the more usual diagnostic tests, when these are available. In those cases in which visual acuity and field studies are impossible, for whatever reason, the capillary number test may afford the only clue to diagnosis.

SUMMARY

In this study, 125 eyes—49 normal and 76 atrophic—were examined. The number of small vessels on the disc was counted according to the Kestenbaum capillary number test. The visual acuity and area of field were determined in each case. These findings were correlated with the number of small vessels and expressed in graph form.

CONCLUSION

The capillary number test as elaborated by Kestenbaum is a valuable adjunct in the diagnosis of optic atrophy from whatever cause and would seem to be a reliable measure of the degree of atrophy present.

129 Clinton Street.

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EPITHELIAL TUMORS OF THE CILIARY BODY*

Joseph A. C. Wadsworth, M.D.
New York

Introduction

The significance of certain tumors of the ciliary body has been a controversial subject, since Treacher Collins,[1] in 1891, first reported a case of primary tumor of the ciliary body in a woman, aged 63 years. Following Collins's report, Alt[2,3] and Fuchs[4] wrote rather extensively on the subject. Both of these authors endeavored to classify the various growths and discussed their etiology. Fuchs,[4] in 1908, reported eight cases and classified the tumors according to the microscopic morphology.

The description of some of these tumors led Collins[5] to postulate the glandular nature of the ciliary epithelium, a point which is still adhered to by some observers (Leber,[6] Rados,[7] Seidel,[8] Carrére,[9] and others).

General discussion

Most writers have agreed on the main factors influencing the classification of these primary tumors of the ciliary body. The main factors generally considered are: (1) Cell morphology, (2) age of the patient, (3) extent of growth, and (4) significant past history.

Fuchs[4] laid the greatest stress on the first factor in his classification; however, he was influenced by the second and fourth factors also. The extent of growth was of comparatively little importance in his classification.

Nordmann[10] gave less attention to the past history and gave a greater significance to the extent of growth.

For the purpose of this discussion Nordmann's classification is acceptable and will be used:

I. Benign tumors
    A—Hyperplasia
    B—Benign epithelioma (adenoma)

II. Malignant tumors
    A—Embryonic type (dictyoma)
    B—Adult type

Collins[1] described his first case as an adenoma and numerous subsequent reports of different authors have used the same term for the small tumors originating from the ciliary epithelium. Fuchs[4] in his thorough treatise on the subject coined the term "dictyoma" (net-tumor) to describe those tumors of the ciliary body whose cells are embryonic in type.

Those tumors which show evidence that the cells are embryonic in type may even form what appears to be an embryonic retina. Often these are indistinguishable from retinoblastoma (neuro-epithelioma).

For the most part these tumors have been found only in children; whereas, the more differentiated cells are seen in adults around the age of 50 years. The large majority of the latter type have no clinical signs or symptoms referable to the presence of an intraocular new growth. These tumors have been found in globes enucleated for various reasons and have had no demonstrable influence on the condition of the ocular illness.

A comparatively large percentage of the patients who reveal these small epithelial tumors of the ciliary body have a past history of ocular inflammation so that this point has been seriously considered as an etiologic factor (Fuchs,[4] Alt,[11,12] Duke-Elder,[13] and others). However, the percentage incidence of inflammation is not sufficiently high in these cases to render it significant statistically.

Following Nordmann's classification will facilitate the discussion of the various primary epithelial tumors of the ciliary body.

I. Benign tumors

A. Hyperplasia

The simple hyperplasia of the ciliary epithelium may form cell masses resembling a small neoplasm. There may be a pigmented or nonpigmented epithelial mass originating from the ciliary epithelium. Such growths usually extend toward the interior of the globe and they do not penetrate into the ciliary processes or ciliary body proper. The arrangement of the cells is usually quite irregular without evidence of any typical

tion of the nonpigmented epithelium but the pigment epithelium may participate in the process as well.

For the most part this hyperplasia involves the region of the ciliary processes but frequently long strands and fingerlike formations may extend from the pars plana (Salzmann).

Case 1

History. A 40-year-old man was struck in the eye during childhood. Following the injury the eye gradually became blind. On occasions the eye became injected with moderate discomfort. Symptoms
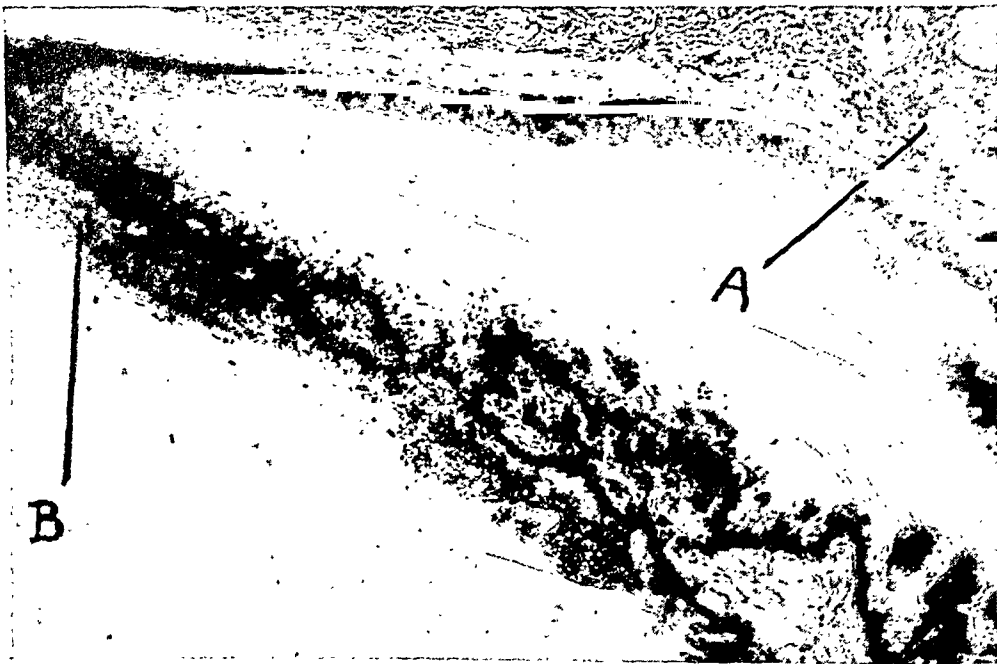
Fig. 1 (Wadsworth). High-power magnification of section in Case 1 at region of ciliary body. (A) Marked hyperplasia of ciliary epithelium extending axialward (B).

organization of the elements. The cells are large with oval nuclei and seem to be simply piled on one another in the form of sheets with occasional folds or scallops.

Eyes with such lesions have a long history of "eye trauma," either as a long-standing recurrent iritis or inflammation following injury. Such changes in the epithelium are frequently seen also in senile eyes. The hyperplasia in some cases may be so general as to push the iris forward and embarrass an already narrowed filtration angle. Generally, the senile hyperplasia is a prolifera-

were not sufficiently severe to consult an ophthalmologist until three weeks prior to admission. At the time he was first seen the eye was painful and exhibited marked ciliary injection, the cornea was steamy, and the tension markedly elevated. Clearing of the cornea revealed a cataractous lens with iris bombé. The eye was excised with a clinical diagnosis of absolute glaucoma, secondary to detachment of the retina, and cataract.

Macroscopic. The globe was of normal size. The anterior chamber was very shallow and there was a complete detachment of the retina.

Microscopic. There is edema of the cornea with a loss of epithelium. A wide peripheral anterior synechia is present completely occluding the filtration angle. A well-formed glass membrane resembling Descemet's extends from the posterior

surface of the cornea onto the anterior surface of the iris. The iris substance shows perivascular round-cell infiltration and some plasma cells. Occlusion and seclusion of the pupil is present and a large fibrous plaque exists on the anterior surface of the cataractous lens. The lens contains calcium.

The muscle of the ciliary body shows some hyaline degeneration, and the ciliary processes have lost, somewhat, there delicate structure and contain a hyalin material. Round-cell infiltration is prominent around the larger vessels. The epithelium of the ciliary body is thickened and reduplicated in places. Numerous vacuoles resembling fat deposits are seen in the nonpigmented layer.

In the region of the pars plana (fig. 1) there is a breaking up of the pigment epithelium with some proliferation. Extending axially from this area is a proliferation of the nonpigmented epithelium. These cells extend centrally and are arranged in sheets and irregular scallops. The central portion of the mass resembles a fibrous core but contains no vessels. In some areas of the proliferation there is marked vacuolation with a pink homogeneous material beneath. No necrosis or active inflammatory response can be found in the tumor.

Enmeshed amongst the zonules are small spheres of large epithelial cells arranged in various forms. These masses have no visible connection with the ciliary body, but are probably cross sections of similar processes described above.

The cells comprising the mass are large, typical epithelial cells with small oval nuclei and moderately clear cytoplasm. No abnormal or immature cells are seen.

This is a good example of hyperplasia of the ciliary epithelium.

B. BENIGN EPITHELIOMA

This tumor may be described as a well-circumscribed cell mass composed of non-pigmented cells encapsulated by a single layer of pigmented cells. These tumors are found by chance in the globes enucleated for various reasons but the high percentage is found among those eyes excised for glaucoma and neoplasms. Nearly all of these growths are seen in patients over 50 or 60 years of age. They are rarely over one millimeter in diameter and have apparently caused no symptoms because of their presence.

The tumor proper is composed of large oval epithelial-like cells with oval nuclei. The outer layer is arranged perpendicularly to the surface and the nucleus is near the base of the cells. This arrangement gives a sort of

palisade along the outer portion of the tumor. The central portion is composed of cellular strands of 1 to 2 layers thick arranged perpendicularly to their long axis. Occasionally one sees an arrangement resembling rosettes. In such a case the polarity of the cells is still present with the nuclei in the outer circumference. The central portion is usually empty or may contain a pink-staining material. The central region of the tumor may show atrophic cells and vacuolization but no necrosis. No vessels or connective tissue are seen in these small tumors.

No true capsule is formed, but the outer surface is lined with pigment epithelium and not infrequently these cells become atrophic and lose their pigment—even disappear in places. On the inner surface of the ciliary body there is always a break in the pigment epithelium and this is the origin of the tumor. This could be called the hilum.

Case 2

History. A 67-year-old married woman with a basal-cell carcinoma of the lid had been given a large but unknown quantity of X ray and radium during the month prior to admission. The eye became injected and painful and an enucleation was done at the time of extensive resection of the lids.

Macroscopic. The globe is of normal size and grossly shows no abnormalities.

Microscopic. There is a complete loss of the corneal epithelium. Bowman's membrane is intact except peripherally where there is marked invasion of new vessels and connective tissue completely replacing the membrane. There is also an invasion of vessels into the stroma peripherally. Descemet's membrane and the endothelial layer appear normal.

The iris shows some hyalinization of the sphincter muscle and generalized atrophy of the stroma with a cellular condensation on the anterior surface. These cells appear to be a proliferation of the endothelial cells.

There is proliferation of the nonpigmented epithelial cells which fill up the recesses of the processes of the ciliary body (fig. 2-a). Embedded in the ciliary processes is a circumscribed collection of epithelial cells arranged in irregular scallops along the outer margin. The central area (fig. 2-b) is made up of irregular strands and numerous spaces of pink-staining material. No necrosis is seen. The tumor contains no true capsule but is surrounded by a layer of pigment epithelium. Numerous areas of atrophy can be seen. A well-marked hilum is demonstrated.

The lens shows proliferation of the anterior
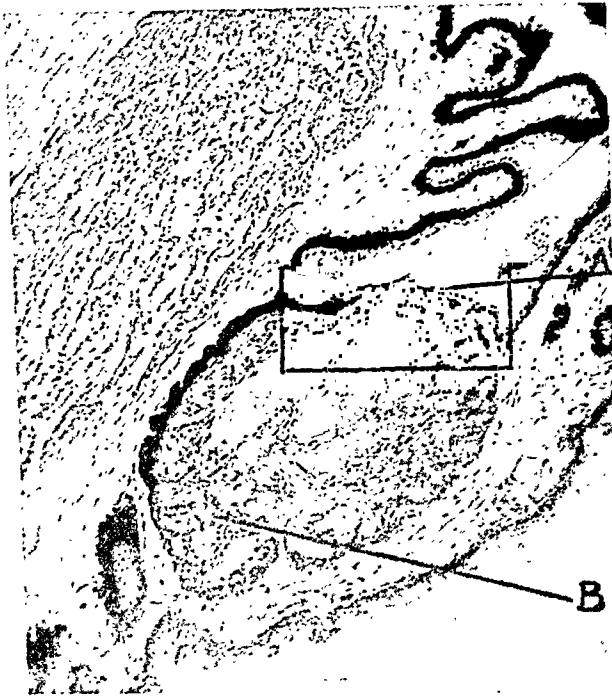
Fig. 2-a (Wadsworth). Benign epithelioma in region of ciliary body demonstrating the proliferation of the nonpigmented epithelium. The tumor shows the typical scalloped arrangement of the epithelial cells (B). (A) points to the hilum.

subcapsular epithelium with some vacuolization and liquefaction of the anterior cortical region. Deep in the cortical region are islands of embedded subcapsular epithelial cells. In the posterior subcapsular region there is also liquefaction, all of which is typical of cataractous changes secondary to radiation (Reese[14]).

There is marked thickening of the lamina vitrea
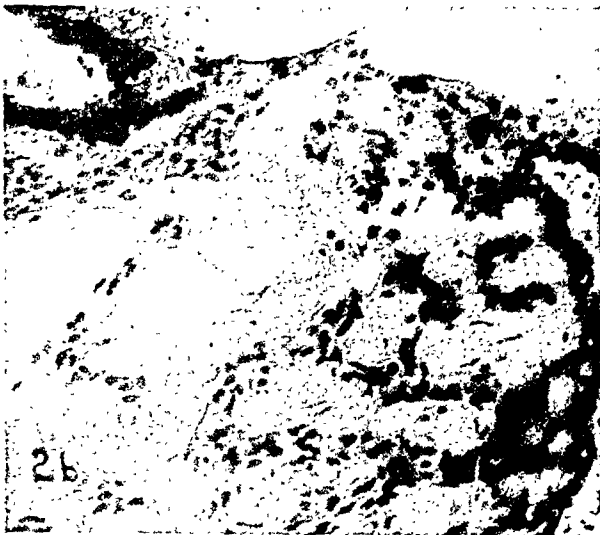
Fig. 2-b (Wadsworth). High-power view of area indicated by square in Figure 2-a, showing the hilum, scalloped arrangement of epithelial cells and the lack of connective-tissue stroma.

and these areas contain fine granules of calcium.

This is a good example of a benign epithelioma of the ciliary body.

II. MALIGNANT TUMORS

A. EMBRYONIC TYPE OR DICTYOMA

This has been called primary carcinoma by Lagrange.[15] It is seen in children between the ages of 1 and 8 years but there are two cases in the literature, one aged 16 years (Böck[16]) and one aged 28 years (Soudakoff[17]), with ciliary body tumors which meet

Fig. 3-a (Wadsworth). Photomicrograph of section from the A. B. Reese collection, showing the malignant nature of the embryonic-type tumor of ciliary body. The tumor has eroded the sclera at the limbus and has extended outside the globe (A). This case was reported by Böck.[16]

all the criteria for their classification as an embryonic type of tumor.

In these tumors there is a questionable inflammatory background. Most observers do not consider inflammation statistically important in these cases.

The structure (fig. 3-a) consists of cell membranes of cylindric epithelial cells with

nuclei arranged in two or more rows with their axis vertically. There may be solid masses of cells like those seen in retinoblastoma and there may be rosettes (fig. 3-b). Invasive nature is a prominent feature and the iris, cornea, and sclera are often affected. The free surface may possess a limiting membrane not unlike the internal limiting membrane of the retina. Tubes, bands, and cavities are common to all tumors of this type.

Fig. 3-b (Wadsworth). A high-power view taken at the area indicated by square in Figure 3-a, showing the cell formation. Rosettes (A) and cords (B).

Case 3

The slide was graciously loaned to me by Dr. A. B. Reese. A 16-year-old girl, who had been blind for about eight months, showed clinically a staphyloma at the limbus nasally. The globe was stony hard. Vision was light perception. This case was described by Böck.[16]

B. ADULT TYPE OF MALIGNANT TUMOR

This is seen in patients between the ages of 10 and 73 years, but the great majority of these patients are seen between the ages of 50 and 65. Of the cases reported in the literature some stress was laid on those cases which gave a history of inflammation or injury. Fuchs[4] reported a case of old septic endophthalmitis with bone formation which demonstrated an epithelioma of the ciliary body that infiltrated into and even destroyed the bone. The majority of the cases have a history of gradual decrease of vision with occasional episodes of pain. Clinically, lenticular opacities associated with appearance of a mass in the region of the angle are the most common signs. Less than half of the cases reported showed elevation of tension.

Case 4

Dr. J. H. Dunnington was kind enough to permit me to include this case in my series.

History. The patient, a 63-year-old man, gave a history of failing vision of the left eye for 3 to 4 years. There was no history of injury or inflammation; no history of pain or tenderness in either eye.

Examination. Vision was: L.E., 20/70; R.E., 20/20. Tension was normal in both eyes. The cornea of the left eye was clear with normal luster. The anterior chamber was of normal depth except in the region between the 12:30- and 3-o'clock positions where the iris was pushed forward. At about the 2-o'clock position the iris was cystic and there was a small pigmented area, 1.5 by 2 mm., in the peripheral region of the iris near the angle. Upon dilatation of the pupil, the lens showed cataractous changes which were dense in the upper nasal region. The lens was displaced backward.

Gonioscopically (fig. 4), the iris was pushed forward obliterating the angle in the region of the 12- and 3-o'clock positions. On the anterior surface of the iris was a heavily pigmented area beginning in about the middle of the iris and extending toward the angle. The pupillary region appeared atrophic in the upper nasal sector. Behind the iris a round heavily pigmented mass was pushing the iris forward and at the same time was displacing the lens backward where the tumor was in contact with the lens and the cataractous changes were most dense.

Because of the clinical appearance of the tumor, a diagnosis of malignant melanoma of the ciliary body and iris was made and the left eye was removed.

Macroscopic. On section of the globe an oval-shaped tumor of the ciliary body and base of the iris was seen. The tumor was covered with heavy pigment and was in contact with the lens pushing it backward. The mass measured about 3 by 3 mm.

Microscopic (fig. 4-a). A section of the cornea has been removed for keratoplasty. The remainder of the cornea is normal except for a region near the limbus which is the area of the tumor.

In the upper temporal aspect of the ciliary body

Fig. 4 (Wadsworth). The gonioscopic picture shown by Case 4. The tumor is pushing the iris forward and is in contact with the lens posteriorly. The dark area on the anterior surface of the iris is the extension of the tumor.

there is an oval-shaped tumor mass measuring 3.5 by 4 mm. The neoplasm appears to have arisen from the base of the ciliary body and pushed the ciliary processes backward. The tumor is fairly well circumscribed except near the base of the iris where it has destroyed this tissue and infiltrated into the corneal lamellae, meshwork of the iris, and ciliary body proper. Sheets of cells are seen on the anterior surface of the iris. These cells are large epithelial-like cells arranged in a sheet.

The cells of the tumor proper are for the most part nonpigmented epithelial-like cells arranged in sheets, cords, and folds that resemble tubules. There are many areas which show atrophy and cystic degeneration but no necrosis. The many spaces are filled with a pink-staining material. In these areas the cells are flattened and lose their distinct cell outline.

Where the tumor (fig. 4-b) involves the base of the iris the cells become heavily pigmented. Otherwise pigment is sparse. However, where the growth has engulfed the ciliary processes the collections of pigment remain.

At the angle (fig. 4-c) the iris is completely replaced by tumor and these cells fill the angle as well as the meshwork. The adjacent tissue shows local infiltration but the cells are well differentiated and maintain their polarity, all of which is indicative of a relatively slow-growing tumor.

Very few new vessels are seen in the tumor and true connective-tissue stroma is lacking.

The infiltrative characteristic, as well as the destruction of the iris, suggests that this tumor has malignant potentialities—certainly it is locally malignant.

This tumor is a primary epithelioma of the adult type.

Butler and others[18] also described a tumor not unlike the above case which also showed extension onto the anterior surface of the iris. This was seen clinically as a tongue-shaped area of pigmentation on the anterior surface extending toward the pupillary area. The case reported by Keyes and Moore[19] showed a replacement of the iris in the region of the tumor and the lens capsule was ruptured and tumor tissue had infiltrated into the cortex of the lens.

Fig. 4-a (Wadsworth). A low-power photomicrograph, showing the tumor in the region of the ciliary body.
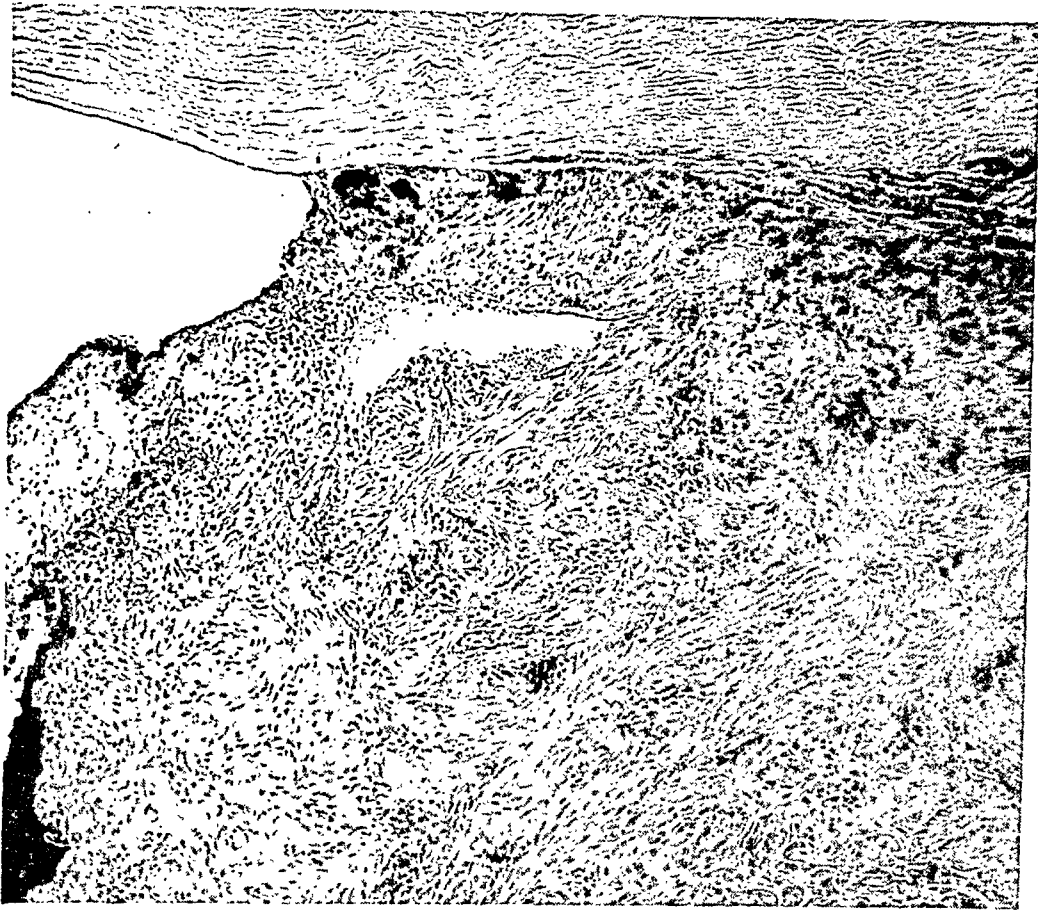
Fig. 4-b (Wadsworth). A high-power view of a section of the tumor taken from the area indicated by the square in Figure 4-a. It shows infiltration of tumor into stroma of cornea. The cells are arranged in cords and bands with very little connective-tissue stroma. Cells at the base of the iris contain pigment.

One of our patients (Case 5)* was younger than usual, being in his 20th year. Clinical signs of cataract were the first symptoms noted two years previously and showed persistent progress. Next, the iris became atrophic and pushed forward into the anterior chamber. At this time dilatation of the pupil revealed the tumor to be in the region of the ciliary body. The tumor (fig. 5) in this case eroded the capsule of the lens by its axial growth. This direction of growth is responsible for the early symptoms before more destruction of the iris and ciliary body could take place. The histology is identical with the previously discussed case.

DISCUSSION

A true picture of the reported cases is a difficult problem because so few of the

benign tumors have been recorded as an individual case. For the most part, the
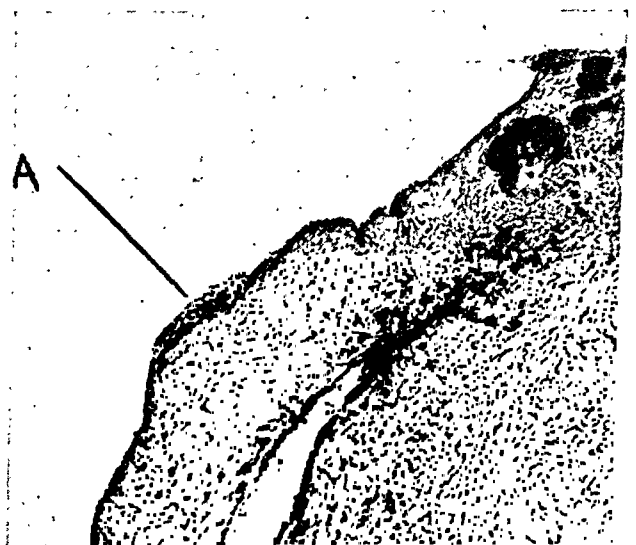
Fig. 4-c (Wadsworth). Section at a different level, showing the infiltration of the iris and the implant of tumor on the iris (A) as was seen clinically in Figure 4.

* See page 1497 for description.
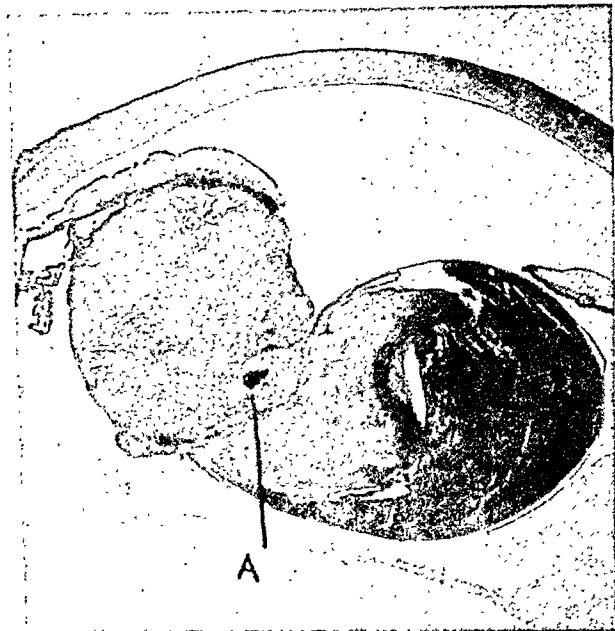
Fig. 5 (Wadsworth). Case 5. This shows the tumor encroaching on the lens with subsequent cataractous changes. At (A) the capsule of the lens is ruptured.

smaller tumors were described in passing while the eye was being reported for some unrelated condition.

Fifty-eight cases of epithelial tumors have been reported in the literature[1-5, 10-12, 17-21] and of these a high percentage have scanty descriptions with insufficient information to classify them accurately. However, Figure 6 is a simple table which gives some comparative data of the three types of tumors. As can be seen, the benign epithelioma (adenoma) was found in older patients but none was seen clinically. The apparently high percentage of inflammation is interesting but not significant since 41 percent of 1,938 consecutive eyes enucleated at the Institute of Ophthalmology, New York, either showed pathologic evidence, or gave a definite history, of inflammation. These large adult epitheliomas showed a very low incidence of inflammation. The statistics on the embryonic type is of no significance since more than half of the cases gave no history at all.

Levy-Wolfe[21] subdivided these small tumors into three classes according to the location in the ciliary body (fig. 7):

TYPE & NUMBER	AV. AGE	AV. SIZE	PREVIOUS INFLAMMATION
CASES FROM LITERATURE			
BENIGN 32	58	1.0 mm.	YES - 66% NO - 12 " ?-22%
MALIGNANT 10 (adult)	34	3.8 mm.	YES - 16% NO - 84 "
MALIGNANT 16 (embryonic)	11	2 mm. to full globe	NO - 43% ? - 57 "
THE AUTHOR'S CASES			
BENIGN EPITHELIOMA 10	61	0.48 mm.	YES - 20% NO - 80 "
MALIGNANT EPITHELIOMA 9 (adult)	56	2.8 mm.	NO - 43% ? - 57 "

Fig. 6 (Wadsworth). Comparative data of the types of epithelial tumors reported in the literature and herein reported.

Class I. The pedunculated type on the surface of the ciliary body.

Class II. Countersunk in the substance of the process.

Class III. Completely embedded in the process.
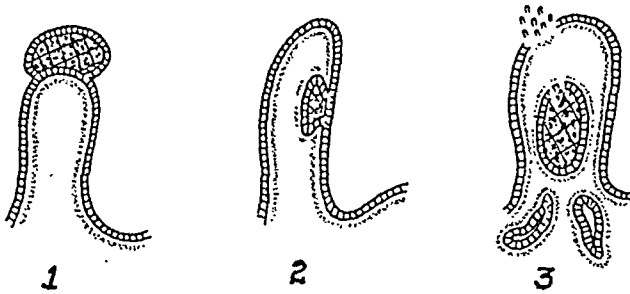
Fig. 7 (Wadsworth). A diagrammatic representation of the three classes of ciliary-body tumors as described by Levy-Wolfe.

Such a classification is an unnatural one and is of no real importance. By study of serial sections a single tumor may fit into more than one classification depending on the level at which the tumor was sectioned.

The first section of our Case 6* (fig. 8-a) shows a small tumor in the substance of the ciliary body which would place the growth

Fig. 8-a (Wadsworth). Case 6. This shows the tumor in the substance of the ciliary body and classified, according to Levy-Wolfe, as Class 3.

* See page 1497 for description.

Fig. 8-b (Wadsworth). The same tumor as shown in Figure 8-a but at a different level and classified, according to Levy-Wolfe, as Class 1.

in Class III. Another section (fig. 8-b) of the same tumor shows an entirely different location and this time the tumor would be placed in Class I.

These so-called benign adenomas may continue to grow and extend beyond the confines of the pigment epithelium and into the substance of the ciliary body proper (fig. 9). As the cells extend into the stroma of the

Fig. 9 (Wadsworth). A small epithelial tumor with cells extending outside the confines of the pigment capsule indicating early malignancy with local extension.

ciliary body, they become larger and more nearly spherical in shape, and they often form small acini. This growth certainly indicates local malignancy.

The formation of these tumors has aroused

Preceded by the invagination of the non-pigmented cells, there is an invagination of the pigmented cells forming a potential cavity into which the nonpigmented cells can grow. If the nonpigmented cells do not keep
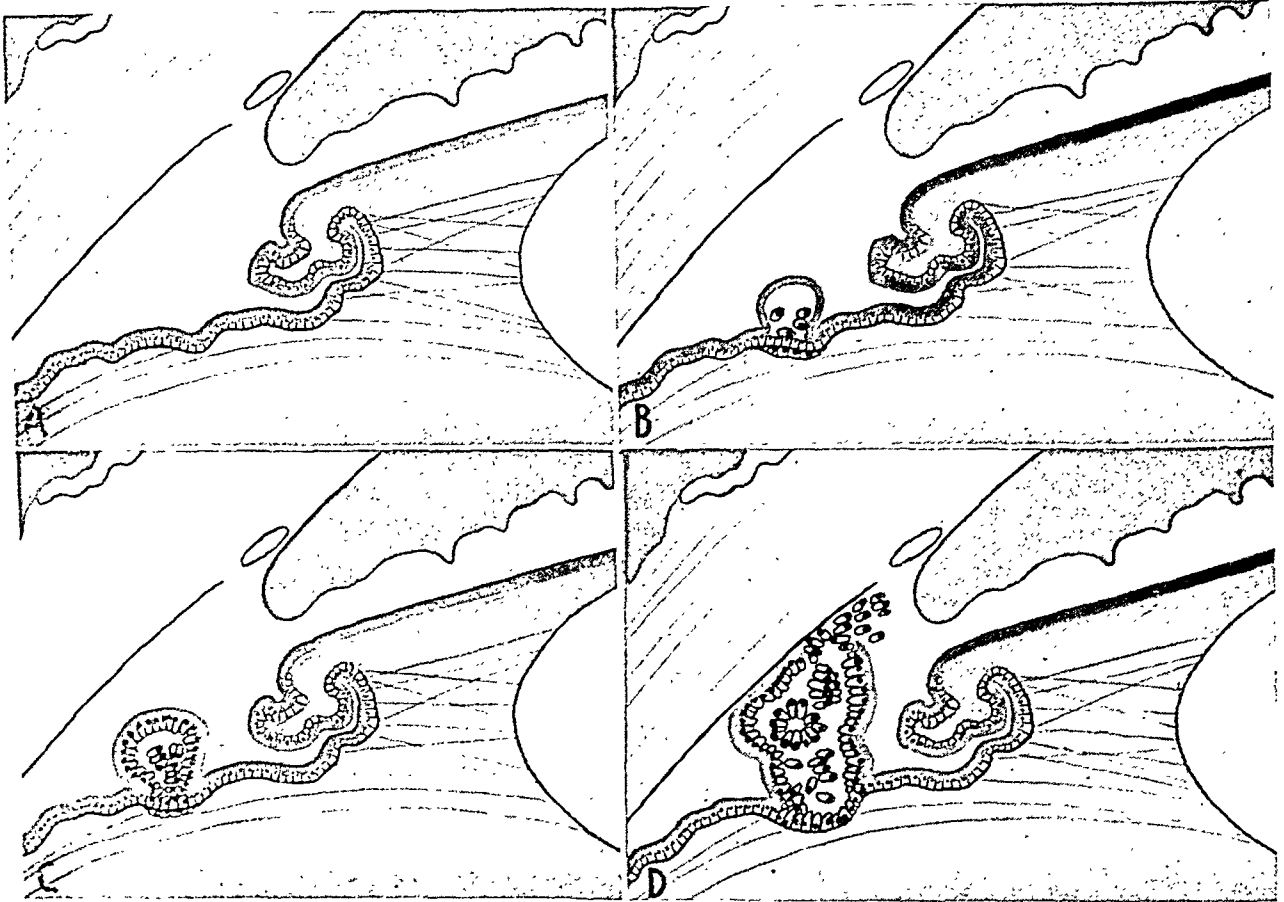
Fig. 10 (Wadsworth). (A) A diagrammatic picture of a normal ciliary body. (B) The beginning formation of a small epithelial tumor, showing the invagination of the pigment epithelium with a proliferation of the nonpigmented epithelium. (C) A further development of the tumor in (B), showing the palisade arrangement of the epithelial cells along the pigmented portion. (D) The progress of the tumor is shown by the rupture of the pigmented layer and the infiltration of the cells into the substance of the ciliary body proper.

sufficient interest to cause some writers to speculate on the manner in which they develop. It is generally agreed that proliferation of the nonpigmented epithelium is the most active process; however, the pigmented epithelium must play a part. All cases of the so-called benign epitheliomas or adenomas are partially, if not completely, surrounded by the pigmented epithelium. There is always a small break in the pigment epithelium through which the nonpigmented cells grow (fig. 10-a, b, c, d).

pace with the pigmented cells, a cyst may be formed.

From the above process there is a hilum formed and a pedunculated tumor in reverse is the result.

In conclusion I believe it is obvious that these small so-called benign epitheliomas may grow and show malignant characteristics as manifested by the destruction of tissue and infiltration. Extension outside the globe in the adult tumors has not been seen because alarming symptoms arise early in the

disease and the eyes are usually removed.

The embryonic type is far more malignant and has the characteristics of a retinoblastoma.

REPORT OF CASES*

In the pathology department of the Institute of Ophthalmology there are 20 cases of primary epithelial tumors of the ciliary body (fig. 6).

Case 5

Graciously loaned to me by Dr. W. T. Boland.

History. A 20-year-old white man had worn glasses for the past 12 years. His refraction has been checked at regular intervals. Two years ago the lens of the left eye showed some cataractous changes but one year later he passed an army test for vision but, after another year, the vision of the left eye was 20/100, not improvable.

The lens was markedly cataractous with the greatest opacification in the nasal half. The iris was pushed anteriorly against the posterior surface of the cornea on the nasal side by a growth in the region of the ciliary body. The iris in this region was atrophic.

Upon dilatation of the pupil, the edge of the growth could be seen. It had a brownish color and was in contact with the lens. The angle was completely blocked nasally. The fundus was poorly seen because of the lens changes. The tension was normal. No family history of malignancy could be elicited.

The macroscopic picture showed a well-circumscribed, brownish mass in the ciliary body nasally. The iris was pushed forward in this region and the lens was pushed temporally and posteriorly. The remainder of the eye was normal.

The microscopic picture reveals the cornea to be normal. Nasally the iris is pushed forward by a round cellular mass originating from the base of the ciliary body. There is a wide posterior synechia over this area with some proliferation of pigment cells of the iris. The tumor mass extends axialward to compress and displace the lens temporally. The nasal portion of the lens is cataractous with some calcium deposits in the lens cortex. The tumor has eroded the capsule of the lens.

The tumor is made up of large epithelial cells with pink cytoplasm and round or oval, lightly stained nuclei. The cells are arranged in cords, bands, and occasional acini. Some areas show atrophic changes characterized by pale, indistinct cell outlines with some cystic degeneration. No necrosis is present. Very few vessels are seen and there is no evidence of inflammation. The greater part of the tumor is surrounded by pigment epi-

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* Cases 1 to 4 have already been described.

thelial cells, but none of the tumor contains pigment and there is very little supporting tissue seen.

The remainder of the ciliary body is normal except for some edema in the region of the tumor. The retina and choroid are normal and there is no evidence of inflammation.

Histologically this tumor is identical with those small "benign" epitheliomas, but this has grown large enough to have been seen clinically and has injured the lens.

Case 6

The patient was a 50-year-old man who had a marked exophthalmos and optic atrophy.

Microscopic. The corneal epithelium shows keratinization. The remainder of the cornea, anterior chamber, and iris are normal. Embedded in the ciliary processes is a well-circumscribed epithelial tumor measuring 0.3 mm. in diameter. One section shows the tumor completely surrounded by the ciliary process; whereas, at another level the small tumor is on the surface of the ciliary body. The basal cells of the tumor are perpendicular to the surface and the center of the tumor is made up of strands of cells arranged perpendicular to the long axis of the strand. Usually these strands are two cells thick. Between these bands is a pink-staining material. This is an epithelioma of the adult type.

Case 7

The eye was removed from a middle-aged man because of a basal-cell carcinoma of the lid with extension to the conjunctiva.

Microscopic. Polymorphonuclear infiltration into the cornea with some extension of the basal-cell epithelioma at the limbus.

Near the base of the ciliary body there is a small, nonpigmented tumor measuring 0.3 by 0.4 mm. The pigment epithelium is invaginated and its continuity is broken at one place where the tumor cells are spreading outside the confines of the pigment epithelium.

The tumor is made up of the large epithelial cells arranged perpendicular to the *outer surface.* The cells in the center of the tumor are roughly ovoid and are arranged in bands and primitive acini. These central cells have variable shaped nuclei; some are round and others are spindle-shaped. No visible supporting tissue can be seen. The cells that have pushed their way outside the confines of the pigment epithelium into the substance of the ciliary body are more nearly round. This is an example of an epithelioma with local extension.

Case 8

History. A 26-year-old man with an intraocular foreign body of six weeks' duration showed chronic inflammation and finally hypopyon. The eye was enucleated for fear of sympathetic ophthalmia.

Microscopic. There is an oblique wound through

the cornea nasally, 2 mm. from the limbus. Some sections show incarceration of the iris in the wound and an increase in vascularization of the cornea between the wound and the limbus. Many polymorphonuclear cells also infiltrate the iris stroma. There is a large laceration of the anterior and posterior capsule of the lens. There is, also, an abscess of the vitreous with a sprinkling of polymorphonuclear leukocytes along the surface of the internal limiting membrane. The choroid and retina are also affected with the same inflammatory process.

In the ciliary body near the base is an aggregation of nonpigmented epithelial cells. The pigment epithelium has become invaginated and forms what appears to be a capsule. Other sections show this to be incomplete and the cells are infiltrating (pushing) out into the substance of the ciliary body. The cells are arranged roughly in rosettes and sheets. The oval nuclei are perpendicular to the outer circumference of the rosettes and located peripherally. The center of these rosettes is filled with a pink-staining material. Several small capillaries are seen and a few scattered connective-tissue cells too. When the pigment epithelium is lacking and the nonpigmented cells are extending from the main mass, the cells are more nearly round and arranged in solid groups. This is an example of epithelioma of the adult type.

Case 9

History. A 77-year-old man had acute glaucoma following the use of atropine five years ago. An iridectomy was done shortly after. There was no history of inflammation.

Microscopic. The epithelium is separated from the cornea by a sheet of connective tissue in the area of the operative incision. Descemet's membrane is incarcerated in the stroma of the cornea. There is a wide peripheral anterior synechia. The ciliary body shows many of its processes to be calcified.

In the region of the base of the ciliary body there is a collection of epithelial cells arranged in whorls and bands with a central structureless pink-staining material. The pigment epithelium is indented and partially surrounds the nonpigmented cells. There is no invasion of tissue. This is a benign epithelioma.

Case 10

History. An 81-year-old man with absolute glaucoma had had a paracentesis two days prior to enucleation. No history of inflammation was present.

Microscopic. The iris is trophic and a membrane of fibrous tissue extends over the anterior surface of the iris.

In the atrophic ciliary body is a small area of proliferation of nonpigmented epithelial cells curled into sheets. The outer portion is lined with the typical large epithelial cell. Several small capillaries can be seen inside the tumor and vacuolization is a

prominent feature. There is no infiltration. Impression—benign epithelioma.

Case 11

Long-standing chronic noncongestive glaucoma. Pneumococcal corneal ulcer two weeks prior to enucleation.

Microscopic. Loss of corneal epithelium with polymorphonuclear infiltration through the layers of the stroma with loss of substance. Anterior chamber contains large numbers of polymorphonuclear cells with posterior corneal abscess. Iris is infiltrated with polymorphonuclear leukocytes.

Near the region of the pars plana of the ciliary body there is a break in the pigment epithelium with invagination of the nonpigmented epithelium. These cells are arranged in sheets and acini. At one area the pigment epithelium is missing and the nonpigmented epithelium is growing free in the stroma of the ciliary body. This is evidence of local malignancy of a small epithelioma.

Case 12

History. A 79-year-old woman had a growth on the inner surface of the lid, bulbar conjunctiva, and cornea of the left eye. The corneal growth proved to be an epithelioma of Bowen's type.

Microscopic. There is a projection of the nonpigmented epithelium into the substance of the ciliary body. Between the cells is a pink-staining material. There is a break in the pigment epithelium.

The nonpigmented epithelial cells are arranged in sheets and cords with some scalloped arrangement. No newly formed vessels are seen. This is a benign epithelioma.

Case 13

History. Age unknown. Failing vision for one year. Irregularity of the pupil and a small elevated area of iris in the pupillary area at the 1-o'clock position. The elevated area increased in size under observation. Tension = 100 mm. Hg (Schiøtz). Enucleation was done because of a blind, painful eye with a suspected tumor of the iris.

Microscopic. The section has badly faded but cytology is possible. The cornea is normal except for irregularity of epithelium. The filtration angle is open but the meshwork of the angle shows thickening and sclerosis of the trabeculas. The iris is thickened in the pupillary region by an infiltration of a spindle-cell tumor which appears to arise from the sphincter. The lens is normal.

In the region of the sims in the ciliary body there is a well-circumscribed tumor, measuring 0.5 by 0.5 mm., composed of large epithelial cells originating from the nonpigmented epithelial cells of the ciliary body. The tumor is partially surrounded by the pigmented cells except in the region of the hilum.

The outer portion of the tumor is lined with the nonpigmented cells arranged perpendicular to the

surface and with nuclei toward the base of the cell. The central area contains many empty spaces. These areas are made up by the numerous bands and sheets of cells forming a coarse network. These bands are two-cells thick arranged perpendicular to the long axis of the bands. No newly formed vessels or connective tissue are seen in the substance of the tumor. No evidence of inflammation is present. Impression—(1) Leiomyoma of iris; (2) benign epithelioma of the ciliary body.

Case 14

History. A 56-year-old woman had had failing vision in the right eye for over one year. There was no pain or inflammation. Physical examination revealed a large detachment of the retina with questionable transillumination. The pigmentation was extremely heavy throughout the eye.

Microscopic. The entire uveal tract is thicker than usual, especially on the temporal side where it is four times its normal thickness and the chromatophores are engorged with pigment.

In the ciliary body near the base is an aggregation of nonpigmented epithelial cells almost completely surrounded by pigment epithelial cells. The outer cells are arranged perpendicularly to the outer margin of the tumor and the nuclei are near the base. The inner portion is made up of irregular bands or sheets and poorly formed acini. No connective tissue or newly formed vessels can be seen in the tumor.

Diagnosis. Melanosis oculi and benign epithelioma of the ciliary body.

Case 15

A 35-year-old woman who had had failing vision for one month presented no history of injury or inflammation.

Microscopic. Arising in the choroid in the lower temporal portion of the globe is a pigmented tumor which has pushed the ciliary body axialward and forward. The tumor has produced a detachment of the retina and the tumor of the choroid is made up of cords of epithelial cells containing pigment. The outermost part of the tumor contains pigment but the central portion shows areas of necrosis and hemorrhage.

In the region of the sims there is a small, circumscribed, nonpigmented tumor composed of epithelial cells resembling those of the nonpigmented cells of the ciliary body. The tumor is almost completely surrounded by pigmented epithelial cells. There is a single layer of nonpigmented cells along the outer surface arranged perpendicularly to the surface and their nuclei are near the base of the cells. The tumor proper is made up of irregular acini and scallops with many spaces. These spaces are filled with a pink-staining, homogeneous material.

Diagnosis. Malignant melanoma of the choroid and benign epithelioma of the ciliary body.

Case 16

No history is available.

Microscopic. The cornea shows some irregularity of the epithelium with some evidence of cornification. In the central region of the cornea Descemet's membrane is irregular and absent in places. In these areas there is proliferation of the endothelium with deposits of pink-staining material. The anterior chamber is of normal depth.

Along the anterior surface of the iris is a sheet of large epithelial cells varying from one cell to 6 or 7 cells thick. These cells are arranged in solid sheets and some have the appearance of columnar cells. One mitotic figure is seen. Numerous empty spaces are seen in the tumor. These cells also course along the inner surface of the cornea and across the angle and completely occlude it. There is occlusion and seclusion of the pupil by extension of the tumor.

In the region of the base of the ciliary body and the base of the iris there is an accumulation of large, nonpigmented epithelial cells arranged in sheets and poorly formed acini. These cells extend into the ciliary body proper and onto the surface of the iris.

The remainder of the eye is not remarkable. There is no evidence of inflammation.

Diagnosis. Malignant epithelioma of the ciliary body; glaucoma, secondary to tumor.

Case 17

No history is available.

Microscopic. The eye has been subjected to a severe inflammation which has subsided with the result of extensive bone formation which almost completely fills the interior of the globe. Many of the internal structures are not identifiable.

In the region of the ciliary body is a mass of epithelial cells arranged in irregular tubes and folds. The outermost group of these cells contain pigment. The central portion of the tumor is atrophic and the cells are arranged in cords and bands. The adjacent bone has been eroded by the neoplasm.

Diagnosis. Malignant epithelioma of the ciliary body in an old phthisical eye.

Case 18

No history is available.

Microscopic. In the region of the ciliary body and the iris there is an epithelial growth extending into the anterior chamber and destroying the immediate portion of the iris. The tumor cells have infiltrated into the inner layers of the sclera near the scleral spur.

The original portion of the tumor is typical in its formation but, as the tumor has extended and gained momentum, numerous bands and membranes can be seen associated with many empty spaces. In the region of the iris the cells contain pigment but elsewhere the tumor is free of pigment.

Diagnosis. Malignant epithelioma of the ciliary body.

Case 19

History. A 77-year-old woman with senile cataracts had had no history of inflammation. The tension was normal. An intracapsular extraction of the left eye was followed by detachment of the choroid and softening of the eye. Six weeks later the tension rose to 70 mm. Hg (Schiøtz) and treatment failed to relieve the pain. The eye was subsequently removed.

Microscopic. The cornea showed some vascularization of the deep layers of the stroma and in the anterior chamber and on the anterior surface of the iris there are two large cystlike areas made up of epithelial cells. The retina is detached and there is marked thickening of the lamina vitrea and proliferation of the pigment epithelium of the retina.

In the ciliary body there is an accumulation of nonpigmented epithelial cells which forms a well-circumscribed tumor. The mass is surrounded by pigmented epithelial cells. Cellular arrangement is typical with the benign epithelioma.

Diagnosis. Epithelization of the anterior chamber; glaucoma secondary to epithelization of the anterior chamber; benign epithelioma of the ciliary body.

Case 20

History. The patient was struck in the right eye 22 years previously and there was no light perception following the injury. The eye was blind and shortly before enucleation the eye became injected and painful.

Microscopic. The globe is somewhat deformed. The cornea is irregular in thickness and irregularity of Descemet's membrane is seen at one place. There is sclerosis of the pectinate ligament with occlusion of Schlemm's canal. Atrophy of the iris with edema is well marked and edema extends to the ciliary body.

In one of the ciliary processes near the base is a cellular collection of nonpigmented epithelial cells which is partially encapsulated by pigment epithelial cells. Near the base of the tumor the pigmented epithelial cells are not present and a well-formed hilum can be seen. The cells in the outer portion of the tumor are perpendicular to their base and the nuclei are in the outer portion of the cells. The central portion is made up of irregularly arranged cells but there is a tendency to form acini, the lumina of which contain a pink material.

Diagnosis. Benign epithelioma of the ciliary body.

73 East 71st Street (21).

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OPHTHALMIC MINIATURE

Egyptian Ophthalmology

In Egyptian writing, the corneal ulcer was symbolized by the crocodile. The Greeks, who did not know the crocodile from first-hand experience, used the crab as a symbol for a painful disease, and corneal ulcer was cancer to them.

Hirschberg, *Graefe-Saemisch Handbuch.*

RETROBULBAR ALCOHOL INJECTIONS*

RELIEF OF OCULAR PAIN IN EYES WITH AND WITHOUT VISION

A. EDWARD MAUMENEE, M.D.

San Francisco, California

The treatment of prolonged severe ocular pain is one of the most trying problems in ophthalmology. Frequently partially seeing eyes and blind eyes which are not disfiguring or otherwise dangerous are removed because the patients can no longer tolerate the pain caused by them. In many instances these patients can be relieved of pain for several months or longer by the use of retrobulbar alcohol injections. If during this interval the cause of the pain is alleviated, the eyes might be saved and in some instances useful vision retained. Retrobulbar alcohol injections should, therefore, have a very definite place in the armamentarium of ophthalmic therapy.

For many years encouraging reports on this procedure have appeared in the German and French literature but its use has not been so well accepted in this country. In the few reports which have appeared in the English literature the possibility of complications in the form of extraocular palsies and injury to the optic nerve have been stressed. It is the purpose of this communication to report the use of retrobulbar alcohol injections for ocular pain in 41 blind eyes and 15 eyes with partial vision. These injections were given by members of the staff of the Wilmer Institute of Ophthalmology between the years of 1942 and 1948.

Grüter[1a] published the first report on the use of retrobulbar alcohol injections in 1918. In 1943[1b] he reviewed the literature and summarized his experiences of 25 years with this therapy. He advocated the use of 1 to 3 cc. of 80- to 90-percent ethyl alcohol without previous injection of novocain in blind painful eyes as an alternative for enucleation. The transient complications of chemosis of the conjunctiva, slight proptosis of the globe, and extraocular palsies which follow alcohol injections were described in some detail. Only a few patients who received an injection of 3 cc. of 80- to 90-percent alcohol developed a permanent paralysis of the ocular muscles. In Grüter's 25 years of experience with this therapy he observed only one case of neuroparalytic keratitis after an injection of 3 cc. of 70-percent alcohol. The complications of herpetic keratitis and corneal ulcer, which not infrequently follow injections of the Gasserian ganglion, were not encountered in his cases.

In 1930 Weekers[2a] reported the use of 40-percent alcohol injections for the relief of pain in patients with seeing eyes who had corneal ulcers, keratitis, uveitis, and primary congestive glaucoma. He injected 1 cc. of novocain, removed the syringe from the needle and, after five minutes, injected 1 cc. of 40-percent alcohol. He again reported the use of this procedure in 1939[2b] and 1941[2c] and stated that he had occasionally observed a temporary paralysis of one or more of the extraocular muscles but had not observed any permanent complications. Damage to the optic nerve was not noted from this procedure. In some cases of primary glaucoma, the ocular tension was reduced for a few days to a week following the injection. He suggested that this therapy be used to lower the ocular tension so that an interval operation might be performed. Weekers thought that alcohol injections had a curative effect in some cases of anterior uveitis and interstitial keratitis.

Magitot[3] has also advocated retrobulbar injections of 1 cc. of 40- to 50-percent alcohol for painful inflammations of the anterior segment of the eye (such as interstitial keratitis, gonococcal iritis, and phlyctenular ker-

atitis) and for acute congestive glaucoma. He stated that he had never seen a permanent extraocular palsy or injury of the optic nerve from this procedure.

There are only a few references to the use of retrobulbar injections of alcohol in the English literature. Fejer[4] in 1932 reported its use in five cases. Gifford[5] in his book on ocular therapeutics mentioned its value for the relief of pain. Hartman[6] in 1942 referred to the work of Grüter, Weekers, and Magitot. Goulden[7] in 1943 reported that he had found 1 cc. injections of 40- to 60-percent alcohol to be of value in cases of interstitial keratitis, uveitis, and subacute glaucoma, but he did not record how many times he had used this procedure. In the discussion of Goulden's communication, Goldsmith mentioned that he had observed a sterile abscess following the use of an 80-percent alcohol injection in one patient. This complication must be extremely rare for it is not mentioned in the reports of Grüter, Weekers, or Magitot.

The only instance of injury to optic nerve recorded in the literature is the report of Cordes[8] in 1929. In this patient, the optic nerve was injected when an attempt was made to inject the sphenopalatine ganglion. The patient saw a sudden flash of light during the injection, and suffered a permanent total loss of vision. He also developed paralyses of the extraocular muscles and ptosis. The optic nerve became atrophic but the motor function of the muscles returned.

METHOD OF INJECTION AND REACTION

The technique for retrobulbar alcohol injections in the series of patients reported here has been similar to that described by Grüter, Weekers, and Magitot. The patient is requested to look up and nasally and a 3.5-cm., 22-gauge needle is inserted into the lateral third of the lower lid just above the rim of the orbit. The needle is then passed through Tenon's capsule between the external and inferior rectus muscles into the muscle cone. An effort is made to keep the needle as close to the back of the globe as possible. The plunger of the syringe is withdrawn slightly to be sure the needle has not entered a blood vessel. One cc. of 2-percent novocain is injected into the muscle cone. The syringe is removed leaving the needle in place. After 3 to 5 minutes, the corneal sensitivity and extraocular muscles are tested to be sure the needle is in the proper position. A syringe containing 1 cc. of ethyl alcohol is attached to the needle and the solution injected into the orbit. The patients frequently complain of a sharp pain in the orbit or a dull occipital headache for a minute or two after the injection. Care should be taken not to make the injection into one of the extraocular muscles or too near the levator muscle. If the injection is given close to the posterior part of the globe and not deep in the muscle cone, fewer muscle palsies occur.

About one hour after the injection chemosis of the conjunctiva and proptosis of the globe develop. This reaction lasts from two days to a week. A partial paralysis of one or more of the extraocular muscles or a ptosis occurs in about 50 to 75 percent of the patients. This complication lasts for a few days to two months depending on the site of the injection. In no instance in this series has a permanent paralysis occurred. Neither neuroparalytic nor dendritic keratitis has occurred in a single case after injection. The patients frequently complain of a feeling of fullness of the orbit for 24 to 48 hours after injection but when the injection has been given properly the ocular pain is relieved. If the injection has not been given correctly and the patient's symptoms are not relieved, the injection can be repeated without danger 2 or 3 days later.

When alcohol therapy was first used at the Wilmer Institute, we were apprehensive about the reactions which might follow, so only 1 cc. of 40- to 50-percent ethyl alcohol was used after an injection of 1 cc. of 2-percent novocain. Pain was not always controlled with this strength solution and the complica-

TABLE 1
RETROBULBAR ALCOHOL INJECTIONS IN BLIND EYES
(Less than 10/200 vision)

Diagnosis	No. of Cases	Diagnosis	No. of Cases
Absolute glaucoma	22	Phthisis bulbi	2
Secondary glaucoma	6	Keratitis after mustard gas burn	1
Parenchymatous keratitis and uveitis	6	Keratoplasty	1
Corneal ulcer	2	Endothelial dystrophy	1

tions were not severe or permanent so 95-percent ethyl alcohol was tried. The results have been more consistent with the stronger solution and the reactions only slightly greater. Therefore during the past four years only 80- to 95-percent alcohol has been used. The blind eyes in which 40- to 50-percent alcohol was given are not included in this report.

ALCOHOL INJECTIONS ON BLIND EYES

A retrobulbar injection of 1 cc. of 95-percent ethyl alcohol was done on 41 eyes with less than 10/200 vision. Many of these eyes would have been enucleated because of pain. A tabulation of the diagnoses in these eyes is given in Table 1. In six patients the pain was not alleviated either because the injection was not given properly or because not enough alcohol was used. Pain was controlled in 35 eyes for at least one month. Eleven of the patients were not seen in the clinic after one month so it is not known whether the pain returned after this time or not. In seven patients the pain returned after two months or longer and the eyes were removed. The remaining 17 patients were followed for two months to three years. In these patients the pain did not return or it returned only intermittently and was not severe enough for the patient to desire enucleation.

Fifteen eyes were removed after alcohol injections affording an opportunity for studying histologically the effect of alcohol injections on the optic nerve. In 13 of these eyes the pain was either not controlled or returned several months after the injection.

TABLE 2
FIFTEEN EYES EXAMINED HISTOLOGICALLY AFTER ALCOHOL INJECTION

Diagnosis		Pain Controlled	Interval Between Injection and Enucleation	Optic Nerve
Absolute glaucoma	(4 eyes)	Not controlled	2 eyes—4 days 2 eyes—1 week	Glaucomatous optic atrophy but no abnormal cellular infiltration
Absolute glaucoma and corneal abscess	(1 eye)	Not controlled	2 weeks	
Absolute glaucoma	(3 eyes)	2 months	2 months	
Absolute glaucoma	(1 eye)	3 months	8 months	
Absolute glaucoma	(2 eyes)	4 months	5 months	
Phthisis bulbi	(1 eye)	Not controlled	1 week	Optic atrophy
Parenchymatous keratitis	(1 eye)	7 months	17 months	Normal nerve
Corneal ulcer	(2 eyes)	1 month	1 month	Normal nerve

In two instances the pain was controlled for one month but the eyes were removed because the patients were elderly; had severe corneal ulcers in one eye, and normal vision in the other eye. The time of removal of these eyes after alcohol injection is listed in Table 2. In the eyes with absolute glaucoma, there was advanced atrophy of the optic nerve but in no case was there a marked cellular infiltration of the nerve or nerve sheath to indicate that damage had been produced by the injection.

In a few eyes removed shortly after in-

will return when the nerves regenerate. Histologic examinations of the optic nerves in 15 cases did not show evidence of injury by the alcohol.

ALCOHOL INJECTIONS ON EYES WITH PARTIAL VISION

Retrobulbar alcohol injections have been done in 15 patients whose final visual acuity ranged between 10/200 and 20/20. The type of ocular lesion, duration of pain before alcohol injection, the amount of alcohol injected, and the visual acuity before and

TABLE 3

RETROBULBAR ALCOHOL INJECTIONS IN EYES WITH PARTIAL VISION
(Final Vision 10/200 to 20/15)

Diagnosis	Duration of Pain	Amount of Alcohol		Vision at Time of Injection	Final Vision and Interval After Injection	
Tuberculous keratitis	8 mo.	1 cc.	45%	1/200	20/50	6 yr.
Epidemic keratoconjunctivitis	3 mo.	1 cc.	45%	20/50	20/20	5 yr.
Epidemic keratoconjunctivitis	4 mo.	1 cc.	45%	20/40	20/20	1 yr.
Uveitis after cataract extraction	4 mo.	1 cc.	95%	10/200	20/100	2 mo.
Uveitis after cataract extraction	5 mo.	1 cc.	95%	20/50	20/15	2 yr.
Disciform keratitis	5 mo.	1 cc.	95%	20/70	20/40	5 mo.
Disciform keratitis	4 mo.	1 cc.	95%	20/30–2	20/20	1 yr.
Disciform keratitis	2 mo.	1 cc.	95%	20/100	20/25	8 mo.
Herpes zoster keratitis	9 days	1 cc. 95% after 2 days 1 cc. 95%		1/200	20/30	6 mo.
Herpes zoster keratitis	11 mo.	1 cc.	95%	4/200	20/100	5 mo.
Postoperative panophthalmitis	8 days	1 cc.	95%	L.P.	20/30	1 yr.
Recurrent corneal erosion	2 mo.	1 cc.	95%	20/200	20/100	9 mo.
Sympathetic ophthalmia in remaining eye	1 yr.	1 cc.	95%	L.P.	20/100	1 yr.
Glaucoma secondary to uveitis	14 days	1 cc.	95%	3/200	20/200	2 mo.
Glaucoma secondary to uveitis	3 mo.	1 cc.	95%	10/200	10/200	6 mo.

jection, there was a slight cellular infiltration of the posterior superficial sclera which might have been caused by irritation from the alcohol. The three eyes removed because of corneal ulcers and parenchymatous keratitis were extremely valuable for they showed no evidence of atrophy or injury of the nerves.

This group of cases indicates that the injection of 1 cc. of 2-percent novocain followed by 1 cc. of 95-percent alcohol will control ocular pain for 1 to 3 months if the injection is given properly. The anesthesia is not permanent, however, and if the primary cause of pain is not remedied the pain

after injection are listed in Table 3. When alcohol injections were first used on eyes with partial vision, we feared that the optic nerves might be injured by this procedure. Therefore, in the first three patients only 1 cc. of 45-percent ethyl alcohol was used after an injection of 1 cc. of 2-percent novocain. Vision was not reduced following this treatment.

During the interval these patients were being followed, 95-percent alcohol was found to be much more effective in controlling pain in blind eyes and histologic examination of several eyes after injections of this strength alcohol failed to show evi-

dence of injury to the optic nerves. We therefore began to use 95-percent alcohol in eyes with partial vision. Twelve eyes have been injected with the stronger solution of alcohol and in no instance has the visual acuity been reduced from this procedure.

CASE REPORTS

The results of alcohol injections in these eyes with vision have been so striking that several of the cases will be described briefly.

The first patient with a potentially seeing eye to be injected had a parenchymatous keratitis with marked photophobia and blepharospasm. The lesion was located primarily in the central portion of the cornea, the pupil would not dilate adequately with atropine, and his vision was reduced to hand motions at two feet. He had not been able to work for eight months because of his pain. An enucleation was considered because his keratitis did not respond to the usual forms of therapy and because of the protracted course of this illness. One cc. of 45-percent ethyl alcohol relieved his pain completely and his pupil became more dilated so that his vision improved to 20/70. It has now been six years since the injection. Vision is 20/70 with a full visual field. The patient has had several minor exacerbations of his keratitis during this interval but none of them have been severe enough to warrant a second alcohol injection.

A second patient had a persistent low-grade anterior uveitis following a cataract extraction. The uveitis failed to respond to antibiotics, typhoid-fever therapy, salicylates, and local atropine. He had been confined to his house and hospitalized for five months. His vision was 20/50 but he requested enucleation for the relief of his pain. A 1-cc., 95-percent alcohol injection completely relieved his pain. During the next three months his uveitis gradually subsided and his vitreous opacities cleared. It has now been two years since his alcohol injection and his vision is 20/15 with a full visual field.

A third patient had a disciform lesion fol-

lowing a dendritic keratitis of four months' duration. His vision was 20/30—2 but he was unable to work for several days each week because of photophobia and ocular pain. A 1-cc., 95-percent alcohol injection relieved his pain. This patient suffered a partial paralysis of the external rectus muscle which caused diplopia for two weeks. The eye was occluded during this interval and the patient was able to return to work. The edema of the cornea subsided during the next two months and the patient now has a small scar in the inferior portion of his cornea. It has been one year since the injection and his vision is 20/20 with a full visual field.

In a fourth patient with herpes zoster keratitis, the first injection of 1 cc. of 95-percent alcohol did not control the pain and a second injection was given two days later. He developed a marked orbital reaction and a paralysis of several of his extraocular muscles which lasted for a month. This patient's visual acuity six months after injection had improved from counting fingers at two feet to 20/30.

In most eyes in this series alcohol injections have had little effect on the basic inflammatory lesions. It has merely relieved the patient's pain while the lesions have undergone their natural process of healing. In four cases of keratitis, however, two which followed epidemic keratoconjunctivitis and two which followed herpetic keratitis, the course of the disease might have been shortened by alcohol injections. In these patients the epiphora and blepharospasm, which might well have been contributing to the continuance of the keratitis, were relieved by the alcohol injections.

In this series of cases injections have not been used to reduce the ocular tension in primary congestive glaucoma as advocated by Weekers and Magitot. It was used in two eyes with secondary glaucoma, however. In one eye the tension was lowered and in the other it was not affected.

In summary, retrobulbar alcohol injec-

tions have been done on 15 patients who have had severe or protracted ocular pain and partial vision. No permanent complications have followed the injections and in most cases the final visual acuity has been better than it was at the time of treatment.

DISCUSSION

Retrobulbar alcohol injections are a valuable adjunct to ophthalmic therapy for the relief of severe protracted ocular pain. The fear of permanent extraocular palsies, neuroparalytic keratitis, and injury to the optic nerve does not seem to be warranted when the method of alcohol injection described in this report is used. No permanent complications have been noted following such injections in 41 blind eyes and 15 eyes with partial vision.

Alcohol injections into peripheral nerves relieve pain by interrupting the transmission of the nerve fibers. The proteins in the fibers are coagulated at the site of injection and the fibers degenerate peripherally from this point. If the nerve is not injected but the surrounding area is infiltrated with alcohol all of the fibers may not be destroyed but transmission is depressed. The peripheral portion of the fibers usually regenerate in a few months after injury by a migration of the axones from the uninjured part of the nerve.

Injections into sensory ganglions, on the other hand, destroy the ganglion cells and cause a permanent anesthesia of the area supplied by the nerve. Permanent anesthesia of the eye is not produced by retrobulbar alcohol injections for the ganglion cells of the sensory nerves from the eye are located in the Gasserian ganglion and not in the orbit.

It is, therefore, not necessary to inject alcohol into the posterior part of the muscle cone near the ciliary ganglion to relieve ocular pain. Infiltration of the more anterior portion of the muscle cone will interrupt the nerve transmission just as effectively and has the advantage of causing less damage to the extraocular muscles.

It is interesting that corneal sensation which is either lost or markedly diminished following the injection of alcohol usually returns to some degree within a few weeks after injection even though the pain is controlled. A similar return of corneal sensation and not pain has been noted after sectioning of the fifth nerve for trigeminal neuralgia.[9] Likewise the sensation of touch returns before pain after injections of other sensory nerves of the body.[10]

The parasympathetic motor nerves to the pupil and ciliary body are interrupted to some extent after retrobulbar alcohol injections. Contraction of the pupil and accommodation, however, return within several weeks.

The optic nerve is apparently protected to a marked extent from the effects of alcohol by its sheath. There was no reduction of vision after the injection of alcohol in 15 eyes with partial vision nor was there evidence of injury to the optic nerve in 15 eyes examined histologically. It is possible that injection of larger amounts of alcohol than were used in this series of patients might injure the optic nerve. The case of Cordes demonstrates that injection of alcohol into the nerve will destroy it. The use of a preliminary injection of novocain should indicate whether the tip of the needle is in the optic nerve or not.

In this series of cases alcohol injections did not seem to have a detrimental effect on the course of ocular lesions. However, in other studies Kornblueth and I have found that corneal transplants do extremely poorly when they are grafted into eyes of rabbits which have previously received retrobulbar alcohol injections. These poor results were not due to an anesthesia of the cornea, for all of the nerves could be sectioned in the periphery of the cornea of the recipient animal and clear grafts could be obtained.

Kornblueth[11] has made further studies on the effects of retrobulbar alcohol injections in rabbits and rats and has found that the rate of mitosis in the epithelial and stromal

cells was reduced. The healing of small lesions in the corneal epithelium was not impaired but the regeneration of the epithelium was definitely impeded when the whole cornea was denuded. This would suggest that retrobulbar alcohol injections might be detrimental to healing of large corneal ulcers.

Weekers and Magitot, however, have advocated the use of alcohol injections for corneal ulcers and have not reported a delay in the healing of these lesions. We have not used alcohol injections in enough cases with corneal ulcers to establish what effect it will have on repair, but the experimental findings in rabbits suggest that it should be used with caution in patients with corneal ulcers. They also suggest that, if a keratoplasty or keratectomy is contemplated, an interval of at least 3 to 4 months should elapse between the time of injection and operation.

Alcohol injections did not reduce the ocular tensions in patients with absolute glaucoma in this study. However, it may be indicated in less advanced cases of glaucoma which fail to respond to medical therapy, for Weekers and Magitot have reported that the tension is reduced in some patients with acute congestive glaucoma, and Kornblueth has found that the ocular tension and rate of formation of the aqueous is reduced in normal rabbit eyes following alcohol injections.

The relief of ocular pain by alcohol injection should not be allowed to influence one in deciding whether an eye should be removed in a patient with questionable sympathetic ophthalmia or intraocular tumor. It should also be established that a patient's pain is real and not imaginary before an alcohol injection is given.

SUMMARY

Retrobulbar injections of alcohol have produced a dramatic relief of pain in 35 patients with blind eyes and in 15 patients with partial vision for at least 1 to 3 months. No beneficial effects have been noted from the alcohol injections other than relief of pain and blepharospasm. Transient extraocular palsies have occurred but no permanent complications such as injury to the optic nerve, extraocular palsies, neuroparalytic keratitis, or sloughing of the cornea have been noted.

Stanford University Hospital (15).

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ACUTE SECONDARY GLAUCOMA DUE TO SPONTANEOUS RUPTURE OF THE LENS CAPSULE*

H. SAUL SUGAR, M.D.
Detroit, Michigan

Recent experience with three cases of spontaneous lens capsule rupture indicates the importance of this condition in the differential diagnosis of the secondary glaucomas. It was not included in the classification of the glaucomas which I have been elaborating and modifying during the past several years not only because I had never seen such a case, but because of the difficulty of classifying the cause of the increased intraocular pressure.

Two diseases of the crystalline lens must be considered in discussing spontaneous lens-capsule rupture. These are lenticular intumescence and so-called spontaneous absorption of cataract. The first, lenticular intumescence, is ultimately the cause of spontaneous lens-capsule rupture. Intumescence lasting several years leads to thinning of the capsule to such a degree that small rents in the membrane result. In the cases presented here, the cataracts in the involved eyes were present for 8, 10, and 25 years, respectively.

The ophthalmic literature contains many cases in which the lens substance was absorbed through an allegedly intact lens capsule (Hess[1]). In relation to these, cases of spontaneous lens-capsule rupture are few in number. Since the latter involve the anterior capsule, it would be expected that they would be fewer in number than those involving the thinner posterior capsule. The relative numbers of these cases suggest that the cases of spontaneous lens absorption are really cases of posterior lens-capsule rupture. Experience with morgagnian cataracts and lens absorption after perforation of the capsule suggests that the lens cannot be absorbed without capsular rupture and that these cases of spontaneous lens absorption are really due to the presence of dehiscenses in the posterior capsule. It is probable that in posterior capsular rupture the lens material cannot find its way into the aqueous but is held back by the zonular ligament if the particles are large.

The frequent occurrence of glaucoma and iritis in connection with the so-called spontaneous absorption of cataract is further suggestive evidence of the relationship between the absorption of the lens and capsular rupture since the increase in intraocular pressure and anterior uveitis are associated with the capsule tears in the known cases of spontaneous capsule rupture.

Four instances of glaucoma occurred in the 34 cases of spontaneous cataract absorption collected by von Reuss.[2] Natanson,[3] Verry,[4] Gifford,[5, 6] and others reported similar cases.

The first reported case of spontaneous capsular rupture associated with increased intraocular pressure was that of Ulrich,[7] in 1882. Von Szily[8] reported a case and mentioned that of Ulrich and one of von Arlt. Gonzales and Gonzales,[9] Rollet and Genet,[10] Knapp,[11] and Kaufman[12] reported cases of this type.

The cause of the glaucoma in spontaneous lens-capsule rupture is important. Three possibilities are apparent: (1) Chemical irritation by lens substance, (2) increased protein content of the aqueous which tends to lessen the osmotic differential between the aqueous and the blood serum, and (3) obstruction of the trabecular spaces by particles of lens substance.

The first is the only condition which appears to be present in every case. I am, therefore, placing this form of glaucoma in the classification of the secondary glaucomas under the group of secondary glaucomas which are probably due to over-production

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of aqueous as a result of irritation of the ciliary processes:

SECONDARY GLAUCOMAS

Each may be subdivided into a noncongestive and a congestive phase. Some never enter the congestive phase.

A. *Secondary glaucomas due to mechanical blockage of the trabecular spaces*
 1. Obstruction by iris
  a. Acute secondary glaucoma due to lenticular intumescence
  b. Acute secondary glaucoma due to dislocation of lens into anterior chamber
  c. Glaucoma following operation for cataract—aphakic obstructive glaucoma—due to delayed reformation of the anterior chamber
  d. Glaucoma associated with essential progressive atrophy of the iris
 2. Obstruction of the trabecular spaces by particulate matter
  a. Glaucoma capsulare
  b. Pigmentary glaucoma
  c. Glaucoma due to obstruction by lens particles
  d. Glaucoma due to tumor growth
  e. Glaucoma due to cellular debris associated with active or healed iridocyclitis
B. *Secondary glaucomas due to lack of communication between the anterior and posterior chambers*
 1. Secondary glaucoma due to seclusion of the pupil
 2. Secondary glaucoma due to total posterior synechia
C. *Secondary glaucomas probably due to overproduction of aqueous as a result of irritation of the ciliary processes*
 1. Glaucoma associated with posterior dislocation of the lens so latter touches ciliary processes
 2. Glaucoma associated with cyclitis and anterior choroiditis
 3. Glaucoma due to spontaneous lens capsule rupture
D. *Secondary glaucomas due to obstruction of venous drainage*
 1. Experimental and clinical glaucoma due to vortex vein obstruction
 2. Secondary glaucoma in pulsating exophthalmos
E. *Secondary glaucomas due to newly proliferated anastomotic vessels involving the Schlemm's canal mechanism in rubeosis iridis (diabetic and arteriosclerotic) and following occlusion of the central retinal vein*
F. *Secondary glaucomas resulting from trauma*
G. *Secondary glaucomas associated with epidemic dropsy*
H. *Secondary glaucomas associated with choroidal angioma*

CASE REPORTS

CASE 1

History. Mrs. R. K., aged 69 years, was first seen by me on July 2, 1948, through the kindness of Dr. Joseph Kopel. She was too uncomfortable to leave her bed. She complained of severe pain in her left eye of two days' duration. The right eye had been successfully operated for cataract eight years previously. The left vision had been obscured by a cataract for nearly eight years and had never been examined during that time.

The right eye was pale, soft, and showed evidence of an iridectomy and aphakia. The left eye was somewhat congested but the anterior chamber appeared clear. The intraocular pressure was 60 mm. Hg (Schiøtz). The anterior chamber did not appear to be particularly shallow. The pupil was not dilated, and showed a hypermature cataract. Physostigmine was instilled and 0.25 gr. morphine sulfate was administered. The pain was relieved and the intraocular pressure was reduced to 32 mm. Hg. Pilocarpine nitrate (2 percent) was ordered for instillation four times daily.

On the following morning the patient began to have severe pain in the left eye associated with nausea and vomiting. The eye was moderately congested and the aqueous was somewhat cloudy, although the cornea was clear. Because of lack of coöperation, slitlamp biomicroscopy could not be done. The patient was hospitalized and an iridectomy-iridencleisis operation was done.

Following the conjunctival closure there was a sudden motion of the contents of the lens which at the time suggested dislocation of the lens. Atropine was instilled. The eye was red on the following day, and the intraocular pressure remained high for a week, during which time a considerable amount of fibrinous material was present in the anterior chamber. Scopolamine and penicillin were used locally.

By July 22, 1948, the eye was much paler. There was no evidence of lens dislocation,

but the lens nucleus could now be seen clearly with little overlying cortex. No perforation of the anterior capsule could be found. Gonioscopically, the angle was open except at the limbus of the coloboma. The tension was within normal limits. Within six weeks after the operative interference the eye was entirely pale.

The diagnosis was not made in this case until the appearance of Case 2, when it was realized in retrospect that this was an instance of posterior lens-capsule rupture. The inability to do slitlamp biomicroscopy delayed proper evaluation of this case. At the onset of symptoms, the anterior chamber was clear by gross observation. The normal anterior-chamber depth and the absence of pupillary dilatation were against the diagnosis of acute glaucoma due to lenticular intumescence.

The subsequent gonioscopic appearance of the chamber angle tends to corroborate this. I can only speculate that a small perforation of the posterior capsule was causing a chemical irritation of the ciliary body producing a type of secondary glaucoma such as appears with cyclitis.

The lowering of intraocular pressure by the use of eserine for a brief time, although it suggests that chamber angle block was relieved, cannot be considered significant, since it was transient and since the angle was subsequently found to be wide and completely free of synechias except at the coloboma area.

The motion of the lens capsule following the operation was evidently a sudden increase in the size of the opening in the posterior capsule so that the liquid cortex was suddenly evacuated. The subsequent course, including the fibrinous iritis and the rapid subsidence with marked thinning of the lens, is evidence of sudden expulsion of the liquid cortex into the aqueous. Since there was no visible anterior-capsule dehiscence at this time or subsequently, a rupture of the posterior capsule must be assumed.

Comment. I have recently had an opportunity to observe the process of absorption of a lens in which the posterior capsule was ruptured. This occurred in a 15-year-old boy who was struck in the left eye on April 29, 1949. The lens was not dislocated but a vertical linear rupture of the posterior capsule was visible. The lens material bulged through the tear giving the appearance of a posterior lenticonus. The lens became opaque in its posterior aspects gradually, and separation of the fibers, with thinning of the lens, occurred. No conjunctival injection remained after the first week. The anterior chamber remained clear during the process. There was no increase in intraocular pressure. The absence of a beam in the aqueous fitted in with the observations in Case 1.

CASE 2

History. Miss A. A., aged 52 years, was first seen on August 17, 1948. She complained of severe pain in her left eye for about one day. She had had a uveitis associated with the formation of a cataract 10 years previously. Tuberculin treatment was used at that time.

Eye examination. The visual acuity was 20/20 with the right eye and light perception with inaccurate projection, left eye. The right eye was entirely normal. The left conjunctiva was moderately injected. The anterior chamber was so cloudy as partly to obscure the iris and lens. No deposits were present on the posterior corneal surface. Particularly noteworthy was the inability to distinguish by optical section the separation between posterior corneal surface and anterior chamber. The intraocular pressure was over 70 mm. Hg (Schiøtz).

A diagnosis of capsular rupture was made and an anterior chamber puncture done with a 27-gauge needle from the temporal side. The aqueous was examined microscopically and found to contain finely granular particulate matter. Scopolamine was instilled.

The eye was reexamined 30 minutes later, at which time the secondary aqueous was quite clear. A morgagnian cataract was present. Two tiny holes in the anterior capsule near the nasal margin of the pupil were

seen. Tiny tufts of lens material protruded through these openings. The eye was treated with scopolamine instillations.

Four days later the tonometric reading was 28 mm. Hg (Schiøtz). A week after this it was 14 mm. Hg. The lens capsule was apparently closed, the cortical material having been evacuated. The eye remained completely quiet for five months. The original picture then recurred. An anterior puncture was done. The aspirated aqueous contained 230 mg. percent protein. The eye became quiet within 48 hours.

Comment. The differential diagnosis of spontaneous capsular rupture may be very difficult, especially since the anterior chamber may be cloudy with anterior capsular rupture and relatively clear with posterior capsular rupture. The history of long-standing cataract with breakdown of the cortex is the necessary background for such an occurrence. Such a history in the presence of increased intraocular pressure should always suggest the possibility of capsular rupture.

With a very cloudy anterior chamber and the above history anterior-chamber puncture may make possible both diagnosis of anterior-capsular rupture and cure of the glaucoma as in the second case reported. From the literature and the experience with these two cases, it is evident that once the liquid cortex is vacuated, closure of the defect is possible.

CASE 3

History. This patient, J. R., a 64-year-old man, was first seen by me on July 6, 1949. He complained of redness and pain involving the left eye, for the previous six days. He had had a cataract in this eye for the past 25 years.

Eye examination. The right eye was entirely normal, with a normal tension and anterior-chamber depth. The left visual acuity was limited to light perception, temporally. The tension was 70 mm. Hg (Schiøtz). The corneal epithelium was hazy. The anterior chamber was of normal depth with some clouding of the aqueous. A morgagnian cataract was present.

An anterior-chamber puncture was done. The aqueous which was removed was slightly opalescent. Biomicroscopic examination immediately after the anterior-chamber puncture showed an outpouring of fibrinlike material into the anterior chamber. No anterior capsular perforation could be seen in the 4-mm.-wide pupil area.

Atropine was instilled daily. The tension was 60 mm. Hg on the next day and 48 mm. Hg on the following day.

Operation. On July 11, 1949, under local anesthesia, a bevelled keratome incision was made 2 mm. from the upper limbus, penetrating the anterior capsule. The milky cortical material was allowed to escape through the wound. A small nucleus filled the pupil area. A cystotome was introduced and the nucleus pushed downward. A Daviel spoon was then introduced and the nucleus broken up by crushing it between the spoon and cornea by using a lens expressor externally. The entire nucleus was removed. The anterior chamber was irrigated.

The capsule was then observed anterior to the iris above. This was removed with a capsule-remnant forceps. No vitreous was lost. The pupil was entirely clear. Atropine was instilled.

On the following day the anterior chamber contained fibrinous exudate and the tension was hard. The wound remained intact and the chamber cleared slowly under atropinization. On the third postoperative day the tension became soft and has remained so, with brief rises to 32 mm. Hg.

CONCLUSION

Three cases of spontaneous capsular rupture with acute secondary glaucoma are reported.

The difficulties of differential diagnosis and the place of the condition in the classification of the secondary glaucomas are considered.

It is suggested that cases of spontaneous lens absorption are due to posterior capsular rupture.

76 West Adams (26).

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THE RETINAL ARTERIOLES IN COARCTATION OF THE AORTA*

14-YEAR OBSERVATION OF A CASE

BEATRICE W. CONNELLY, M.D., AND GLEN GREGORY GIBSON, M.D.
Philadelphia, Pennsylvania

Coarctation of the aorta, a congenital or developmental partial or complete stenosis of the artery at or near the insertion of the ductus arteriosus, produces an elevation of the systemic blood pressure above the lesion, and relatively normal tension below the level of the constriction. This elevated blood pressure is presumably present in the retinal arterioles. There has not been much ophthalmic interest in this vascular anomaly because there are no ocular symptoms produced by it.

Since the cause of this form of hypertension is most probably a simple mechanical obstruction which increases the peripheral resistance to the flow of blood, uncomplicated by toxic, hormonal, neurogenic, and other unknown factors which operate in essential hypertension, we have at our disposal, in these rare cases, an opportunity to observe the responses of the retinal arterioles to simple increased blood pressure. Since the complicated mechanisms are not completely understood, by which the changes of essential hypertension are produced, it is possible that some information about this process might be forthcoming from the observation of what occurs in the retinal arterioles in patients who have coarctation of the aorta. It is possible, however, that the mechanism of the elevated blood pressure is not simple increased peripheral resistance but that other factors, such as renal ischemias, are operating in these cases.

It is known that there exists a relationship between the degree of the retinal arteriolar changes in essential hypertension and the two factors which seem most important in determining the effect of the hypertension on the patient. Those two factors are the severity and the duration of hypertension. It is also recognized that, in a comparatively

small group of patients with hypertension, the relationship is disproportionate between arteriolar change, on one hand, and severity plus duration, on the other. This disproportion may be either more or less than the amount that is expected.

Ophthalmologists who have studied large series of these patients and correlated the retinal and clinical findings are able to recognize these disproportionate cases. The patient whose record is reported here, represents an instance of this disproportion. It seems reasonable to assume that the disproportion, in this case, between the actual and the expected amount of sclerosis is due to the difference in the mechanisms of the two entities; namely essential hypertension and coarctation of the aorta.

One of the unknown points in hypertension is which comes first, the hypertension or the attenuation or uniform narrowing of the retinal arterioles. It is an unsettled question whether the attenuation is the cause of the hypertension or the result of the hypertension. Likewise, the mechanism of the sclerosis is unknown. While one can draw no conclusions from one case, it would seem that the findings in this case of coarctation offer material for thought on these interesting and important points. There are numerous references in the literature about the retinal changes in coarctation of the aorta and all the findings observed in our case have been recorded as occurring in previously reported cases.

PREVIOUSLY REPORTED CASES

Schwartz,[1] in reporting five cases, found the retinal picture to vary from normal in the mildest case, to tortuosity, spasticity, arteriovenous nicking, and increased reflex stripe in the more severe cases.

Blue,[2] in one case, found minimal early arteriosclerosis of the retinal vessels. Rhodes and Durbin,[3] in one case, reported narrowing and tortuosity. Draper,[4] in a report of one case, found normal fundi as did Shapiro.[5]

Christensen and Hines[6] found that, among 80 patients who had fundus examinations, only 22 had essentially normal fundi. Generalized narrowing of the retinal arterioles was frequent. Higher grades of sclerosis were found in cases when the diastolic pressure was over 110 mm. Hg. No patient had severe hypertensive retinopathy.

Among the many other references are listed fundus findings similar to those herein. These range from normal fundi in cases with little or no hypertension to more advanced changes in cases with hypertension. However, reports of repeated fundal examinations over an extended period of time in the same patients were not encountered in the literature. The justification for this report is that cases of long-time observation on coarctation were not found, and there was no reference to an attempt to correlate the significance of the findings in these cases with the significance of the findings in cases of essential hypertension.

CASE REPORT

History. The patient, a white man, was first examined at the age of 21 years, in June, 1933. The chief complaint was occasional diffuse pain in his legs and lower abdomen for the past four years. The past history revealed that he had also had pain in his legs at the age of 10 years which lasted for three years.

The clinical examination showed a well-developed white male weighing 155 pounds, showing redness of the face and neck. There was no cyanosis and no clubbing of the fingers. A large pulsating vessel was seen and felt in the upper right interscapular region, also on the left side at the level of the first thoracic segment. The subclavian arteries likewise showed marked pulsations. The radial arteries had a slightly increased amplitude, while the femoral arteries could not be felt. The blood pressure was, in the right arm, 200/80 mm. Hg, and 160/95 mm. Hg in the left arm. Auscultation of the heart revealed no significant murmurs and the

heart showed no enlargement.

Electrocardiograms showed a regular sinus rhythm. There was no axis deviation. X-ray examination of the thorax revealed the typical erosions of the under surfaces of the ribs which is commonly noted with coarctation of the aorta. The heart shadow was not above the upper limits of normal size.

The clinical diagnosis was coarctation of aorta, and a fundal examination was requested by the cardiologist, Dr. Roesler.

The external ocular examination, the visual fields, and the ocular media were negative. The fundal examination was negative except for the blood vessels. All the arterioles were more tortuous than normal and two were mentioned as being unusually tortuous. There was a slight accentuation of the reflex stripe on the retinal arterioles. All the arterioles, instead of being larger than normal, showed a moderate attenuation or generalized narrowing of caliber in their entire courses, and this change was very marked in their peripheral thirds. There was no sclerosis, no angiospasm, no pulsation, and no retinitis. The patient would not consent to fundus photography.

Course. The patient was reëxamined in October, 1934, and there were no significant changes. He was reëxamined in June, 1947. He complained of shortness of breath on exertion, dragging of the legs, and occasional epistaxis. He was now aged 35 years and his weight was 190 pounds. The blood pressure was 180/100 mm. Hg in the right arm, and 184/90 mm. Hg in the left arm. The heart was normal in size. The electrocardiogram showed a regular sinus rhythm; there had developed a minor degree of left axis deviation and the initial deflection showed increase in voltage in the chest leads.

The fundus examination was the same with exception that there were now present very slight focal caliber constrictions indicating retinal arteriosclerosis, grade one, on the basis of four, of the hypertensive type.

COMMENT

It is usual in essential hypertension of the degree and duration known to exist in this patient, that one should expect more advanced and severe changes than those which were found. There are two possible explanations for this disproportion, the first of which is the relatively low diastolic pressure. It is well known that the damage to the arteriolar tree is determined not by the height of the systolic but by the height of the diastolic blood pressure. The relatively low diastolic pressure in our patient accounts, in part, for the disproportion between the clinical and the retinal findings.

This fact is somewhat, although not entirely, balanced by the fact that the diastolic pressure in coarctation cases does not undergo the fluctuations nor remissions which occur in many types of essential hypertension. The second possible cause for the absence of more advanced changes is the absence of any hormonal, toxic, or neurogenic influences on the arterioles themselves.

The presence of the severe attenuation or uniform narrowing in this mechanical type of hypertension, where none of the factors which produce essential hypertension are active, would seem to offer strong implications that the attenuation observed in essential hypertension is not the cause of the hypertension but rather represents the reaction of the vascular tree to hypertension.

The criterion for the presence of hypertensive sclerosis in this case are the ones included in Wagener's[7] report on hypertension for the American Ophthalmological Society; namely, the presence of slight focal constrictions or localized areas of caliber narrowing. The marked tortuosity of the main arterioles is matched by the veins and is considered to be a vascular anomaly and is not an indication of sclerosis. This was present in the same degree in the later examination.

The fact that these changes occur in coarctation suggest that sclerosis per se may repre-

sent a further degree of reaction of the arteriolar tree to simple pressure. The fact that the sclerosis is of such slight degree, after such a long duration, suggests that the more advanced changes encountered in essential hypertension are the result of a combination of causes working on the arterioles as well as to higher degrees of diastolic pressure.

It is admitted that the evidence in this one case, and the changes and interferences drawn from this case are not sufficiently convincing to constitute proof of the premises which have been offered but, on the other hand, it seems that their significance is worthy of attention of students of this problem.

SUMMARY

A case of coarctation of the aorta, in which detailed fundus examinations were recorded when the patient was aged 21 and 35 years is reported. On the first examination no sclerosis of the retinal arterioles was present but, 14 years later, there were minimal signs of sclerosis.

It is pointed out that one would expect much more sclerosis to be present than was found on the basis of observations in essential hypertension. There was uniform narrowing (attenuation) of all the arterioles on both examinations.

It is postulated, but not proved that attenuation is the reaction of the arteriolar tree to elevated blood pressure, and that the elevated pressure of essential hypertension produces the attenuation.

Likewise, it seems fair to conclude that sclerosis can be produced by, or is a reaction of the arteriolar tree to, simple elevated blood pressure. The rate and degree of the sclerotic process is increased considerably in the case of hypertension due to higher diastolic pressure and other factors which may be operating in essential hypertension.

255 South 17th Street (3).

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ENUCLEATION AND ALLIED PROCEDURES*

PART I: A REVIEW

JACK S. GUYTON, M.D.
Baltimore, Maryland

Removal of an eye by the mutilating and seldom utilized operation of "extirpation," which consists of slashing the eyeball from the orbit without attempting to preserve remaining orbital structures, was rendered obsolete in 1841 by the introduction of "enucleation," a procedure whereby the eye is shelled out of Tenon's capsule. During the succeeding century rather little actual progress was made in the field of eye removal.

True, descriptions of "evisceration" (1872), and of implantation of a foreign material within the sclera (1885), or within Tenon's capsule (1886), led to collection of considerable data as to the relative merits of these procedures with respect to cosmetic appearance, prevention of sympathetic ophthalmia, and prevention of postoperative meningitis. Introduction of the Snellen "reform eye" in 1898 greatly reduced the discomfort and disfigurement so prevalent with the older "shell" prosthesis. Reactions of orbital tissue to various grafts and to foreign substances embedded within it were recorded. Countless descriptions of minor variations in operative technique permitted the sifting out of a few with value. Methods were devised for at least partially correcting deformed or contracted sockets. Introduction of the plastic "acrylic" afforded a lighter, more durable, easier shaped material than glass for making well-fitting prostheses. Finally, recognition that cosmetic defects were likely to follow removal of an eye by any of the methods in use stimulated many ingenious, if largely unsuccessful, attempts to prevent or correct such blemishes.

In 1945 Ruedemann[1] described an artificial eyeball (first used in January, 1941) which he placed in Tenon's capsule at the time of enucleation and to which he actually attached the rectus muscles. He therewith initiated a new era in the enucleation field. In 1947, Cutler[2] described a semiburied implant (his "ring" implant, first inserted in October, 1945) to which the rectus muscles were attached and to which a prosthesis could be coupled after healing of the socket. This two-piece principle made it possible to assure correct orientation of the prosthesis by varying the size and shape of the anterior segment and the position of its coupling pin.

At the Wilmer Institute, utilization of Ruedemann eyes was begun in June, 1945, and of Cutler ring implants in March, 1946. The early cosmetic results were amazingly good, especially with Cutler implants, but a number of these implants extruded some months after successful insertions.

A technique was therefore devised which embodied the two-piece principle of Cutler, but also satisfied an additional new principle. When healing is complete, there is no epithelial-fibrocytic transition at any point, and the "exoplant" is in contact with nothing but epithelium rather than partially buried within tissue; this was accomplished, without any sacrifice of motility, by attaching the recti directly to each other at the juncture of two perpendicular tunnels through the exoplant, there being no actual attachment of muscles or other tissues to the foreign body. With this procedure, epithelium grows completely around the muscles as well as behind the exoplant.

From July 15, 1946, to April 1, 1948, 45 of these exoplants were inserted at the Wilmer Institute. The results have exceeded original expectations. Motility of the prostheses has equalled that obtained with the

Cutler implant; there have been no late extrusions of this exoplant nor late infections around it, and it is suitable for delayed insertion as well as for use at the time of enucleation.

A number of modifications of the semiburied implants embodying the principles of Ruedemann and of Cutler have more recently been devised. The best of these appears to be that of Whitney and Olson,[3] wherein the muscles and Tenon's capsule are attached to a circular strip of tantalum mesh surrounding the implant.

This present report consists of a condensed review of enucleation and related procedures utilized prior to the introduction of semiburied implants with directly attached prostheses (1945), a more complete review of the procedures under development since Ruedemann opened these new vistas, and a description of a new technique involving insertion of an "exoplant" which gives cosmetic results which may prove more uniform and permanent than those attained with any enucleation procedure previously described.

PROCEDURES WITHOUT DIRECTLY ATTACHED PROSTHESES

EXTIRPATION

The first recorded technique for complete removal of the eyeball was described by Bartisch[4] in 1583. Much earlier, Celsus[5] had described obliteration of the anterior segment of the eyeball, and Paré[6] (1579) had advocated excision of unduly prominent staphylomas.

The procedure of Bartisch, "extirpation," consisted in passing a needle and thread through the eyeball and then, while making traction on the thread, passing a knife or sharp-edged spoon into the orbit behind the globe and severing its attachments. This operation was so brutal that Bartolini[7] is cited as pulling out a cancerous eye by hooks, a procedure he considered milder than that of extirpation—although the patient died in convulsions three days later.

It is significant that while Paré,[8] the father of modern surgery, described prostheses as early as 1579 for use after loss of an eye because of trauma or suppuration, he did not mention operative removal of the eyeball. Yet he described such operations as couching a cataract, correcting an entropion, and even restoring a drainage pathway between the conjunctival sac and nose.

Certainly the operation of extirpation was so severe and mutilating it was used only for removal of eyes with cancerous or fungoid growths; globes which were merely painful or suppurating were simply incised and allowed to drain. The severity of extirpation is well illustrated by Bowman's report[9] that from 1839 to 1848 (immediately preceding adoption of "enucleation" as the means of removing an eyeball), only four extirpations were performed at the Royal Ophthalmic Hospital in London, although during that period 1,419 eye operations of all types were performed and 2,302 cases of injury, 23 cases of "fungus of the globe" and 16 cases of orbital tumor were examined.

The dread in which the extirpation operation was held was largely a result of the accompanying pain, since anesthesia was not generally available until about 1850. However, actual mutilation resulted from the complete disregard of the integrity of the orbital structures surrounding the eyeball, leading to a socket generally unsuitable for a prosthesis and consequently cosmetically disfiguring.

SIMPLE ENUCLEATION

Tenon's capsule was first described in detail in 1806, but it then appears to have been forgotten until 1841.[10] In that year, Ferrall[11] and Bonnet[12] independently reëmphasized its significance and proposed the operation of simple enucleation. Ferrall had actually performed such an operation, but Stoeber[13] (1842) is generally credited with popularizing it. This operation consisted of making a circumcorneal incision of the conjunctiva, cutting the muscle insertions without disturb-

ing Tenon's capsule, and cutting the optic nerve close to the globe.

Enucleation did not immediately replace extirpation as the more common procedure, because introduction of general anesthetics about that time made the latter operation far less horrible, though no less disfiguring, than formerly. Not until about 1855 did enucleation come into general use for cases other than malignant growths, especially as a result of Critchett[14] advocating it for cases of staphyloma, intraocular foreign bodies, symblepharon, inflamed and painful blind eyes, and inflamed eyes where sympathetic ophthalmia was feared.

As originally described, no sutures were used following simple enucleation. However, during the succeeding century practically every conceivable type of suture for closing the conjunctiva, and/or uniting two or more of the rectus muscles, and/or closing Tenon's capsule has been described.[15-18] About the close of the 19th century considerable emphasis was placed on the exact methods of closure, but conclusions of different authors were, on the whole, variable. It seems probable that the only suture of real advantage was that which closed the conjunctiva and thus shortened the healing time.

For many years after simple enucleation was first described, minor details of technique were emphasized or argued about and many special instruments (each bearing a proper name) were devised: for example, Landolt's enucleation scissors, Brazil's enucleation knife, Luer's optic-nerve hook, Schweigger's enucleation hook, deWecker's, Terson's, and deWelt's enucleation spoons, and Joseph's hook neurotome. Even in recent years a few descriptions of minor technical details, *rarely original and in no way important*, have crept into the literature.[19-22]

In retrospect, the most important details of technique which have been added to the original decriptions of simple enucleation are those designed to preserve as much conjunctiva as possible. It is generally considered advisable to suture the conjunctiva horizon-

tally because an excess of conjunctiva is available from above and below, but not from each side, for covering the space previously occupied by the cornea. In the presence of preoperative infection no sutures should be used.

Insertion of a conformer at the time of enucleation is of definite value in preventing contracture of the conjunctiva, as well as in preventing conjunctiva from prolapsing between the lids should moderate postoperative hemorrhage occur within the orbit.[23] Should postoperative infection occur, it is especially important that a conformer with a large central opening be kept in the socket to prevent contracture.[24]

SIMPLE EVISCERATION

Evisceration of the globe with retention of the sclera was first described as a deliberate procedure by Noyes[25] in 1872. He merely incised the anterior aspect of the globe and wiped out all contents except cornea and sclera. Graefe,[26] in 1884 advocated evisceration as preferable to enucleation as a means of obviating danger of meningitis from cutting the optic nerve in the presence of a purulent infection. Graefe removed the cornea as well as the intrascleral contents.

In 1898 Hall[27, 28] described an addition to simple evisceration which consisted of removal of a disc from the posterior sclera together with a small piece of optic nerve, after excising the cornea and wiping out the intrascleral contents of the globe. Gifford[29] (1900) advised leaving the cornea intact in order not to reduce the amount of available conjunctiva, and stated that "evisceration" was a misnomer unless the cornea was left intact. Nicati[30] advocated removal of all sclera posterior to the attachments of the rectus muscles, scooping out the anterior segment, and leaving the cornea intact.

Gifford[31] (1914) later reported using a pressure bandage to flatten the corneoscleral envelope after evisceration, thereby obtaining as a stump a large flat disc which was quite satisfactory from the standpoint of the

prosthesis. Dimitry[32] redescribed the Hall operation, and shortly afterward[33] advocated sewing the anterior and posterior lips of the sclera together to give a flat stump.

Lister[34] advised removal of all the sclera except a frill around the optic nerve when evisceration was performed because of pan-ophthalmitis, thus cutting down the prolonged healing time incident to suppuration of the anterior portion of the sclera. This procedure was again advocated by Weve[35] in 1939. Khramelashvili[36] advised opticociliary neurectomy at the time of simple evisceration as a means of reducing postoperative reaction.

ENUCLEATION OR EVISCERATION WITH IMPLANTATION

In 1885 Mules[37] reported burying hollow glass spheres within the scleral envelope at the time of evisceration. He removed the cornea, inserted the implant, and sewed the sclera vertically and the conjunctiva horizontally. Out of the nine cases he originally reported, the implants had to be removed or were extruded in four and in one other there was a fistula at the site of the scleral incision.

Mules initiated his operation with the idea of utilizing the implant to take up space formerly occupied by the ocular contents and thus prevent sinking in of the socket and also to have a stump which moved as well as a normal eye. When he reported this work, before the Ophthalmological Society of the United Kingdom, he demonstrated a patient on whom he had performed this operation. In the discussion, Frost commented that he could see no better movement of the prosthesis than after simple enucleation, although the stump itself moved perfectly.

In 1886 Frost[38] reported burying hollow glass spheres within Tenon's capsule at the time of enucleation. He performed this operation on six patients, but the implant was retained in place in only one instance. In 1887 Lang[39] independently reported a similar

operation with implantation of glass, celluloid, or hollow silver balls. Out of 16 cases, the implant was retained in place in 14. He advocated this procedure because he believed the cosmetic results were better than after simple enucleation and he preferred it to Mules's operation because it gave less postoperative reaction, pathologic specimens were not damaged, and complete removal of the globe obviated the possibility of late development of sympathetic ophthalmia.

During the years succeeding the reports of Mules, Frost, and Lang, the literature became redundant with reports of varied techniques for insertion of implants either into Tenon's capsule or the scleral cavity, with descriptions of implants of various materials and of different sizes and shapes, and with arguments as to the relative merits of theses types of operations as compared with each other and as compared with simple enucleation and simple evisceration.

As the years passed, improved techniques gradually reduced the percentage of implants which were extruded. Thus Verrey,[40] in 1898, collected 343 cases of Mules's operation with extrusion of the globe in 21.3 percent, while Burch,[41] in 1944, reported failures in only 9.6 percent of 52 operations.

Huizinga[42] (1900) described what was essentially Mules's operation but with removal of a disc of sclera from the posterior aspect of the globe along with a portion of optic nerve, and implantation of a fenestrated aluminum ball. He believed removal of the posterior disc reduced postoperative reaction, a view which was later expressed by Ray[43] and by Dimitry.[44] Fox[45] advised tenotomizing the recti as an addition to Mules's operation. He believed this reduced the incidence of extrusions of the implant.

Dimitry at one time preferred leaving the cornea intact in performing Mules's operation, but he soon afterward condemned this procedure because of late thinning and often eventual rupture of the cornea.[33] O'Connor[46] advocated retention of the cornea, with cruciate incisions through cornea and sclera,

and closure by suturing the apices of the corneal incisions and then covering the cornea with a conjunctival flap. Poulard[47] likewise retained the cornea, and implanted ovoids instead of spheres in those cases where he did not retain the cornea.

Burch[48] described his technique as consisting of making a scleral incision around two fifths of the circumference of the globe and just anterior to the superior rectus, removing the intraocular contents, wiping the endothelium off the back of the cornea, inserting a hollow gold ball (usually 18 mm. in diameter but varying from 14 mm. to 20 mm.), and closure of the incision with six fine white silk mattress sutures. This procedure was followed by moderately severe reaction with protrusion of edematous conjunctiva in about half the cases, but Burch believed the reaction was less marked than with the original Mules's operation. The cornea became vascularized in 3 to 6 weeks, but it did not become completely opaque, and Burch did not note thinning or late perforation of the cornea as occasionally described by others.[49]

The size of an implant to be inserted after evisceration must depend on whether or not the cornea is preserved. The implant should not fill the scleral envelope completely, because allowance must be made for some contracture. In general, the implant should be 10 to 14 mm. in diameter if the cornea is removed, or 14 to 18 mm. in diameter if the cornea is retained.

For implantation within Tenon's capsule, Frost originally united the inferior and superior rectus muscles with a silk suture, the same stitch including the overlying conjunctiva, and used another suture to unite the internal and external recti and conjunctiva. Lang also included Tenon's capsule in the sutures. Many variations in the technique of closure have been reported. Verhoeff[50, 51] closed Tenon's capsule by means of a double-armed, 3–0 chromic catgut suture passed successively through both layers of the capsule just in front of the retracted end of each severed rectus tendon, and closed the conjunctiva horizontally.

Berens[52] advocated closure of Tenon's capsule by means of a silk suture which is tied outside the conjunctiva and is removed after healing is complete. Other variations in closure have included closing Tenon's capsule with a purse-string suture, uniting the severed ends of the recti over the then-closed Tenon's capsule, and closing the conjunctiva in still a third layer.

Kirby[53] stressed the care which must be taken not to cut Tenon's capsule, because of the resulting danger of the implant becoming displaced outside the capsule and thus outside of the muscle cone. Kirby[54] also advised closure by overlapping Tenon's capsule obliquely instead of vertically and horizontally.

The percentage of extrusions of implants buried in Tenon's capsule has been found to be minimized by careful attention to the following details: (1) Waiting for complete cessation of bleeding before insertion of the implant, (2) selection of an implant which is never larger than 18 mm. in diameter, with a 14 mm. implant probably the optimum,[55, 56] (3) firm closure of Tenon's capsule and of conjunctiva in separate layers, (4) rigid asepsis, and (5) introduction of a conformer into the socket at the close of operation. Displacement of the implant outside of the muscle cone, even though it is not extruded, has been found to occur all too frequently if Tenon's capsule is ruptured and/or if too large an implant is inserted. Such displacement of an implant is certainly far more detrimental to the cosmetic result than insertion of no implant at all.

After implantation following either evisceration or enucleation, a round stump results, the prominence of which depends on the size of the implant used. If it is very prominent, a shell artificial eye serves best, but if a small implant is inserted and the stump is not prominent, a reform eye is used.[55]

. The different implants which have been described are legion. These include: hollow

silver ball,[57] sponge[58, 59] aluminum frame or fenestrated ball,[60] ball of silk,[61] rubber ball,[62] agar-agar,[63] paraffin ball,[64-66] liquid paraffin,[67-70] autogenous cartilage graft,[71, 72, 219] preserved cartilage,[73] autogenous bone graft,[74] charred bone sphere,[75 76] autogenous fat graft,[77-80] hollow gold ball,[52, 81] preserved tendon,[82] hollow glass in the form of either a sphere or an ovoid, or a grooved sphere,[37, 39, 47, 83] polyviol[78, 84] (a soft plastic which causes considerable tissue reaction), acrylic[85-90] in the form of a solid or perforated sphere or pyramidal shaped, or designed so the rectus muscles can be sutured to it, hollow vitallium sphere,[91] perforated tantalum sheet in four-leaf pattern bent into cup shape,[92] celluloid sphere,[39] and dental wax.[44] In addition, freshly enucleated rabbit eyes have been sutured in place of enucleated human eyes,[93-95] and autogenous grafts of skin and subcutaneous fat have been sutured to the muscle tendons, leaving the epithelial surfaces of the grafts exposed.[96]

At present, the materials most suitable for making nonabsorbable rigid implants of inert material are vitallium, tantalum, or acrylic (completely polymerized methyl methacrylate). These materials stimulate the formation of a minimum of surrounding connective-tissue membrane. Gold and glass cause somewhat more fibroblastic proliferation, but not an excessive amount, and are almost as good for buried implants. There is no necessity for using any of the other materials which have been described for this type of implant. It was probably fortunate that Mules, Frost and Lang selected hollow glass spheres for the first implants, because buried glass does not result in a chronic inflammatory reaction inducive to extrusion of the implant. Hollow glass implants are theoretically objectionable in that they might break within the orbit but such accidents are so rare as to be negligible. I can find only one actual report of such an occurrence,[97] but Dr. Clyde Clapp has observed one additional case.[95] In Dr. Clapp's case the implant broke as a result of a blow by a fist; removal of the fragments of glass was laborious but no serious damage resulted.

Pure polyethylene plastic[99] causes as little tissue reaction as any substance known, and should serve best where it is desirable to have a flexible implant which can be molded at the time of the operation.

Implants prepared from animal or human tissues act only as foreign bodies unless they are autogenous grafts, and are in no way desirable. Preserved cartilage, for example, causes a foreign-body reaction and is gradually absorbed.[73] Charred bone (such as Guist's bone spheres) causes considerable tissue reaction ,and O'Brien[100] has reported he had to remove every one he ever inserted because of late erosion anteriorly through the tissue.

Of the various autogenous grafts generally used for burying in the orbit, the amount of eventual absorption is as follows: with fascia lata, almost none; with cartilage, very little but somewhat variable; with dermis, 30 to 40 percent; and with fat, about 60 percent. Cartilage is probably best in that it is rigid, remains viable when implanted, and undergoes little or no absorption; however, tolerance of the orbit for buried implants of the inert materials is so good it seems needless to perform the additional surgery required to obtain cartilage or any other tissue for an autogenous graft.

PROSTHESES

The earliest artificial eyes about which we have information[101] are those in Egyptian mummies. These are of many varieties, such as silver covered with enamel, or marble with colored glass inserts. Aztec and Inca mummies also often have artificial eyes, as do some Greek statues. Mention is made of artificial-eye makers in old Roman literature. However, the first definite mention of artificial eyes being worn by human beings is by Paré[8] (1579). He described and illustrated oval shell prostheses made of gold and silver,

painted and enameled, designed for wearing beneath the lids.

Venetians are credited with making the first glass eyes in 1619.[102] These eyes were molded and were made to order for each individual case. The Venetians' technique was exposed in 1749, and subsequently a few families, especially in France, developed this art and retained what knowledge they gained as family secrets.

Goudard[103] credits a glass blower of Nevers with making the first blown-glass prosthesis in 1740, but Dimitry[102] credits Sauzay with first describing blown-glass eyes in 1867. "Shell" eyes, made of a single layer of glass with relatively sharp edges, were the only ones available until 1898, when Snellen[104-105] first had his "Reform-Augen" made. These eyes consisted of a double shell with a hollow space between the shells and smoothly rounded edges. They represented two advances in the making of artificial eyes: the rounded edges did away with much discomfort, and the prostheses could be made as thick as desired for filling out deep-set sockets. "Shell" eyes were thereafter rarely used except to cover disfiguring or shrunken eyeballs, or in sockets with very prominent stumps.

The Mueller brothers of Wiesbaden began making artificial eyes under the direction of Snellen in August, 1898. Thereafter, most artificial eyes were obtained by choosing the best fit and match from stock collections.[106-107]

Glass eyes have certain inherent faults. A lead-glass prosthesis may last only nine months to two years because of some erosion of the glass by the lacrimal secretion.[108] Soda-glass eyes are more durable, but very fragile. As early as 1863 Davis, an artificial eye maker in this country, stressed the importance of not only obtaining an exact individual fit but also of discarding a prosthesis as soon as it developed any rough surface.[109] Continuation of wearing a glass eye after its surface begins eroding has resulted in much discharge, conjunctival ulceration, and subsequent contracture of the socket, as well as needless suffering.[110]

Hayes[111] collected 14 reports of "explosion" of reform eyes. Such an "explosion" consists of a break occurring in the posterior shell and a sucking in of orbital tissue because of the relative vacuum (approximately one-half atmosphere) within the prosthesis. Such on occurrence is frightening to the patient but is not serious.

Finally, glass eyes can be made to fit a misshapen socket only by an expert glass blower. Thier[112] described a method of actually molding the socket and making the glass prosthesis the same shape as the mold, but such a procedure was not adaptable to very widespread use.

Since 1944, glass eyes have been largely replaced by plastic prostheses of methyl methacrylate.[108, 114-122] Such eyes were only occasionally made[113, 123] before widespread production of them was first begun in that year by dental technicians in the United States Army.

A number of variations in technique may be used for making acrylic prostheses, but the general plan is as follows: An iris disc is made by painting a transparent disc (composed of ethyl cellulose, smooth water-color paper or glass) with permanent pigments, or by utilizing a photographic reproduction of a real iris. This disc is incorporated in a clear acrylic button the shape of the cornea and the anterior chamber. If a large stock of such buttons is available, a direct match can be selected for the fellow eye. Otherwise the iris disc is painted individually to match the other eye. This button is then invested into an acrylic sclera, which may be selected on the basis of stock sizes and shapes or may be prepared from an actual mold of the socket. Opacity of the scleral plastic is obtained by mixing in some titanium oxide for the whitish background and mixtures of red, blue, and yellow pigments to give the desired color. Blood vessels are reproduced on the

scleral portion with red pigment or etching ink, and sometimes red rayon threads. A clear layer of acrylic is then applied and polymerized or "cured."

A great advantage of acrylic prostheses is that they may be ground down to attain the best fit possible. If the prosthesis is shaped from an actual mold of the socket, alterations in shape toward the conventional form are often necessary. Meticulous care must be taken to polish every surface of the acrylic prosthesis.

Disadvantages of the plastic eye consist in its tendency to scratch if handled roughly, and in the occasional hypersensitivity which may develop to the plastic. The occurrence of allergy for methyl methacrylate is reported to be as common as 1 out of 100 or as rare as 1 out of 10,000.[124, 125] Incomplete polymerization is believed to be of importance in the development of such hypersensitivity.

In cases where destruction of the orbital contents is so marked that a prosthesis cannot be retained by the lids it can only minimize, never obviate, the cosmetic defect. The mutilated socket can often be concealed less conspicuously with a plain flesh-colored patch than with a prosthesis shaped and colored like lids and an immovable eyeball. However, prostheses made to cover the entire orbit will often result in a fairly satisfactory appearance. Such prostheses can be made from wax,[126] but are more easily made from latex.[127-130]

For preparation of a latex prosthesis, an impression is taken of the opposite eye and normally opened lids, and a thin prosthesis is cast from latex which has been colored to match the skin. The markings of the eyeball are then painted on and artificial lashes are attached. Latex prostheses shrink with time and the pigments become discolored, so it is usually necessary to recast such prostheses about once a year. These prostheses are extremely light in weight and can be held in place by attachment to ordinary spectacles or

by a small metal band partially encircling the head.

RESULTS OF ENUCLEATION AND EVISCERATION, WITH AND WITHOUT BURIED IMPLANTS

A. DANGER OF MENINGITIS

Cutting the optic nerve during enucleation affords a potential pathway via the meninges of the optic nerve to the meninges of the brain. Evisceration was originally introduced to obviate danger of meningitis in those instances where the eye was removed because of panophthalmitis, and evisceration has been repeatedly advocated for such cases.[131] However, the actual occurrence of meningitis following enucleation is rare. Out of 10,743 collected cases of enucleation reported in 1898,[132] there were only seven deaths from meningitis, all ocurring in cases with panophthalmitis. Out of 768 collected cases of evisceration there were no instances of meningitis.

DeSchweinitz[133] (1900) collected 478 cases of evisceration with no deaths and 2,875 cases of enucleation, of which 273 were for panophthalmitis, with only one death. Out of 52 cases of panophthalmitis with death from meningitis which he collected from the literature, 33 followed enucleation. Proof was lacking that those cases of meningitis occurring after enucleation resulted from the operation rather than in spite of it. No large scale statistics are available as to the occurrence of meningitis following evisceration, but that it can occur is illustrated by the fact that Schuleck[134] had two deaths out of 36 eviscerations.

In the reported cases of meningitis following enucleation, thrombosis of the cavernous sinus has been frequently mentioned. This fact raises the question as to whether meningitis was actually the result of bacteria entering the optic nerve sheaths or whether it resulted from the surgical trauma to infected orbits. If the latter is the usually correct answer, it would be better to perform

simple evisceration rather than the frill operation advocated by Lister and Weve.

In either event, in these days of available antibiotic therapy, it seems probable that fear of meningitis should rarely influence a decision as to whether enucleation or evisceration is to be performed.

B. Danger of sympathetic ophthalmia

In a majority of the reported cases of sympathetic ophthalmia following any form of eyeball removal, there are grounds for suspicion that sympathetic ophthalmia might have developed if no operation whatever were performed or that it was already present in a clinically unrecognized stage at the time the eye was removed. Nevertheless, there are adequate reports in proof that evisceration will not always prevent sympathetic ophthalmia if the eviscerated eye is potentially sympathicogenic, and that evisceration can rarely result in sympathetic ophthalmia even if the eviscerated eye was itself in no way dangerous.

Thus, deSchweinitz[133] (1900) collected 317 cases of Mules's operation with sympathetic ophthalmia occurring afterward in six instances, and in one case (that of Carrow) the original condition excluded the possibility of its having originated the sympathetic ophthalmia.

Gifford[135] (1908) collected 18 cases of probable sympathetic ophthalmia after evisceration. Nine of these cases occurred after simple evisceration and nine after Mules's operation. Most of them occurred two weeks to a year after the evisceration. Gifford was able to collect only three cases of possible sympathetic ophthalmia following enucleation, and none of these cases is really convincing.

Holdener[136] (1930) reported five cases of possible sympathetic ophthalmia following enucleation, all occurring in patients who had suffered perforations of the globe 14 to 29 days before the eye was removed. In these cases an anterior uveitis developed in the other eye between 18 to 35 days after enucleation, but in each instance the iritis was very mild and healed without loss of vision within a few weeks.

Dor[137] found a much higher incidence of subjective symptoms of photophobia, and so on, in patients who had had eviscerations than in those who had had enucleations.

Advocates of evisceration have from time to time stated the belief that this operation does not cause sympathetic ophthalmia more often than does enucleation.[138] Nevertheless, on the basis of reported cases, it must be concluded that sympathetic ophthalmia is a definite, although small, possibility following evisceration[139, 140] and that it probably never actually begins following enucleation. This fact must be weighed as definitely against evisceration in determining which method should be utilized for removal of the eye.

C. Cosmetic appearance

Cosmetic appearance after removal of an eye must be judged on the basis of appearance and movement of the prosthesis rather than on movements of the stump, as was emphasized by Noyes in his discussion of Mules's original report. Most reports concerning the cosmetic results of enucleation and of evisceration agree that motility and appearance of the stump are best after evisceration with implantation, second best after either simple evisceration or after enucleation with buried implant, and poorest after simple enucleation.

However, appearance and movement of the prosthesis bears rather little relationship to the motion of the stump because of lack of transmission of movements of the stump to the artificial eye. The artificial eye simply rests in the conjunctival sac, being held in place by the lids. It derives its movements from retraction of the various fornices, by contraction of different rectus muscles with simultaneous relaxation of the opposing muscles. The stump itself simply slides

around beneath the prosthesis. One exception occurs in sockets with prominent, convex stumps which will support shell eyes similar to contact lenses,[141] but the attainment of such stumps is uncommon. The degree of actual prominence must be exact if the stump is actually to support the shell and still not result in apparent proptosis.

There is no uniformity of opinion as to which procedure results in best motility of the prosthesis. For example, deSchweinitz[133] preferred simple enucleation, Gradle[142] preferred evisceration with implant, Dimitry [113, 114] preferred each of the procedures under discussion at one time or another, and Gougleman,[110] who actually had the task of fitting prostheses, expressed no opinion except that a small ball implant usually gave a better result than a large implant.

Retraction of the upper lid sulcus is perhaps a more noticeable cosmetic defect after removal of the eye than is poor motility. Some degree of sinking of the upper lid is apparent in all cases except those with deep-set eyes. This sinking of the upper lid has been blamed on various factors, but recent experience with prostheses attached to partially buried implants (sinking of the lid rarely occurs after these procedures) seems to prove the sinking is due to the fact that the weight of the prosthesis is supported by the lower lid and that it therefore tends to push the lower lid outward and downward and to tilt backward in its upper periphery, affording improper support to the levator. It cannot be made large enough properly to support the upper lid without pushing the lower lid so far downward as abnormally to widen the palpebral fissure. A flange or ridge on the upper edge of the prosthesis sometimes will reduce the upper lid sulcus, but more often it will produce a staring expression more repulsive than the deep sulcus, as well as reduce motility.

It is rather generally conceded that abnormal deepening of the upper lid sulcus is minimized by insertion of an implant at the time of enucleation or evisceration. However, Gougelman warns against too large an implant on the grounds that a fuller eye than normal is less pleasing than a small or deep-set eye, and that if the stump is too large it is neither possible to keep a normal fold in the upper lid nor to prevent an appearance of unnatural fullness.

Years after prostheses have been worn, there is not infrequently a relaxation of the lower lid with exaggeration of the depression in the upper lid, a backward tilting of the prosthesis, and even loss of the lower fornix with inability to retain any prosthesis in place.

A good cosmetic appearance is probably best obtained after either evisceration or enucleation if a small or medium-sized implant is incorporated in Tenon's capsule or the sclera, and the results are approximately equal following carefully performed operations of either type. However, all patients who have undergone one of these operations have at least some restriction in motility of the prosthesis, and all except those with prominent brows and deep-set eyes have some degree of displeasing sinking in of the upper lid sulcus.

Alt[143] even advised Green's[144] procedure of removing all conjunctiva, tarsi, and lid margins and sewing the skin of the lids together (complete ablation of the socket) as preferable for most working people on the grounds that the plain skin-covered socket did away with all socket irritation and discharge and was often less conspicuous than a socket containing a prosthesis.

Enucleation during early childhood is rather commonly believed to interfere more or less seriously with orbital development. For example, Vorisek[145] described a man with a very small disfiguring orbit which he blamed on removal of the eye at the age of two years. However, recent studies[144-148] have shown that while a measurable defect in bony development occurs if the eye is removed before the age of five years, and possibly even up to the age of 18 years, this deficiency in development is only in the or-

der of 0.5 to 2.5 mm. in orbital height and width, with slight overgrowth of the maxillary antrum. The defect is not cosmetically apparent. Those cases with implantations showed slightly less deficiency in orbital development than those with no implantations.

PROCEDURE FOR CORRECTING COSMETIC BLEMISHES AFTER REMOVAL OF THE EYEBALL

A. RETRACTION OF UPPER LID SULCUS

In cases with sunken sockets, where retraction of the upper lid sulcus is most likely to be very disfiguring, a few ophthalmologists have considered it advantageous to increase the volume of the orbital contents by late implantations. Suker[69] prepared a pocket in the center of the socket about 3 mm. below the conjunctival surface, injected paraffin into this pocket, and sutured the overlying flaps firmly together.

Fox[45] prepared a pocket within the central stump via an incision in the upper temporal aspect of the socket and implanted a 12- or 14-mm. gold ball. Grimsdale[15] believed late implantation of a glass sphere would occasionally improve appearance but would never improve motion of the prosthesis.

Wheeler[83] described a grooved hollow glass implant with an anterior-posterior diameter of 18 mm. for delayed implantation within the muscle cone. He incised the conjunctiva horizontally and dissected it up rather widely, made a vertical incision through the fibrosed mat of collapsed Tenon's capsule, carried this incision down almost to the apex of the orbit, and inserted the implant so that the rectus muscles (if identified) fitted in the grooves.

DeVoe[149] found late implantation of a glass ball was frequently difficult because the muscles pursued an eccentric course as a result of the scarring following enucleation, that it was usually impossible to implant a sphere larger than 16 mm. in diameter without its extruding either anteriorly or posteriorly, and that such implantation did not

improve movement of the prosthesis and would improve the unsightly retraction of the upper lid sulcus only slightly if at all.

Dimitry believed the cause of retraction of the upper lid sulcus was attachment of the inferior rectus to the superior rectus following enucleation; contraction of the inferior rectus, he supposed, would pull the superior rectus downward, thus indirectly pulling the levator and septum orbitale downward and backward because of the partial attachment of these structures to the superior rectus sheath.[150] Because of this theory, DeVoe[149] tried carefully severing the attachments of the superior rectus from the levator at the time of enucleation, but he found the end results were not improved.

Correction of an abnormally deep sulcus in the upper lid has been accomplished by insertion of a buried graft or implant directly within the upper lid. Smith[151] and Devoe[149] employed dermal grafts, Cutler[152] preferred fascia lata strips, Vannas[152a] used autogenous cartilage, and Sugar and Forestner[153] advocated individually shaped acrylic implants varying from 27 to 30 mm. in length and 5 to 8 mm. in width. The graft or implant is placed between the septum orbitale and the orbicularis, just below the brow, and should arch around so as to fill out the upper lid sulcus in as normal a pattern as possible. Cosmetic improvement has been reported as being uniformly worth while. The defect should be corrected as closely as possible at the time of the operation if an acrylic implant or an autogenous fascia lata graft (which do not absorb) is used, but the defect should be overcorrected if a partially absorbable autogenous graft such as dermis (which eventually absorbs by 30 to 40 percent) is used.

Surprisingly, I have been unable to find any mention of tightening the lower lid for the primary purpose of restoring a normal upper lid sulcus. Certainly tightening the lower lid to hold the prosthesis upward and not tilted backward, thereby supporting the levator and septum orbitale, is a logical and

comparatively minor procedure. It does not induce abnormal widening of the palpebral fissure. The results of such a procedure can be determined preoperatively by pinching the skin just lateral to the lower lid into a vertical fold while the prosthesis is in place. I have never seen this procedure used except where actual ectropion was present, but the results in terms of appearance of the upper lid were so good I believe it should be used rather commonly for its effect on the appearance of the upper lid alone.

B. RELAXATION AND ECTROPION OF LOWER LID

Relaxation or actual ectropion of the lower lid, with difficulty of even retaining a prosthesis in place, is best corrected by a lid-tightening operation such as the Kuhnt-Szymanowski.[74, 154]

C. CONTRACTED SOCKET

Partial contraction of the socket may result from wearing no conformer or prosthesis following enucleation, the subjunctival tissue gradually becoming slightly fibrosed and rigid instead of retaining its normal elasticity.[74] However, in such instances the socket can be gradually enlarged to normal size by the wearing of increasingly large conformers, even if the eye was removed many years previously.[155, 156]

More extensive contracture of the socket may result from wearing a prosthesis with a rough surface so that ulceration and gradual scarring of the conjunctiva take place. Even greater contracture may be encountered in sockets where eyes have been removed because of severe infection with conjunctival ulceration or because of trauma from chemical, thermal, or mechanical causes.

If the contracture is not so extensive as to preclude the retention of a very small conformer, and if there is not too excessive subconjunctival scarring, the socket can often be reformed by using increasingly large conformers. Another procedure at times effective consists in strapping or splinting a

normally large prosthesis into the orbit, with application of pressure to the prosthesis (via a pin attached to its anterior apex) for at least two months.[157]

For restoration of sockets so contracted that small conformers cannot be retained, various plastic operations have been devised, most of them dependent on skin grafts.

Free skin grafts are of three varieties: (1) Ollier-Thiersch grafts, first taken by Ollier with a needle and later by Thiersch with a razor, theoretically purely epidermal but actually including a small amount of dermis, (2) split-thickness grafts including epidermis and one half to two thirds of the dermis, and (3) whole-thickness grafts including epidermis and all of the dermis.

The thinner grafts vascularize more quickly and are more likely to remain viable. With a free graft there is more contracture than with a sliding or pedicle graft, and even with a pedicle graft there is a tiny bit of contracture from scarring along the plane of junction of graft and underlying tissue.[158]

Maxwell[159, 160] first described an operation for forming a lower cul-de-sac and increasing the vertical diameter of the socket (by 4 mm.). His operation consisted in preparing a crescent-shaped skin flap, with the upper margin 5 mm. below the lower lid border, and 8 mm. wide in the center, left attached to the subcutaneous tissue in its center; this was inverted through an incision extending through the lower lid, from the upper edge of the flap into the lower part of the socket, so that the epithelial surface could be sutured to the edges of the conjunctival incision.

Schwenk[161] used Maxwell's method for restoring the lower cul-de-sac and, in those cases where almost all of the conjunctiva was lost, also employed a pedicle flap from above the brow for restoring the upper cul-de-sac.

Weeks[162] used a full-thickness skin graft to restore either the lower or upper cul-de-sac. He inserted a rubber mold at the time of operation and overcorrected the defect about 50 percent. Disadvantages of this pro-

cedure consisted in undue thickening of the lid because of the thickness of the graft, often an unpleasant discharge with some odor, and growth of hairs from the graft.

Czapody,[163] in 1935, again advocated use of full-thickness grafts, and kept the cul-de-sacs stretched postoperatively by means of a two-piece form which could be spread like the blades of a speculum. Lugossy,[164] however, criticized the Czapody operation because late scarring often resulted in an immovable and very disfiguring appearance of the lids.

Esser[165-167] introduced his "epithelial inlay" in 1916, and was the first to describe use of a Thiersch graft for replacement of conjunctiva in contracted sockets. His procedure consisted of full dissection of upper and lower cul-de-sacs and insertion of the graft wrapped around a mold of dental stent.

Esser's procedure has been redescribed many times with minor variations[168-179] and is still the most commonly used operation for restoring severely contracted sockets.

Several details of technique which have been emphasized are worthy of mention.

Dissection beneath the lids should be kept very superficial in order not to end up with lids which are too thick; all scar tissue and granulation tissue should be removed and, if tarsal conjunctiva is involved, the tarus should be split and thinned to reduce the resulting thickness of the lids. The dissection should be carried down one-fourth inch below the infraorbital ridge, up to the levator and one-half inch to each side of this muscle. The graft should be as thin as possible and 50 percent larger than the defect.

The epithelial surface of the Thiersch graft is usually kept against the mold or conformer either by suturing the graft around the mold or by sticking it on with rubber cement, but the graft margins may be sutured directly to the edges of the defect.

A conformer or prosthesis should remain in the socket at least three weeks, keeping the cul-de-sacs stretched. Various conformers of rubber, latex, or acrylic have been advo-cated in place of a mold of dental compound. Flexible conformers such as one simply cut from a hollow rubber ball[174] are probably best, because these can be quite large and yet can be inserted without a canthotomy. After healing is complete, small blisters will indicate the positions of occluded lacrimal ducts, and these can be opened with a hot needle to allow a moist socket.

O'Connor and Pierce[170] advocated use of any available conjunctival flap from elsewhere in the socket, or otherwise a very thin bipedicled skin flap from the upper lid, to replace tarsal conjunctiva of that lid, because a Thiersch graft over the upper tarsus often contracts sufficiently to buckle the upper tarsal plate and concentrate the cilia in the center of the lid.

A combination of skin and mucous membrane as a lining for the socket has most generally been condemned, but Marcks and Zugsmith[74] have recently reported obtaining more flexible sockets by leaving a central area of intact conjunctiva if any is available, or, in case there is no conjunctiva, using a two-stage procedure of suturing a central epidermal graft in place and later reforming the fornices with Esser's procedure. They found that, in sockets with a combination epidermal and mucous membrane lining, there was a period of increased secretion which gradually reduced, with the epidermal graft becoming soft and flexible within a year. They also emphasize the importance of a normal-appearing caruncle for proper cosmetic appearance, and advise that, if it is bound down with scar tissue, it should be freed by means of a "Z" plastic or a mucous membrane graft.

Free mucous membrane grafts have occasionally been advocated for repair of contracted sockets. For women, Clay and Baird[180] advised use of two grafts, each about 3 by 5 cm., taken from each side of the vagina, from between the inner margins of the labia minora and the outer margins of the hymen. In men, they preferred mucous membrane from the prepuce but, if the con-

junctival defect was large, insufficient mucous membrane could be obtained from that site. MacKenzie[181] lists the preferable sites for obtaining donor grafts as follows: in the male, (1) mouth, (2) prepuce; in the female (1) vagina, (2) mouth.

De Roetth[182] employed fetal membranes for repair of conjunctival defects, the chorion surface being placed against the raw surface and the amnion forming the free surface, but found very marked shrinkage after three weeks. Law and Phillip[183] used amnioplastic and noted some shrinkage after three months but retention of a fornix of fair depth.

Berens[184] devised an operation to restore the lower cul-de-sac which preserved the overlying conjunctiva, and thus obviated the necessity of any grafting, for use in those cases where the lower fornix was obliterated by subconjunctival scar tissue but where there was no serious shortage of conjunctiva.

He made a 2-cm. vertical incision into the lower cul-de-sac at the outer canthus. Working through this incision, he undermined the conjunctiva and removed all scar tissue down to and along the entire extent of the anterior surface of the lower orbital margin. He then passed three double-armed silk sutures through the mobilized conjunctiva, into the depths of the reformed cul-de-sac, and out through skin at the orbital margin, tying the sutures over rubber pegs (Snellen sutures). With this procedure, he found it unnecessary to insert any conformer or prothesis at the close of operation.

For reformation of an obliterated lower fornix, Nordlow[154] dissected the conjunctiva from the lower lid and carried his dissection down beneath the orbital margin, shortened the lid with a Kuhnt-Szymanowski operation, and sutured the conjunctiva into the resulting cul-de-sac with Snellen sutures. Weskamp[155] described Damel's technique for restoration of the lower cul-de-sac as incising the conjunctiva horizontally 6 mm. back of the lid margin, undermining the palpebral

conjunctiva, dissecting the lid free to the orbital margin, and suturing the edge of the undermined conjunctiva to the inner surface of the skin of the lid near the orbital margin. The remaining bare surface in the lower portion of the socket is simply allowed to epithelialize over.

Occasionally it is desirable to widen the external canthus. Noyes[186] described the use of a small temporal skin flap for this purpose.

D. DEPRESSED FRACTURE OF ORBITAL FLOOR

Not infrequently, eyes are enucleated because of an injury which is sufficiently severe to fracture the floor of the orbit into the maxillary sinus, with prolapse of orbital structures downward and backward; there is usually an associated comminuted fracture of the zygoma.

If such a fracture is recognized within 2 or 3 weeks of the injury, the proper orbital shape can generally be restored by packing iodoform gauze in the antrum. Later, such a defect is more easily repaired by a subperiosteal implantation along the depressed orbital floor, but the bony orbital floor should be completely healed before an operation of this sort is performed.

For building up the orbital floor fascia lata, cartilage, bone, tantalum, acrylic, and glass wool (fiberglas) have been utilized.[158, 187, 188] Autogenous cartilage or fascia lata grafts have the least chance of resulting in infection, while glass wool or tantalum wool is easier to insert in proper position for correcting the defect.

E. PARTIAL OR COMPLETE EXENTERATION

After exenteration of the orbit the defect is generally best covered by a latex prosthesis or simply an inconspicuous patch. However, a few surgical procedures, none of them very satisfactory, have been advocated for partial cosmetic repair.

Golovine[189] utilized a pedicle skin flap from the temporal region which he carried through a vertical incision behind the outer

canthus and sutured into the orbit along the edges of conjunctiva, the lids having been preserved. After the graft had taken well, the pedicle was cut, the skin incision outside the canthus was closed, and an artificial eye could be retained within the lids.

Goldstein[190] freed the lids, after healing was complete, and lined the undersurface of each lid with Thiersch grafts. He then split the lids and inserted Thiersch grafts, and the patient was able to wear a prosthesis which would fit into these slits.

Hagedoorn[191] described a four-stage operation for use after complete exenteration but with retention of skin of the lids. The first stage was implantation of fat and connective tissue beneath the lining of the lower part of the orbit; the second stage was mobilization of the overlying epithelium and moving the fat back to the apex of the orbit; the third stage was mobilization of the skin of the lids and completing the filling of the orbit by means of another fat transplant; and the fourth stage was an Esser operation for contracted socket.

Kolen[192] described an ingenious method of reconstructing the eyelids by making pockets beneath abdominal skin and lining the insides of the pockets with mucous membrane grafts. Later, slices of cartilage from the ear were grafted between skin and mucous membrane, and finally the ready-made lids and socket were transferred to their final position via pedicles. Filatov[193] also advocated use of this procedure for reconstruction of a completely exenterated orbit, but he had not actually performed such an operation.

(To be continued)

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EVALUATION OF NIGHT VISION*

PHILLIP ROBB McDONALD, M.D.

Philadelphia, Pennsylvania

INTRODUCTION

The physiology of rod and cone vision has been under investigation for many years. Schultze[1] was the first to suggest, in 1866, that the retina possesses two types of receptor cells, but it was not until 1895 that the duplicity theory was finally established by von Kries.[2] In brief, this proposed that the cones are concerned chiefly with visual acuity and color discrimination at high intensities of illumination while the rods are responsible for vision at low intensities. Parsons introduced the terms "photopic" for vision at high intensities and "scotopic" for vision at low intensities of illumination.

The phenomenon of retinal adaptation was first measured by Aubert[3] in 1865. During the latter part of the 19th century other investigators, notably Koenig and Ritter[4] and Abney and Festing,[5] were concerned chiefly with the effect of wave length on the threshold of the dark-adapted eye. With the development of more precise physical equipment, this work has been repeated several times, the most accurate measurements being those of Hecht and Williams[6] and Kohlrausch.[7]

Shortly after the original measurements of retinal adaptation,[3] Boll[8] discovered visual purple (1876), and Kühne[9] was successful in extracting it from the retina (1879). It was natural, therefore, to associate it with the visual process. In fact, Parinaud,[10] in 1895, suggested that night blindness was caused by a deficiency in visual purple.

The correlation of the physiologic studies of retinal sensitivity with the photochemistry of the retina is a most fascinating story,[11] the nature of which was gradually revealed by the work of many investigators. Lythgoe and Tansley,[12] in England, and Hecht[13] and Wald,[14] in this country, have been the principal contributors to this problem.

Coincident with the evolution of our knowledge concerning dark adaptation and the chemical nature of the visual process was the interest shown by the nutritionists in the isolation of the vitamins. It had been known for many years that a nutritional deficiency might cause impairment of night vision. Studies on the relationship of vitamin A to visual purple and the isolation of vitamin A from the retina by Wald[14a] provided further impetus to the study of dark adaptation as a measure of vitamin-A deficiency. The literature on this subject has recently been reviewed by Schmidtke.[15] The results varied with the socio-economic status of the group tested, the apparatus used, and the enthusiasm of the reporter. It became apparent that vitamin-A deficiency did raise the light threshold of the dark-adapted eye. However, the subjective nature of the test and the many variables that had to be considered did not permit its acceptance as a routine method for the determination of vitamin-A deficiency.

Numerous instruments have been devised for testing the light sense. Until the advent of our interest in the test as a measure of vitamin-A deficiency, most of these were well-standardized models relegated to the research laboratories of those interested in visual physiology. The popularization of the test, however, led to the development of some instruments that could not fulfill the claims of the manufacturers. The literature on the instruments available prior to World War II has been adequately reviewed by Sloan.[16]

With the onset of the war, it was soon realized that, although great advances had been made in our knowledge of visual capacities at scotopic levels of illumination,

there were still many problems of a practical nature that were left unsolved. The hours from dusk to dawn assumed a new importance. The evaluation of night vision became of paramount interest both from the point of view of identification of enemy aircraft and the operation of aerial attacks against the enemy.

The problem presented to the military services, especially with regard to aviation, can be briefly stated as (1) what variation in the visual threshold might be expected in a highly selected group of individuals, (2) what type of night-vision test suitable for mass testing could best reduplicate the visual tasks required in night operations, (3) providing a satisfactory test were developed what would be its reproducibility and reliability, (4) what would be the validity of the test, (5) what means, if any, could be used to improve the visual threshold of supposedly normal individuals?

The investigative work to be reported here relates to the first, third, and fifth parts of this problem. It will be described in the order in which it was carried out and will be followed by a general discussion of the problem as outlined in the preceding paragraph.

EXPERIMENTAL WORK

OBJECTIVES

1. To determine the variations in certain criteria of dark adaptation in a group of individuals of the same age who had passed the rigid physical examination for aviation cadets and who followed the same dietary regimen.

2. To determine whether large doses of Vitamin A as a supplement to an adequate diet would improve the visual threshold.

3. To study the reproducibility and reliability of two different tests of night vision.

The dark-adaptation tests were conducted on 162 aviation cadets stationed at Randolph Field, Texas, during the summer of 1941. These cadets, selected at random by their officers, were all supposedly in perfect health, with uncorrected visual acuity of 20/20 or better and with no evidence of ocular disease. The examinations were made by me during the second 10-week period of their flying training. The cadets, all of whom lived in permanent barracks, were fed in a central mess hall. The food was excellent and unlimited quantities of milk, butter, eggs, and green vegetables were provided. In accordance with military procedure the cadets were allowed off the post only on Saturday nights; on other nights—except while flying at night—they were in their barracks by nine o'clock.

The examinations were conducted in a photographic darkroom, adequately ventilated to insure comfort. Unless stated otherwise, the dark adaptometer devised by Hecht and Shlaer[17] was used and the procedures recommended by them followed. On calibration of the standard lamp, the logarithm of its intensity in micromicrolamberts ($\mu. \mu. 1$) was 12.962. The right eye of the examinee was used in all experiments, the chin rest being adjusted to the right height by means of a pinhole disc temporarily inserted into the eyepiece of the instrument.

For light adaptation, the right eye was adapted to an intensity of 982 millilamberts for three minutes. The test field was three degrees in angular diameter and fell seven degrees to the nasal side of the macula. A violet filter (Corning 511) was used in the test field which was exposed in flashes of one fifth of a second. The intensity of the testing light was controlled by means of a neutral wedge and filters. This intensity was usually set by means of the wedge below the expected threshold value for the first flash and then was increased by steps of 0.1 (log $\mu. \mu. 1$) until the observer reported seeing a flash.

The rod threshold was determined by the "method of limits" described in the following part of this paper. Dark adaptation was measured over a period of 30 to 35 minutes. Threshold readings were recorded as the logarithms of the intensity expressed in micromicrolamberts (ordinates) and plotted

against time in minutes (abscissa).

Range of dark adaptation threshold. The first factor to be determined was the variation in the range of the dark adaptation threshold in such a group of cadets, whose ages ranged from 19 to 25 years. The entire course of dark adaptation was recorded for all individuals. The criteria selected for study were the cone threshold and final rod threshold. In the entire sample 81.5 percent had final rod threshold values between 2.7 to 3.0 (log μ. μ. 1) and 75.3 percent had cone threshold values between 5.6 and 5.9 (log μ. μ. 1). If the data are analyzed statistically, the logarithm of the mean cone threshold in micromicrolamberts was 5.75 with a standard deviation (δ) of 0.198 logarithmic units. The logarithm of the mean rod threshold in micromicrolamberts was 2.84 with a standard deviation (δ) of 0.156 logarithmic units. The correlation coefficient of the two final thresholds is 0.20. This value is on the border line of statistical significance. The low correlation between these two thresholds had been previously reported by Hecht.[18]

Three categories were arbitrarily chosen to classify performance in the dark adaptation tests. Listed as *good* were all observers whose final rod threshold fell within one standard deviation above or below mean (2.68 to 3.00 log μ. μ. 1); as *excellent,* all those whose thresholds were lower than one standard deviation (2.68 log μ. μ. 1 or less); and as *fair,* those whose thresholds were greater than one standard deviation from the mean (3.00 μ. μ. 1). None of those examined had thresholds high enough to suggest any evidence of night blindness or to warrant their performance being classified as poor. The cone threshold was not considered in this classification.

Vitamin-A effects on night vision. In a study such as this, it is only natural that one of the features to be investigated should be factors that might improve the visual threshold. Of the group of 162 cadets examined in the preliminary survey, the last 40 were detailed for this experiment. When reporting for further night-vision tests, every alternate cadet was used as a control subject. No selection was attempted to include persons with high or low thresholds. The subjects were examined twice before starting the experiment. One group received 50,000 units of vitamin A a day as a supplement to their usual diet, the other group received only the ordinary cadet mess diet. The vitamin A was taken in the presence of an officer immediately following the noonday meal. The entire group was examined weekly for a period of eight weeks.

The total number of examinations in the control group was slightly less (9) than in the vitamin-A group because of examinations unavoidably missed. Half the group was examined in the morning and half in the afternoon, since this fitted their flying schedule. One week each group was seen before exposure to much sunlight and the following week was seen after 1 to 2 hours of flying. This balanced the rise in threshold that might occur following exposure to bright sunlight for a period of several hours.[19]

The statistical analysis is based on 38 individuals since two "washed out" before the experiment was completed. The results are listed together in Table 1. In order to appreciate fully the improvement that may take place as familiarity with the test increases, the data have been further broken down so that one can compare the mean thresholds of the first two and last two examinations.

In the group receiving vitamin A, the drug was not started until after the second examination. Those receiving vitamin A showed an improvement in their mean cone thresholds of 0.158 logarithmic units while the control group improved by 0.108 logarithmic units. The difference (Δ) 0.050 between these two values is not significant statistically since it is less than twice the standard error of 0.051.

Similarly the improvement in the mean rod threshold of those receiving vitamin A was

0.150 logarithmic units while the control group showed an improvement of 0.108 logarithmic units. The difference (Δ) 0.042 between these two values is also less than twice the standard error of 0.050, again not

it was found (in the control group) that there was no significant improvement in the mean cone or rod threshold after the first two tests. One might expect slight improvement with practice but this was to all intents

TABLE 1

LOGARITHM OF THE MEAN CONE THRESHOLDS IN MICROMICROLAMBERTS

Vitamin A		Controls
$5.727 \pm .0133$	Eight-week period mean cone threshold	$5.721 \pm .0162$
146	number of examinations	137
.161	standard deviation (δ) (logarithmic units)	.190
	First two examinations	
$5.803 \pm .024$	mean cone threshold (log I $\mu \mu$ l)	$5.797 \pm .024$
38	number of examinations	38
.148	δ (logarithmic units)	.146
	Last two examinations	
$5.646 \pm .024$	mean cone threshold (log I $\mu \mu$ l)	$5.689 \pm .030$
38	number of examinations	38
.148	δ (logarithmic units)	.186
Δ_v .158	improvement (log I $\mu \mu$ l)	Δ_c .108
Difference $\Delta_v - \Delta_c = .050$		
S.D. of the		
difference $\delta (\Delta_v - \Delta_c) = .051$		

LOGARITHM OF THE MEAN ROD THRESHOLDS IN MICROMICROLAMBERTS

Vitamin A		Controls
$2.720 \pm .0124$	Eight-week period mean rod threshold	$2.746 \pm .0155$
146	number of examinations	137
.150	standard deviation (δ) (logarithmic units)	.182
	First two examinations	
$2.810 \pm .0165$	mean rod threshold (log I $\mu \mu$ l)	$2.800 \pm .0265$
38	number of examinations	38
.101	δ (logarithmic units)	.158
	Last two examinations	
$2.660 \pm .0238$	mean rod threshold (log I $\mu \mu$ l)	$2.692 \pm .0323$
38	number of examinations	38
.146	δ (logarithmic units)	.200
Δ_v .150		Δ_c .108
Difference $\Delta_v - \Delta_c = .042$		
S.D. of the		
difference $\delta (\Delta_v - \Delta_c) = .050$		

statistically significant. The improvement in the control group can be ascribed only to the "learning" factor which is a common observation in subjective tests of this nature.

Reliability and reproducibility of night-vision tests. In any test of night vision, it is essential that the test be reliable and that the results be reproducible. In the experiment reported (*Vitamin-A effects on night vision*)

and purposes negligible after the second test.

The fact that one particular test of night vision is reproducible and reliable does not necessarily mean that all other tests of a similar nature will have the same reliability. Even if another test proves to measure reliably the functions it purports to measure, there may be a poor correlation between the two tests. This is especially true if the two

tests are measuring visual functions at different levels of illumniation.

To evaluate the reliablity and reproducibility of a night-vision test using form discrimination, 85 cadets were examined by at a level high enough so that all presentations should be seen readily and finishing at a level at which, in most instances, none could be seen. The test therefore has yielded a score between 0 and 40.

TABLE 2
SCORES ON SUCCESSIVE TESTS ON THE AAF NIGHT-VISION TESTER

Case Number	Test Number				Case Number	Test Number			
	1	2	3	4		1	2	3	4
1	20	28	28	31	44	9	11	13	10
2	13	25	17	24	45	15	20	19	20
3	8	22	19	22	46	24	19	17	29
4	7	19	23	26	47	27	27	23	31
5	12	22	19	24	48	10	7	13	16
6	19	23	20	21	49	27	24	25	33
7	16	14	11	13	50	18	22	26	27
8	16	22	15	24	51	17	20	16	14
9	20	15	19	22	52	21	27	21	22
10	32	34	34	34	53	21	30	32	32
11	14	25	21	24	54	24	25	23	26
12	24	21	19	21	55	13	21	17	23
13	27	32	27	24	56	18	17	21	16
14	15	22	24	21	57	20	26	26	24
15	14	14	12	13	58	23	28	30	27
16	16	15	13	21	59	26	30	24	28
17	25	25	20	23	60	6	4	10	6
18	13	19	16	23	61	20	21	22	25
19	16	24	26	28	62	20	24	24	25
20	26	25	20	27	63	16	17	15	23
21	10	14	19	20	64	16	22	20	19
22	22	30	31	32	65	28	31	36	32
23	14	25	22	24	66	24	27	30	32
24	25	20	18	21	67	17	20	21	25
25	9	22	17	20	68	12	22	18	20
26	24	29	22	30	69	17	29	26	31
27	5	6	7	10	70	32	29	31	31
28	30	32	27	30	71	15	25	17	21
29	16	22	22	19	72	27	26	30	29
30	12	17	13	12	73	22	25	22	18
31	17	21	22	24	74	9	22	17	20
32	9	15	17	10	75	16	13	14	19
33	21	24	21	20	76	11	18	21	23
34	17	15	21	19	77	7	10	8	8
35	18	19	18	17	78	34	32	36	36
36	16	19	14	15	79	25	32	36	31
37	3	4	8	4	80	25	22	23	28
38	14	24	25	23	81	19	17	21	20
39	21	20	18	21	82	31	28		26
40	25	27	22	26	83	27	33		25
41	22	23	26	29	84	16	26		15
42	8	6	11	11	85	4	14		14
43	7	20	13	12					

another test using the method of "frequency of seeing" [43b] described later. This required the recognition of a Landolt C subtending a visual angle of two degrees. The test object was automatically presented five times at eight different levels of illumination, starting

The test was carefully explained to the cadets and, after thorough dark adaptation, the value of parafoveal vision was demonstrated by means of a preview of the test. Table 2 lists the scores on the four tests. It must be pointed out that the first and second

tests were given on the same day and the third and fourth approximately one week later.

The statistical analysis of the data is presented in Table 3. This shows that the practice effect is greatest between the first and second tests, the mean difference between the scores being less than 3.72. Subsequent retests are of little value. The mean difference between the scores on the second and fourth totals is 0.68. The relation between the second and fourth tests can be seen in Figure 1. The correlation between these two tests is 0.797, which is very good. Again this shows that after the second test there is little subjective improvement in a test of this nature.

DISCUSSION

Before adopting any test of night vision, it is essential to know what variation might

TABLE 3

RELIABILITY OF AAF NIGHT-VISION TESTER
(*Comparison of scores on first, second, and fourth tests*)

Mean difference, trials 1 and 2	=	3.72
S.E. of mean difference	=	0.54
Interpretation P	=	.01
Mean difference, trials 1 and 4	=	4.40
S.E. of mean difference	=	0.55
Interpretation P	=	.01
Mean difference, trials 2 and 4	=	0.68
S.E. of mean difference	=	0.46
Interpretation P	=	.20 to .10
n	=	85
$\overline{x^1}$	=	17.96
$\overline{x^2}$	=	21.68
$\overline{x^4}$	=	22.36

be expected in the population to be tested. Several surveys of fairly large numbers of supposedly normal individuals have been published. The results have varied somewhat,
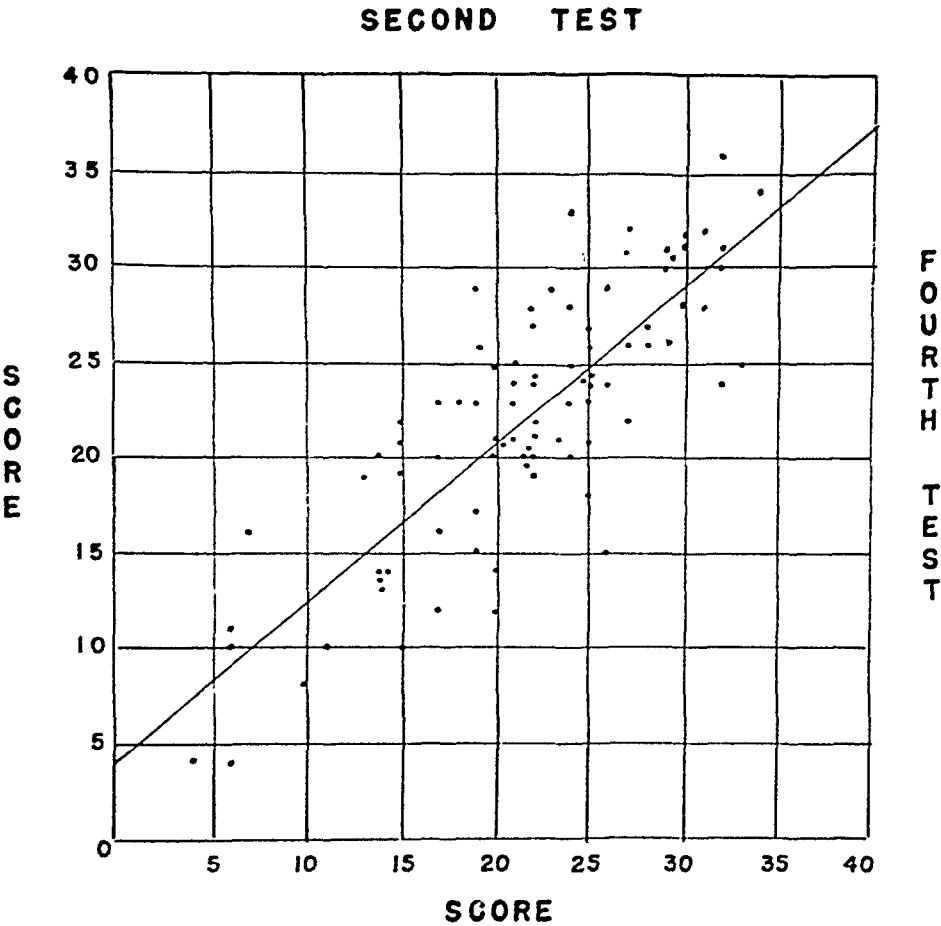
Fig. 1 (McDonald). The scores of the second and fourth tests on the A.A.F. night-vision tester, plotted together to show the correlation between the two tests.

depending upon the type of instrument employed. The one used in this survey was the same as that used by Hecht and Mandelbaum[18] in their study of 110 university people. Solandt and Best[20] used a later modification of the same instrument, while Yudkin and Robertson[21] used one embodying the same general principles. The results of these surveys are in close agreement. Bishop Harman,[22] Rycroft[23] and Lister,[24] in England, have also reported on large groups of individuals. Their respective instruments required the recognition of a form at a low level of illumination. Their data, though significant, are hardly comparable, since the results are not expressed in units of brightness or illumination.

The Hecht instruments measure the threshold with a well-controlled patch of light. As Godding[25] has pointed out, however, there is a difference between the measurement of the absolute threshold and the recognition of various forms or letters at low intensities of illumination. This fact alone may account for the apparent differences in the results that have arisen in the various studies of night vision. This will be amplified in the discussion of the various instruments that recently have been developed.

At the time my experimental work was done, the only available material was that of Hecht and Mandelbaum.[18] The data on both these groups were compiled on the results of the individual's first performance of such a test. The results show striking similarity. As might be expected in a group of younger individuals, the final rod threshold is slightly lower, although the cadet group was essentially the same as the 21-to-25-year age group reported by Hecht and Mandelbaum.[18] Since the cadets were a highly selected and physically homogenous group, all eating the same food and living under the same conditions, a greater difference might have been expected between these two groups.

The spread of the final rod threshold was approximately one log unit which is also the same as reported by others.[18, 21] This means that the threshold of the poorest individual was 10 times higher than that of the best. When one considers that the total threshold change is at least four log units, or 10,000 to 1, this variation is comparatively small. One may expect therefore that the visual threshold may vary by a factor of 10 in a group of aviation cadets.

The study of visual perception under conditions of threshold illumination has not been evaluated without some difference in opinion attested to by the several instruments that have been developed to measure this function. Each one has had certain purported advantages such as ease of administration, rapidity and simplicity of the test, and so on. Hecht,[18] Craik[26] and Tansley[27] have repeatedly emphasized that the fundamental physiologic principles must be fully appreciated and followed to insure reliable measurements and the basic criteria for a satisfactory test of dark adaptation have been fully discussed by them. Briefly the factors to be considered are: 1. Time and intensity of the preadapting light; 2. location of the retinal area tested; 3. size of the retinal area stimulated; 4. time of exposure of the test flash; 5. wave length of the testing light.

These criteria must be followed to devise an accurate test of some basic visual function at low levels of illumination such as the measure of the absolute threshold to a flash of light, or of some simple visual task such as the recognition of the direction of an arrow, at any given low level of illumination. The advantages of such a test are that in measuring one visual function over a fairly narrow range of illumination, the test would be fairly simple to give and might readily lend itself to mass testing. Another argument in favor of a simple test of threshold or visual acuity at low levels of illumination is based on Shlaer's[28] studies, which showed that visual acuity at such levels varies as the logarithm of the intensity; therefore, such a test might give sufficient

information as to visual acuity at higher levels of scotopic vision.

Additionally, the requirements for a test of night vision peculiar to the needs of the military services demanded that it reproduce as closely as possible the visual discrimination encountered in night operations.

The most difficult task was to define what visual discriminations might be encountered in night operations. These may vary from determination of the absolute threshold to the recognition of forms of varying size and contrast, from low levels of illumination to the wide ranges of sky brightness found in starlit or moonlit nights. It is obvious that no one test could fulfill this range of requirements. However, one could aim at a test of form discrimination at intensities well within the range of scotopic vision. A test which approximates these conditions has been called by Livingston[29] "a test of night visual capacity," a term that would seem more appropriate to denote the visual discriminations required.

Such a test would have the advantage of approaching more closely to actual operating conditions and by so doing should make performance on the test correlate better with actual practice. One of the disadvantages is that it must needs be a compromise, since it would not be feasible to measure any one visual function over the wide range of intensities encountered in night operations.

Another disadvantage is that extraneous factors would be introduced that would have no real bearing on the visual task to be measured. Craik[26b] and Godding[25a] have clearly shown that the perception of a silhouette or other more complicated material is not a test of dark adaptation. Consideration must be given to visual, adaptive, psychologic, and training factors in any such test. True, good dark adaptation is a requirement for a high standard of night visual capacity but, as Craik[25b] has shown, there is little correlation between such tests and the absolute threshold of rod vision.

These objections, however, were outweighed by the desire to produce a test that would more closely approximate the visual discriminations encountered in night operations. How best could this be done without disregarding the basic fundamentals for a satisfactory test of dark adaptation?

The first point to be considered was the necessity of *preadapting the eye* or eyes to a light of unknown intensity for a fixed interval of time. The purpose of preadapting the eyes to a bright light is to bleach the visual purple in the retina with a known quantity of light. This enables one to measure the course of dark adaptation from a known standard level and permits comparable measurements which are independent of the level of the environmental illumination. This difference in rate of adaptation is clearly demonstrated on entering a darkened theatre on a bright, sunny day or during a dimout.

If one is not particularly concerned with the course of dark adaptation, a common level of dark adaptation can be obtained by keeping the subjects in a darkroom for a minimum of 30 minutes, after which there is, for most practical purposes, little change in the rod threshold. An important consideration here is that, in measuring thresholds during the course of dark adaptation, the final rod threshold has been found to be the most reliable measurement.[21, 25a, 30, 31]

Another argument against the measurement of the rate or course of dark adaptation is the time factor—numerous determinations would have to be made and the value of this information in contrast to a few more accurate measurements at the desired levels of illumination is questionable. (This was evident in the measurements of the complete course of dark adaptation on the 162 cadets in the experiments reported above.)

Because of these factors and because of a desire to measure visual efficiency at various levels of low illumination rather than the rate of adaptation or a threshold at one fixed

level, it can be assumed that, for the purposes of the military services, preadaptation could be dispensed with and an equal retinal level could best be reached by a carefully regulated period in which all subjects were kept in darkness.

This is the procedure that has been followed in most of the night-vision tests used by the various armed services. The wearing of red goggles[32, 33] transmitting light only beyond 620 μ can considerably reduce the time to be spent in actual darkness. The effectiveness of the goggles depends upon their cutting down the total amount of light transmitted and upon the difference in the stimulating power of white and red light on the rods.[34]

The *location of the retinal area* to be tested can be determined by the use of some fixation device.[35] If binocular vision is used, corresponding areas of retina will be stimulated. Hecht[17, 18] has emphasized that the control of fixation gives greater accuracy to the test since a predetermined area of the parafoveal retina is stimulated. Godding,[25a, b] however, feels that if a larger test field is used, that is, one subtending a visual angle of seven degrees, fixation devices can be dispensed with.

The use of a fixation device would not be in keeping with the desire to reproduce as closely as possible the actual conditions encountered in night operations. It must also be borne in mind that the region of the retina having the maximum scotopic acuity may vary from individual to individual and an alert examinee may do better if he is not required to fixate.

All pilots and gunners are taught to scan and to use a roving gaze, although through force of habit the tendency is to fixate an object to see it clearly. Hence, an examinee who did not use his parafoveal vision although instructed to do so might fail the test, in which case his unsatisfactory night vision would be due to inattention and not to a defect in his visual apparatus.

Nevertheless, even though some individuals may be penalized, the advantages of permitting free movement of the eyes is believed to outweight the use of a fixation point. This is especially true if the examinees are given a practice test to demonstrate to themselves that in the dark-adapted state "off center vision" is better than direct vision. This can serve as a graphic proof of the increased sensitivity of the parafoveal retina.

The total *area of retina stimulated* necessarily depends to some extent on the nature of the test. In determining the visual threshold to a flash of light, Hecht[17, 18] advocated that the testing light subtend a visual angle of at least two degrees, this being large enough to give a uniform cross section of the retina. It was assumed, of course, that a fixation device would be employed. Godding[25a, b] favored using a seven-degree field without fixation, since threshold brightness is independent of area considerations in a test field of that size. However, if one is to measure visual *acuity* at scotopic levels of illumination, the size of the test object used will depend upon the level of illumination at which the test is to be conducted. This can be understood best by reference to Figure 2 which is adapted from some unpublished data (Hartline and McDonald).

Since visual acuity is dependent upon illumination,[28] a larger test object must be used if one is to test visual acuity at levels of illumination below that of a starlight night than if one were to test it at brightness levels between those of starlit and moonlit nights; conversely, a decrease in the size of the test object must necessarily be accompanied by an increase in the general level of illumination.

Thus, if a test letter subtending a visual angle of two degrees is used, it should be exposed on a test field subtending a visual angle of four degrees; otherwise the character will tend to fill up the field and clues other than visual acuity will come into play, that is, if a letter T subtending a visual angle of two degrees were exposed on a 3-degree

field, one could tell the position of the T by determining the darker side of the field; exposed on a 4-degree field this clue would be eliminated. Therefore, in a test of visual acuity, the area of retina stimulated will depend on the criteria established for the general level of illumination at which the test is to be conducted.

The *time of exposure of the test object* also depends on the nature of the test.

tion at low levels of illumination. Minor variations in the brightness of the light source at photopic levels are not of great importance, but in the measurement of the threshold of vision at scotopic levels such variations become of much greater significance. Hence, it must be insured that the light source is not subject to variations in intensity. This should be controlled by neutral density filters and not by varying the
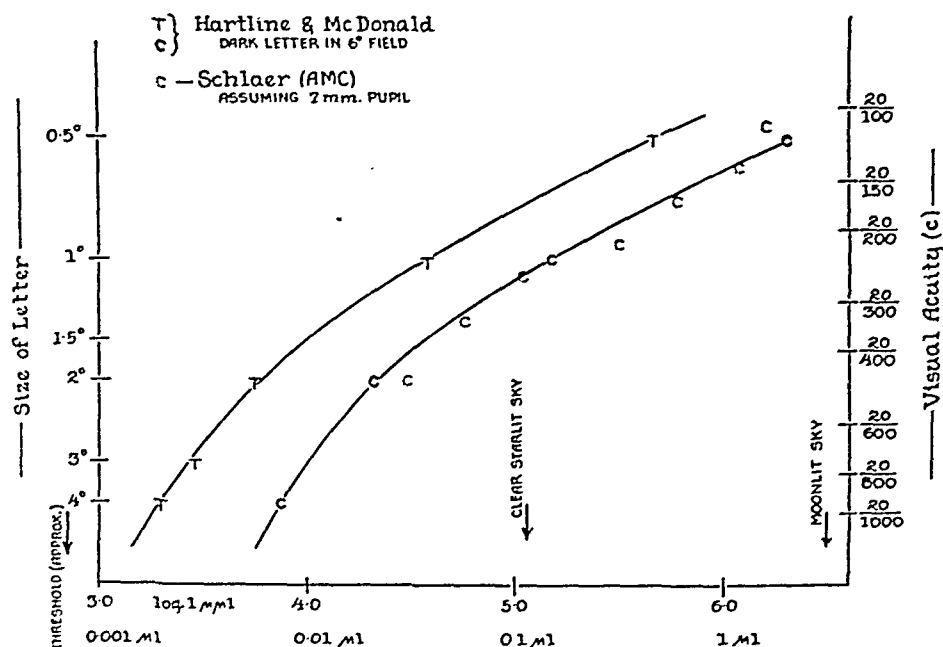
Fig. 2 (McDonald). A composite graph to show the relationship between visual acuity and illumination. The approximate brightness of the starlight and moonlight skies is also recorded. The size of the letter and visual acuity are plotted against the intensity which is recorded as the logarithm of the intensity expressed in micromicrolamberts and also in microlamberts.

Hecht[17, 18] advocated that, in the determination of flash thresholds, the duration of the flash be one-fifth second, since this is long enough to be well within the physiologic limits of the retinal reaction time. When a test object without a fixation spot is being used, longer exposures are necessary to obtain threshold readings.[25a, b] At low levels of illumination, exposure should be long enough for the examinee to be able to shift his gaze or try several areas of his parafoveal retina and yet not be long enough to induce fatigue. An exposure of 5 to 10 seconds should amply fulfill this requirement.

The source of *light* is one of the most important features of any test of visual func-

brightness of the light. The latter method would cause variations in the color temperature of the test light which in turn would give rise to the Purkinje phenomenon and affect the results of the test.

In order to produce maximum stimulation of the rods a blue filter (480 μ.) of constant density should be used in the path of the test light. This wave length produces maximum stimulation of the rods and also approximates the spectral characteristics of the night sky more closely than white light. The use of white light, however, would be quite satisfactory provided the same means of controlling the intensity were used.

Of the criteria mentioned for a satisfac-

tory test of dark adaptation, one can therefore omit a period of light adaptation, since the rate of adaptation is not under consideration and for practical purposes a period of 30 minutes' dark adaptation will insure a standard level for all examinees. Likewise, in an attempt to simulate operative conditions, the use of a fixation point to insure testing the same retinal area in all individuals can be omitted. A test of night visual capacity, therefore, resolves itself into a test of form discrimination at whatever level of illumination will most nearly approximate conditions under which night missions are performed.

The exact duplication of the specific conditions of night operations would require a fairly complicated test with many variables. Some compromise must, therefore, be made between comprehensiveness and practicability. Actually the visual task varies from the use of the threshold of vision to the discrimination of various size forms of varying contrast over the range of illumination of the night sky. The upper limits of these visual discriminations would necessarily involve some measurement of photopic acuity—such levels being reached on a moonlit night.

Since it is desired to measure scotopic acuity only, the level of illumination should therefore be restricted to that no higher than the starlit sky. At this level, however, one could devise a test in which the test object would vary in size and contrast (black to gray) and be presented on a white background, the brightness of which was kept within the desired limits. Such a test involves three variables and the more variables introduced the more difficult is the test to control. Wright[36] has devised a test of this nature. A series of Landolt C's, varying in brightness from white to gray, are exposed on a black background. The source of illumination is a plaque of luminous radium compound placed to one side of the test plate.

A simpler test would be to have either a test object of fairly large size and constant contrast which is viewed at varying levels of illumination well within the scotopic range, or to have test objects of varying size viewed at a fixed level of illumination also within the scotopic range. Measurements of dark adaptation[18, 21, 37] have shown that rod or scotopic vision covers a range of illumination of approximately 2.5 log $\mu.\mu.$ 1 (flash threshold) to 5.5 log $\mu.\mu.$ 1.

Reference to Figure 2 shows that a Landolt C subtending a visual angle of four degrees (visual acuity 20/1000) can be seen at a level of illumination of approximately four log $\mu.\mu.$ 1, whereas a similar letter subtending a visual angle of one degree (20/250) requires a level of illumination of approximately 5.2 log $\mu.\mu.$ 1.

The recognition of the letters T or E subtending the same visual angle could be accomplished at lower levels of illumination since the visual task is somewhat easier. However, no matter what is used as a test object—airplane silhouette, boat, or other symbol—the correct visual angle can be determined if the levels of illumination at which it is desired to conduct the test are decided upon.

To recognize a test object subtending a visual angle of one degree or less requires a level of illumination at the borderline of scotopic and photopic vision. Many night operations are carried out at sky brightnesses varying between starlight and moonlight, but such a test is not one of rod vision. At these relatively higher levels of illumination, it is difficult to determine exactly what one is measuring. Visual tests below this level of illumination correlate fairly well with each other as do tests which involve predominantly cone vision. Tests which involve both rod and cone vision show very poor intercorrelation with tests of either rod or cone vision.

TEST INSTRUMENTS

Most of the instruments described since 1939 embody some but not all of the criteria which have been described above; they all differ to some extent. Haines[38,] described a simple instrument which provides for a

period of light adaptation after which the time taken to recognize the position of an arrow at some predetermined low level of illumination is recorded. As many readings as desired can be taken by resetting the intensity and one can therefore measure the change in threshold over a period of time. Yudkin[39] made some further improvements in the same instrument and used it for threshold measurements of a spot of light rather than of the recognition of an arrow.

Bishop Harman[22a, b] has described a simple test in which the examinee is required to recognize the number of discs on a black screen. There are four groups of discs, the number of discs varying in each group. The light source is a standard candle set at a predetermined distance. The examinee approaches the test screen until he answers correctly. This test has met with considerable criticism.[40]

The two most widely used tests in England during the war were those designed by Craik and by Livingston.[29a, b] The Craik test, described by Rycroft,[23] was known as the Pentagon test and was used by the British Army. It consisted essentially of a five-sided figure on each face of which was a letter V in different positions. The light source was within the instrument but the sides were so arranged that the intensity was different on each face. The candidate was scored on a basis of 5/5, 4/5, and so on.

The rotating hexagon described by Livingston[29a, b] was a much more elaborate instrument, designed to test six individuals simultaneously. On each face of the instrument there are 16 figures, crosses, silhouettes, letters, and so on. The test figures are exposed at different levels of illumination and the candidate scored on a basis of the number correct out of the 32 presentations. The figures are stated to subtend the same visual angle though they vary rather markedly in difficulty of recognition. Because of the mechanical nature of the test there are many places where errors could arise

such as variations of intensity from panel to panel, from instrument to instrument, and so on. However, the principal criticism of the test is that raised by Godding[25a, b]: it is not a test of dark adaptation. Livingston designed it, however, as a test to determine night visual capacity, and even though other visual, psychologic, and training factors had to be considered, it probably served its purpose.

Both of these tests were concerned with measuring visual acuity at low levels of illumination. The size of the test object was kept constant but the illumination was varied. The only objection that might be raised is that the range of intensity, especially in the Craik test, was not broad enough to permit an adequate quantitative evaluation of the results.

Godding[25a] and Koch[30a, b] have also described instruments for testing the light sense. Both of these adhere strictly to the essential criteria for a satisfactory instrument. The Koch instrument was used by Michaelson[41] in testing army personnel and, contrary to the statements of most other military personnel, he believes that an instrument determining the minimum light threshold is of more value than one determining the minimum form threshold.

The Canadian Army and Air Force used some of the instruments designed by the English though they were chiefly concerned with night-vision training.[42] At the end of the training period the examinees were required to spot the direction of a black disc on a contrasting background, that is, was it vertical, right or left? The relative merits of night-vision training and night-vision testing are not pertinent to this discussion. The Canadian Navy[20] used a modification of the Hecht-Shlaer instrument. The only essential change was to make the instrument more compact and to permit binocular viewing of the test field. In their hands, this instrument proved satisfactory.

In this country there was just as much

diversity of opinion about the best instrument as elsewhere. The Army Air Corps had four different types of instruments to test night vision.[43a, b, c] The large instrument mentioned in the first part of this paper was designed to test large numbers of individuals at training centers, and to be as free of human error as possible. The test object was automatically presented five times at eight different levels of illumination in 1 of 8 positions. The exposure time of 10 seconds and the change in illumination were all automatically controlled. Six examinees were tested at one time. Each had in front of him a model of the test object, a letter C made out of plastic. They were required to turn the break in the C to correspond with that of the test object; the response was automatically recorded if correct. Although the more complicated the mechanical device the greater the chance for mechanical failure, the instrument definitely fulfilled a purpose.

The other three types of instruments available were of the so-called portable variety: the Hecht-Shlaer instrument as designed for the Canadian Navy and the night-vision testers of the School of Aviation Medicine, and the Aero Medical Laboratory.[43a, c] The School of Aviation Medicine night-vision tester required the recognition of a Landolt C subtending a visual angle of two degrees. The source of illumination was a plaque of self-luminous paint behind the test letter, the intensity being controlled with neutral density filters. The test was conducted at 12 inches. The Aero Medical Laboratory's night-vision tester was similar in principle. The source of illumination was radium salt in a moisture-proof cell. The test letter was also a Landolt C. The candidate was first tested at 11 feet from the instrument; if he did not get 4 out of 5 presentations he was moved up to 9, 7, or 5 feet. The results were recorded as the distance at which the examinee got 4 out of 5 presentations correctly.

The United States Navy[44] employed a test somewhat similar to the Aero Medical Laboratory's test. The source of illumination was a radium plaque. In front of it was the test letter. A fixation device was attached to the side of the instrument.

Thus the instruments in general use by the Armed Services had one thing in common, that is, the recognition of a form at a low level of illumination. Some of the silhouettes, as in Livingston's[29] instrument, were rather complicated and the criticism that this was not a test of dark adaptation would appear justified. In this country, a test of much simpler form discrimination was employed. The size of the letter was determined by experiment to be one which would test scotopic acuity below the level of a starlit night (fig. 2).

Probably the most important feature of any such test is the control of illumination of the test object. This can be either a light bulb or a luminous plaque of a radium compound. Both have advantages and certain disadvantages. A properly controlled light source with provisions to check its brightness periodically is probably the better of the two. Trained personnel and adequate equipment are needed to do this properly. The radium plaques have the disadvantages of deteriorating slightly in intensity and of being affected by exposure to light. However, if the proper precautions are taken, they prove to be quite satisfactory in the smaller types of instruments. They have the distinct advantage of not requiring elaborate devices to ensure constant brightness.

TEST SCORING

No matter how accurate or elaborate a test one may devise, the entire value of the test may be nullified by improper scoring. Unfortunately, many investigators have not paid sufficient attention to this aspect. Thus, in the routine laboratory or clinical tests of dark adaptation the usual method of determining the threshold is by the "method of limits," that is, starting with flashes that can-

not be seen, the intensity of the test light is increased in small fixed steps until a flash is reported as seen, the intensity is then reduced about 0.2 μ. μ. 1 and after a brief pause the flash is repeated. After 3 or 4 flashes two values are arrived at—one where the flash is seen and one where it is not. If there is not too great a difference between the two values, the intensity at which 2 out of 3 flashes are seen is called the threshold. This method is not too laborious and was employed by Solandt and Best[20] in testing a large group.

A more accurate method of determining threshold is by "frequency-of-seeing curve" (unpublished data, Hartline and McDonald). Knowing the approximate threshold, a specified number of flashes are given in random order at each of several intensities, approximately 0.10 log μ. μ. 1 apart. At the highest intensity the flashes should be seen on every presentation, and at the lowest, none; at the intermediate intensities, some are seen and others are not. The mean threshold is therefore somewhere between these intensities, theoretically at that intensity where one half the flashes are seen and one half are not.

The number of correct responses may be used to determine the actual mean threshold or they may be used as a score to differentiate individuals. If an individual sees 25 out of 40 presentations, he is obviously better than anyone who sees only 15 out of 40. (This method of measuring stimuli is fairly commonly used in psychophysical methods of measuring sensation.) It has one distinct advantage in that it lends itself to scoring a routine or semiautomatic test. This is the method employed with the American Army Air Force Night-Vision Tester.[43b] It would appear laborious for a manually operated test but actually it would not be if the test were set up correctly. In an instrument allowing four different positions of the test letter, the test object could be presented 12 or 16 times at 3 or 4 levels of illumination. The score of number correct would be easier to tabulate and would be more accurate than just reading the intensity or the distance at which 4 out of 5 presentations were called correctly. If a candidate did that on his first trial the tendency would be to record that as his score and not make any further examination.

It must be remembered that in any subjective test of this nature, there are many factors to be considered apart from the instrument. For many this test is an entirely new experience. In a desire to do well, some may forget to use the parafoveal retina. Others, trying to avoid certain types of duty, may deliberately fail the test.

One must also consider the individual giving the test. Hour after hour in a dark, poorly ventilated room may soon dampen his enthusiasm and result in carelessness and inattention. These and other intangible factors must all be evaluated.

RELIABILITY AND VALIDITY

Finally, in any test of visual function, it is important to know the reliability and validity of the test. As is to be expected, there was little opportunity to investigate this problem in time of stress. To say a test is reliable means that it must align individuals about the same way each time the test is given. This in turn depends primarily upon (1) the accuracy and standardization of the instrument, technique, procedure, and so on, and (2) the size of the intraindividual variation as compared with the interindividual variation in the population tested.

It has been shown in the group of 162 cadets that there is an interindividual variation of the visual threshold of one log unit. If each individual were to show a day-to-day variation of one log unit (intraindividual variation), the test could not be considered reliable since it could not align individuals in the same way at each test. This would not be a criticism of the instrument, but, in statistical terms, the test would not be reliable since in the visual function tested each individual

might vary as much as the whole group.

The two different tests of dark adaptation in this report show good test-retest reliability. The correlation between the two tests has not been made because these studies were carried out at different times and on different individuals. Since most of the different instruments described above were modified from instruments known to have good reliability, the authors have for the most part not retested large groups of individuals. Yudkin, and others,[21] reported that on retests of the same individual the final rod threshold varied by about 0.2 log units. This is in close agreement with my findings and those of Hecht and Mandelbaum.[18]

The validity of the test is the correlation of the results of the test with some measure of performance, that is, flying ability (accident rate, success or failure in flying training, enemy planes shot down at night, and so on). The validity will be low (1) if the function tested has little or no correlation with the test of flying, (2) if the test is not reliable due either to poor technique and instrumentation or to little difference in the intraindividual variation as compared to the interindividual variation, or (3) if the test scores do not have a high correlation with the critical function purportedly measured.

Unfortunately, there has been no validation of these tests against actual performance. This is true for most of our tests of visual function. In fact most of our physical standards have been established without any validation. Moreover, any one function we measure contributes such a small part to the actual performance of flying that its validation is extremely difficult.

Most of the studies on dark adaptation within the past few years have been concerned with factors that impair night vision. The role of vitamin A deficiency in causing impairment of night vision is now well established and it is well recognized that the response to vitamin A therapy varies from individual to individual.[14 6, 15, 18, 21] It has also

been clearly shown[45] that there are various ocular conditions that may account for an abnormal rise in the visual threshold, and that there are also certain other physiologic factors that may cause such a rise. One of these is the deterioration of night vision with age[46, 47] which has been attributed to a decrease in the pupillary diameter. Anoxia has also been shown[48-51] to cause such a rise. This is believed to be brought about by the effect of anoxia on the central nervous system and not on the visual purple.

In any study of night vision, it would seem logical that an attempt be made to improve the visual threshold of normal individuals. Anything that might improve the transparency of the ocular media or increase the concentration of visual purple in the outer limits of the rods should improve night vision. Since there is no known means of improving the transparency of the ocular media, the first obvious approach was to attempt to improve the threshold by feeding large amounts of vitamin A in the hope that this might be reflected in an increase of this protein in the visual purple. In the experiment that was conducted there was no significant improvement in the visual threshold following eight weeks of vitamin-A therapy. This might be expected since the individuals in this age group were in perfect health and their threshold of vision approximated the absolute limit.[131]

Yudkin[52] has reported on the effect of vitamin A, alcohol ,and benzedrine on the final rod threshold. Most of his subjects, however, had thresholds that were considered abnormal. He found that 100,000 units of vitamin A caused an improvement in the threshold within 4 to 10 hours but by 24 hours the threshold had returned to its previous level. Alcohol and benzedrine both caused a transitory improvement of the threshold for 30 to 60 minutes but the effect was not noticeable after 90 minutes. Kekcheev,[53] in a paper that is poorly documented, states that caffeine, kola, and alcohol im-

prove night vision. He also states that stimulation of one sense organ increases the sensitivity of the other sense organs. Listed are stimulants to taste and smell that will improve night vision. In general he believes that pleasant sensations lower the threshold and unpleasant sensations raise the threshold. There is no other literature available to corroborate his claims.

Lythgoe[54] and Craik,[55] in papers that appear to be frequently overlooked, stress the fact that the mechanism of dark adaptation cannot be explained solely on the basis of the bleaching and regeneration of visual purple. Lythgoe believes that the increase in retinal sensitivity to light is brought about by both the regeneration of visual purple and some change in the neural mechanism of the retina. Since Yudkin[52] does not think that the effect of alcohol and benzedrine is brought about by a change in the vitamin-A content of the blood it is possible that these drugs may affect the neural component as proposed by Lythgoe.[54]

The search for some method to improve the visual threshold in normal individuals has not been very productive. In evaluating the effect of substances that affect the entire nervous system, that is, alcohol, anoxia, and so on, great caution must be paid to be certain that the results are accurate.

In some unreported experiments (Hartline and McDonald) on the effect of choline on the visual threshold it was found that in some instances trained individuals reported seeing many more blanks than usual. This might not have been noted except for the fact that the threshold was being measured by the frequency-of-seeing method and it was customary to give each individual a certain number of blank presentations. Unless this had been detected, it is quite probable that the true effect of the drug would have been missed.

CONCLUSIONS

Prior to World War II most of the investigative work on night vision was concerned with physiologic studies of the mechanism of vision or the effect of nutritional deficiencies on the visual process. This work fortunately provided the basic information needed for the tremendous problem of trying to evaluate and protect the night vision of those civilians and soldiers who were required to perform their various duties at night.

Since all physical examinations prior to the war were concerned only with tests at photopic levels of illumination, satisfactory tests at scotopic levels had to be devised. Of necessity some tests were devised and put into operation without much preliminary evaluation. Some sacrificed accuracy for simplicity though, for the most part, the tests were able to detect those who showed defective night vision. Practically all the tests developed during the war had one thing in common: they measured the threshold for form rather than that for light.

The introduction of a measure of visual acuity even at scotopic levels of illumination complicated the test. The criticism that such a test was not a test of scotopic vision was justified especially if the test objects were difficult to recognize or if they were so small (fig. 2) that to be recognized the level of illumination approached that of photopic vision. Most of the tests, especially the more elaborate ones, attempted to assess the examinees' night vision on a quantitative basis.

In the experiments that have been reported the tenfold variation in the final rod threshold of healthy young adults confirms the findings of other investigators. The two different night-vision tests employed, one a test of the visual threshold to a flash of light and the other the recognition of a 2-degree C, have both shown good reproducibility or test-retest reliability. It has also been shown that the visual threshold in normal individuals is not improved with large doses of vitamin A.

In discussing the improvement of the visual threshold, no mention was made of the various means used to protect the thres-

hold, that is, the use of goggles, red lights, developments in instrument panel illumination, the use of oxygen at night, and so on. These do not enter into a discussion of the evaluation of night vision.

The ideal of any test of night vision is that from the results one could eliminate the poor and select the best for special assignments that might involve night operations, and so on. As is frequently the case, the ideal is seldom achieved. If failure on the test means removal of the trainees from certain types of training, especially if such training is none too desirable, the elimination rates goes up once that fact becomes known. In subjective tests of this nature it is very easy to fool the examiner. Given sufficient retests and individual examination the true situation can frequently be uncovered but the excuse can always be given that the test was not understood.

As a means of selecting the best individuals for a particular job, the test is again none too satisfactory when employed on a large scale. There are so many other factors such as motivation, intellect, natural skill with a particular instrument or airplane, and others, that the performance score on a night-vision test is frequently overshadowed by other considerations.

Most of the individuals who complained of difficulty in performing their assigned duties at night were found to have normal night vision. (Such complaints are frequently the earliest manifestation of anxiety.) Despite this, however, it is believed that a test of night vision on all military personnel is worth while—some cases of night blindness are always discovered on routine examinations, especially in groups less highly selected than cadets. Also in the vast majority of individuals this test proves to be the first demonstration they have ever had that, at low levels of illumination, eccentric vision is many times better than central vision.

Like many tests of physical capacity it is no better than the person doing the testing. Given a satisfactory instrument and an interested examiner, a test of night vision becomes an important diagnostic aid as well as a means of demonstrating the important aspects of scotopic vision. However, until this one aspect of visual function is correlated with actual performance, no opinion can be expressed as to its value in a battery of tests for selection of individuals for flying duties.

1930 Chestnut Street (3).

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RIBOFLAVIN TREATMENT OF SPRING CATARRH

H. J. Stern, M.D.
Utica, New York

In 1944, Castellanos[1] published a paper on his experiences with riboflavin in the treatment of spring catarrh (vernal conjunctivitis). He found that 92 percent of 105 patients improved within a short time (35.7 percent in 3 to 4 days and 65 percent in 10 to 15 days) when 1 to 3 mg. of riboflavin were given daily by mouth. During this treatment, the patients also received eyedrops containing adrenalin. He explained this favorable effect by assuming that riboflavin is rapidly destroyed in summer by the increased ultraviolet radiation, and concluded that spring catarrh is actually a riboflavin deficiency.

In a reply in the same journal, Lehrfeld[2] attacks this paper vigorously, denying that riboflavin can conceivably be of any use in the treatment of spring catarrh because this disease has been proved to be of allergic origin. Lehrfeld assumes that the improvement observed by Castellanos in his cases is solely due to the local treatment with adrenalin.

To treat patients with spring catarrh by administering a substance well known to give considerable relief in this condition while experimenting with a new therapeutic agent must be regarded as an inconclusive experimental set-up, and to claim full credit for riboflavin without considering that adrenalin might have had a share in the successful treatment is not justifiable. Moreover, the explanation offered by Castellano was not convincing. Riboflavin deficiency is

a reasonably well-defined clinical picture, and to ascribe a condition to a lack of riboflavin because this substance gives relief can hardly be defended. Moreover, it seems that riboflavin is present in the cornea in its coenzymatic form which is light-stable.[3-5]

However, in view of recent observations on the antiallergic properties of several members of the vitamin-B complex, the idea of testing them on cases of spring catarrh seemed attractive, and the results of this investigation are to a certain degree a vindication of Castellano.

INVESTIGATION

Twenty-two cases of spring catarrh were treated. Of these, 13 presented the palpebral form of the disease, four of them showing only milky conjunctival edema while nine suffered from papillary hypertrophy giving the conjunctiva the typical cobblestone appearance.

Seven cases showed the bulbar form with hyperemia and edema of the bulbar conjunctiva and grayish gelatinous "epaulettes" encroaching upon the cornea to a varying degree. Two cases belonged to the so-called mixed form with involvement of the bulbar as well as the palpebral conjunctiva. In all cases, the history and subjective complaints were typical for the disease.

RESULTS

The nine cases suffering from the palpebral form with papillary hypertrophy re-

ceived 5 mg. of riboflavin twice daily, three of them together with 25 mg. nicotinamide. They responded uniformly well. No other treatment was given during this time.

After the first few days, the subjective symptoms—burning, itching, and photophobia—improved considerably, and the pathologic changes of the palpebral conjunctiva receded to a varying degree, leaving the conjunctiva less hyperemic and smoother. The cobblestones were less marked, although they never disappeared altogether.

The improvement was not maintained when the treatment was discontinued. Riboflavin could be replaced by preparations containing the whole B complex (Betotal, Bevitex, yeast tablets) with satisfactory results, and the combination of riboflavin (5 mg.) and nicotinamide (25 mg.) twice daily seemed particularly effective.

The four cases of palpebral spring catarrh, without papillary hypertrophy but with milky edema only failed to derive any benefit from treatment with riboflavin by mouth or injections of the B complex.

One of the two cases with the mixed form improved somewhat with 3 gm. of yeast tablets daily, the second one did not respond to riboflavin, B complex, nor nicotinamide by mouth.

The same negative results were recorded in the seven cases with the bulbar form of spring catarrh.

DISCUSSION

It is interesting, but cannot be explained at present, why the patients with the bulbar and mild palpebral form of spring catarrh failed to improve under a therapy which proved so beneficial to the cases with papillary hypertrophy (cobble-stones) of the palpebral conjunctiva. Further investigations will have to be made, and it is anticipated that some ideas may be derived from the results as to the peculiar fact that one and the same disease can produce so fundamentally different clinical pictures—if it really is one and the same disease.

An attempt will be made, however, to explain the results obtained in the light of recent knowledge of the antihistamine properties of riboflavin and nicotinamide, by assuming that it is a histamine sensitivity which constitutes the physiopathologic basis of the nosologic entity in the cases deriving benefit from the treatment described.

There can hardly be any doubt that spring catarrh is an allergic condition. Berens[6] and Gifford[7] are the exponents of a small number of authors who doubt this and do not admit allergy as the cause of it in every case. It seems, however, undeniable that a large amount of evidence points to the allergic nature of spring catarrh. The clinical picture with its recurrences; the climatic and seasonal incidence; the frequent association with other allergic conditions as asthma and hay fever; the absence of bacterial agents or inclusion bodies and the presence of eosinophilia; the frequent finding of a positive Prausnitz-Küstner reaction to specific allergens; the reaction of the conjunctiva to adrenalin—all these facts are, according to Lagrange and Delthil,[8] proof of the allergic nature of the condition.

The physiopathologic basis for allergic manifestations is an abnormal response of the capillary system to physical stimuli which causes a disturbance in the capillary circulation. This results in disorders of the cell nutrition, liberation of histamine in the tissue, and disturbances of the fluid and electrolyte metabolism. The manifestations are localized because they are transmitted by the parasympathetic nervous system, reactions of the sympathetic system only being generalized (Otfried Mueller).

Best and Taylor[9] summarize the present views in the following words: "It is now generally accepted that the antigen-antibody reaction in some way brings about the liberation of histamine by the affected tissues and that the action of this amine is re-

sponsible for the allergic manifestations."

Magitot[10] describes how the irritation of the subepithelial layers leads to follicle formation in the mucous membranes and points out that the participation of the nervous system in an inflammatory process consists of stimulation of the sensory nerve terminals, whereby histamine is liberated, resulting in vasodilatation.

Histamine and adrenalin are antagonistic in their effect upon the capillaries, and adrenalectomized animals show an increased susceptibility to histamine administration. This fact may be an explanation of the beneficial effect of adrenalin in spring catarrh. It does not simply act as vasoconstrictor, thus alleviating the symptoms, but, as an histamine antagonist, it exerts its therapeutic action on a more basic level as well.

A considerable number of antihistamine agents have been found recently. One of them is riboflavin. It is known that this vitamin plays a rôle in the dehydration and destruction of histamine. It is a component of a diamino-oxidase which is essential in this process.

This has been proved experimentally by Doxiades and Lemke[11] who could desensitize guinea pigs against an allergic shock by previous administration of riboflavin. Kalter[12] has treated asthma successfully with riboflavin and has also had some success in the treatment of hay fever.

It has been shown by Daïnow[13] that nicotinamide also exerts a very beneficial influence on such allergic conditions as hay fever and asthma. In collaboration with Halpern,[14] he showed in animal experiments that guinea pigs can be protected from an asthma attack in an atmosphere containing histamine by premedicating them with nicotinamide. A similar attack of asthma provoked by acetylcholine cannot be prevented with nicotinamide. Halpern and Daïnow conclude from this that nicotinamide possesses a specific antihistamine property.

The same authors[15] showed that nicotina-

mide prevents and even relieves the spastic contraction of the isolated uterus and intestine of guinea pigs suspended in a solution containing histamine. In similar spasms caused by acetylcholine or the hormone of the posterior lobe of the hypophysis, nicotinamide failed to be effective.

In view of these experiments and clinical trials, it seems undeniable that riboflavin and nicotinamide are to be regarded as antihistamine agents. It is not surprising, therefore, that these substances are very effective in alleviating the symptoms of certain forms of spring catarrh, which, as has been shown, must be regarded as an allergic condition due to histamine liberation in the tissue.

Theoretically, the effect of nicotinamide on allergic conditions can perhaps be regarded as due to its regulating action on the cell metabolism as a prosthetic element of the dehydrating enzymes (cozymase). Colldahl[16] has shown that in experimental asthma of guinea pigs the lack of cozymase leads to a reduction of oxidative processes in the tissues which can be normalized again by administering this enzyme.

One can assume that histamine is not the only body responsible for allergic reactions and that other substances (acetylcholine, and so forth) also play a rôle. This may explain the fact that not all cases of palpebral spring catarrh were benefited alike from the administration of riboflavin by mouth, that the bulbar form did not respond at all. There must and will always be allergic conditions which will fail to respond to riboflavin or nicotinamide.

Moreover, one must always keep in mind that the therapy with antihistamine agents is a symptomatic therapy which does not remove the underlying cause for the allergic reaction but only alleviates its symptoms. Active antiallergic procedures, such as isolation from the guilty allergen or desensitization against it will remain paramount in the therapy of spring catarrh.

If and when isolation and desensitization

are not possible, however, we can regard riboflavin and nicotinamide as valuable allies in the symptomatic treatment of this annoying and sometimes even incapacitating disease.

3 Hopper Street..

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OPHTHALMIC MINIATURE

The ophthalmoscope was discovered by Hermann von Helmholtz in December, 1850, and the account thereof was published in the following year. In speaking of this invention some years later, he said:

"The ophthalmoscope has become the most popular, perhaps, of my scientific achievements, but I have already told the ophthalmologists how luck played an incomparably greater part than my merit in this matter. I had to explain to my students the theory of ocular luminosity, which stemmed from Brücke. Actually, Brücke had missed the discovery of the ophthalmoscope by a hair's breadth. He had only neglected to ask himself the question: To which optical image do the rays returning from the luminous eye belong? Had he raised this question, he could have answered it just as quickly as I did, and the ophthalmoscope would have been discovered.... I immediately set about to construct the instrument out of spectacle lenses and cover glasses for microscopic preparations. At first it was quite difficult to use, and without a firm theoretical conviction that it must work, I would perhaps not have persevered in my efforts. But after about eight days I had the great pleasure of being the first to see clearly a living human retina."

THE REACTION OF VARIOUS TYPES OF FAT TRANSPLANTED INTO THE ORBIT OF GUINEA PIGS PRIOR TO THE DEVELOPMENT OF EXOPHTHALMOS*

GEORGE K. SMELSER, PH.D., AND V. OZANICS, M.S.

New York

Thyroidectomized guinea pigs receiving daily injections of extracts of anterior hypophysis develop exophthalmos which is accompanied by swelling and edema of the orbital and some fat tissues. These changes have been reported by several observers.[1-4] The edema, although noted in fat tissues other than in the orbit, is more marked there than in other regions such as in the perirenal or testicular fat bodies.[5] The reason for this difference is not clear and is of interest because of the importance of the role the edema may play in the production of the exophthalmos.

The edema of the orbit may be a local manifestation due to anatomic peculiarities of that region or, as suggested by Gailli Mainini,[6] a result of reduction in tissue pressure occasioned by the forward movement of the globe. If this concept is correct, the edema found in these animals should be restricted to the orbit, which, as has been shown, is not the case. Conditions in the orbit may simply exaggerate a generalized condition due either to factors as suggested by Gailli Mainini, or inadequate lymphatic drainage, and so forth.

Another possibility, which is in agreement with the available data, is that the permeability of the vascular bed varies with the tissue which it supplies, and that the vessels are not very permeable in these animals in the testicular, axillary, or perirenal fat but are in the orbital fat, as well as in the fat depots near the Fallopian tubes or the ureter.

These several concepts may be tested by transplanting fat from various parts of the body to the orbit and then producing an exophthalmos by the injection of anterior pituitary extracts. The histologic structure of the orbital fat of the intact and operated orbits could be compared with that of the graft and with donor type of fat tissue in its normal location.

If the transplanted tissue retained the characteristics shown in its original position, it would indicate that purely local orbital conditions were negligible in the production of the changes seen in the orbital fat of exophthalmic guinea pigs. If, on the contrary, transplanted fat were affected in the same manner as orbital fat, the importance of local factors would be emphasized. It was necessary, of course, to determine whether transplantation alone affected the response of the tissue to the injected extracts. Therefore, grafts of orbital fat were also made using as donors the male parent of the recipient.

EXPERIMENTAL

Forty-nine guinea pigs of both sexes were used in these studies. In seven cases, transplantation of fat to the orbit was done when the guinea pigs were young adults, in all others the grafts were made in 1- or 2-day-old animals. The Harderian gland which occupies a large space in the orbit was removed from the right orbit through a small conjunctival incision on the nasal side of the globe where its ducts open. The gland could be withdrawn from the orbit through this opening with a minimum of trauma and no bleeding save when the vessel to the gland itself was severed. The donor fat tissue was obtained from the same individual at this time and placed in the orbit. The con-

junctival incision did not require sutures. Donor tissue was taken from the right axilla in nine cases, the right testis fat body in 13 cases, the right ovario-uterine mesentery in 10 cases. Seventeen grafts of orbital fat were made in the same manner excepting that the transplants were from another, although related individual, rather than from the same animal.

The guinea pigs were thyroidectomized when several months of age and 7 to 10 days later daily injections of an anterior pituitary extract were administered to 39 of the animals. Representatives of each type of transplant, totaling 10 animals, were reserved as uninjected controls. The preparation and amount of extract administered was the same as reported in previous communications.[7, 8]

The length of the injection period varied widely; in some cases treatment was continued for 55 to 76 days. Eight animals, however, were injected for only 10 days. Each type of graft was represented in both long and short injection groups. Exophthalmos, as judged by inspection and postmortem measurement of the unoperated left eye, was present at the conclusion of the experiment.

At autopsy the fat in the operated orbit was carefully examined to determine if two (donor and host) zones could be distinguished, the tissue was then fixed in Bouin's fluid and histologic sections were prepared.

The block of embedded tissue was oriented so that the sections passed through both the host and transplanted portions and showed the interface between the two.

The removal of the Harderian gland and transplantation of fat in its place resulted in a variable displacement of the globe inward and slightly downward. The injection of the anterior pituitary extract caused an exophthalmos which was evident in the intact left side. Protrusion of the operated right eye was not as marked as that of the intact left eye and exact measurements of the exophthalmos (skull-limbus distance) made postmortem were not as dependable as usual, because of the displacement of the globe caused by the operation. However, the operated right eyes averaged 0.5 to 0.6 mm. greater protrusion postmortem than their controls.

All of the autotransplants were well incorporated in the orbit and had greatly increased in weight since grafting. Their growth was demonstrated in a few instances by comparison of the weight of the donor tissue at the time of transplantation with that obtained at autopsy.

The orbital fat of exophthalmic animals has a translucent appearance due to edema which differentiates it very sharply from the normal, dense, opaque character of ordinary fat tissue. This appearance was also characteristic of the native orbital fat in operated

Figs. 1 to 6 (Smelser and Ozanics). (Fig. 1). Section of orbital fat from an unoperated orbit of an exophthalmic guinea pig showing the edematous character of the tissue.

(Fig. 2). Section of transplanted orbital fat of an exophthalmic guinea pig. The graft had been made at birth and was from a related normal adult.

(Fig. 3). Section of orbital content of an exophthalmic guinea pig showing the interface between the edematous host orbital fat and the testicular fat transplant which remained unchanged by the pituitary extract injections and the development of exophthalmos.

(Fig. 4). Section of testicular fat in situ of an exophthalmic animal showing a region including some epididymal tubules. Note the presence of edema in the connective tissue surrounding the tubules and its absence in the purely adipose tissue.

(Fig. 5). Low magnification of a section through the orbital fat and graft of testicular fat of an exophthalmic guinea pig showing both the host and donor regions. Note that the host portion is edematous, whereas the grafted portion is not, except in the region of grafted epididymal tubules where edema is found. The situation is similar to that shown in Figure 4 where edema is noted near the epididymal tubules in testis fat in its normal location.

(Fig. 6). High-power view of the epididymal tubule region included in the graft shown in Figure 5.
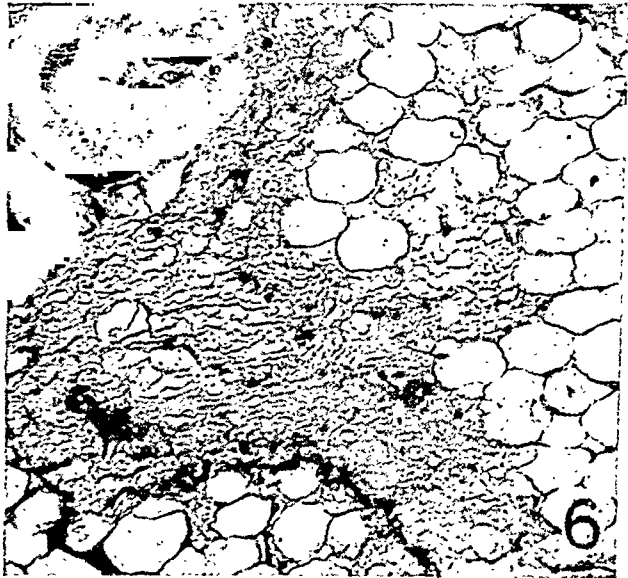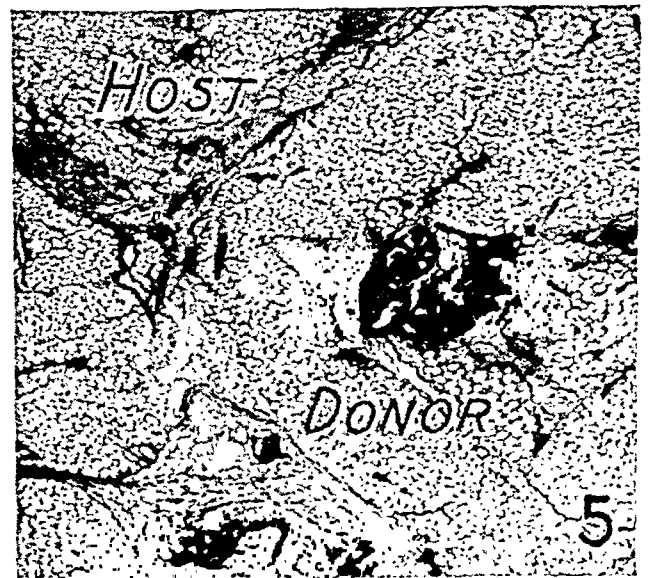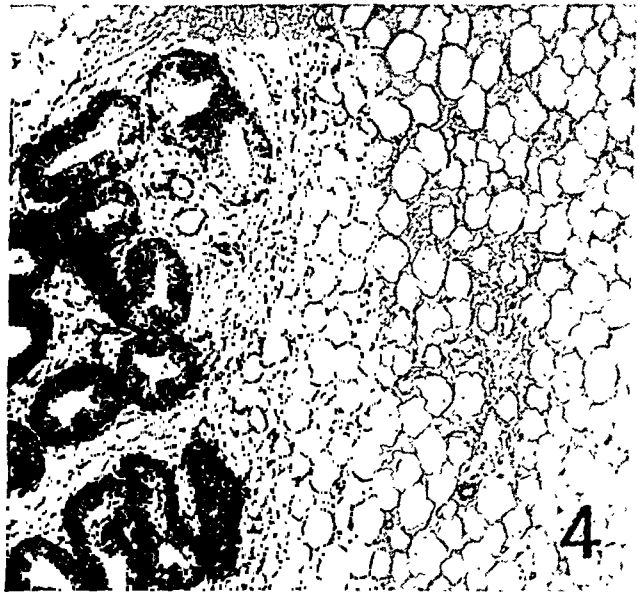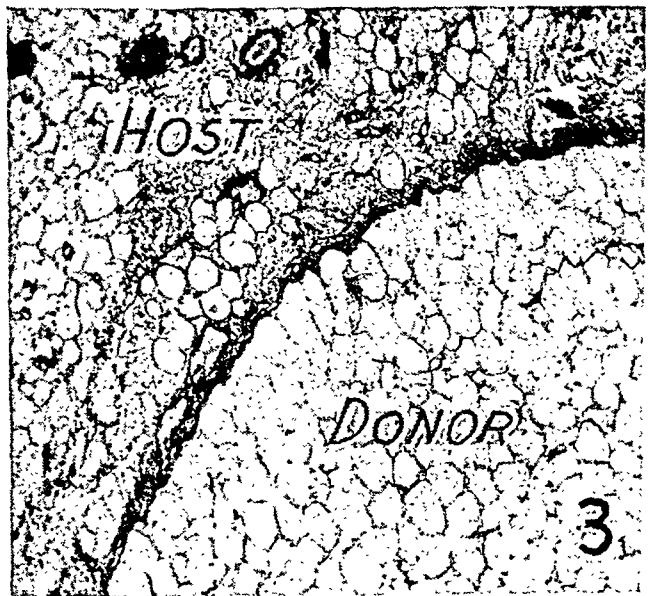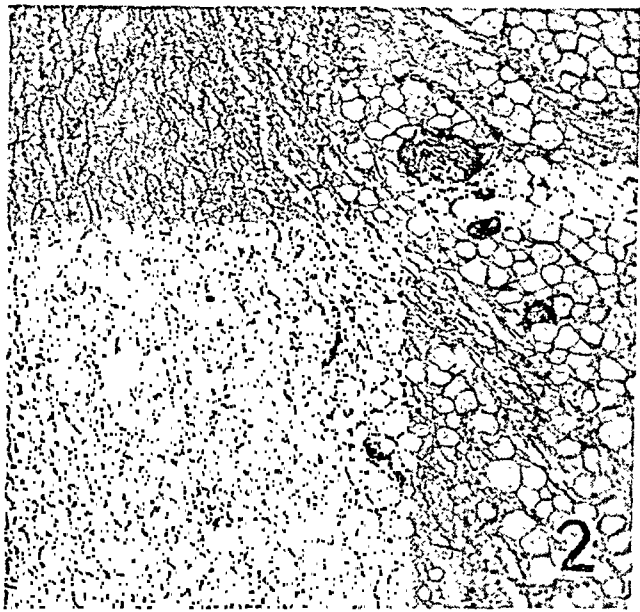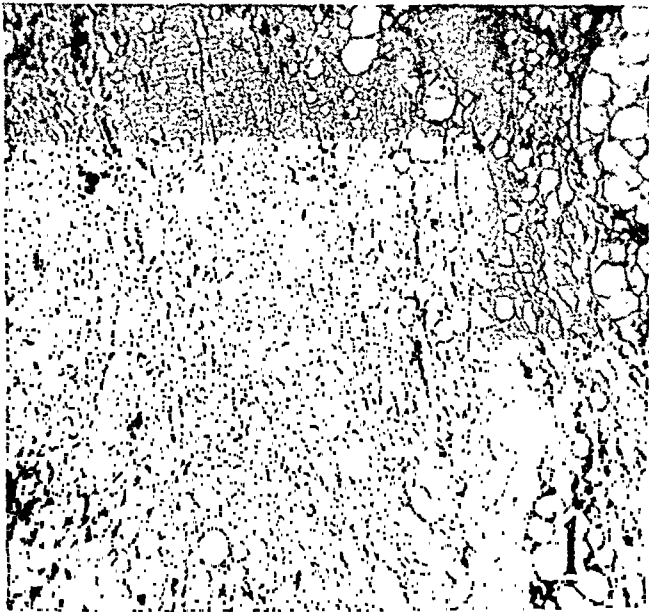
orbits of the exophthalmic animals and contrasted sharply with the transplanted tissue of axillary, testicular, or uterine origin. Specimens of these donor-type fat tissues were removed from the appropriate regions, but from the side opposite that from which the fat used in making the graft had been removed. The orbital and transplanted fats of the 10 uninjected, control animals maintained the appearance of these tissues as observed in other thyroidectomized guinea pigs with intact orbits.

Gross observations of the orbits to which orbital fat had been transplanted did not reveal distinct separation of the fat into zones different in appearance or texture, and the entire mass appeared to be edematous. In a few instances it is possible that the major part, at least, of the graft had degenerated. This was indicated by a mass of dense connective tissue in the region where the implant had been made. In the other cases, however, the size of the homogeneous mass of fat in the orbit in the region of the graft together with the absence of scar tissue indicates that these transplants were well incorporated, and that the transplanted portion reacted to the injected pituitary hormone as did the original fat tissue of the host.

Sections were prepared of all the grafts as well as the orbital fat from the intact orbit and a specimen of the donor tissue. These where stained with Masson's trichromic stain, because with this stain the protein containing edematous infiltrate is particularly well shown. Sections of orbital fat from the intact orbits showed marked edema such as was reported earlier. Sections of the fat from right orbits which had been recipients of

orbital fat grafts showed two zones, both edematous. They were separated by a line of connective tissue forming an interface between graft and host. The histologic character of the two zones was similar and like the orbital fat in the unoperated orbits of the same animals (figures 1 and 2).

This condition was not found to apply in the case of the orbits containing grafts of axillary fat or in some cases from the testicular fat body or fat from the uterine mesentery. In these cases two distinct zones of fat tissue of different character were observed (figs. 3, 7, and 11). One was, in each case, typical orbital fat and the other was a mass of adipose tissue composed of solid masses of fat cells separated by a few delicate strands of connective tissue, characteristic of the fat depots from which they came (figs. 8, 9, and 10). The two masses of fat were separated by a band of connective tissue, as were the host and graft of orbital fat. In several cases the graft appeared to have been pushed into the host tissue and was partly surrounded by a narrow zone of edematous connective tissue, presumably of host origin.

Most of the grafts of testicular fat (13 cases) behaved exactly as did those of uterine mesentery or of axillary origin. Two types of fat were seen in these orbits, one edematous and containing nerves, vessels, and muscle fibers (retractor bulbi) characteristic of orbital fat, the other one not edematous but consisting of masses of closely packed fat cells containing a few strands of connective tissue (fig. 3). Sections of the fat from the testes of these animals did not exhibit evidence of the edematous infiltration,

Figs. 7 to 11 (Smelser and Ozanics). (Fig. 7). Section of orbital content of an exophthalmic guinea pig showing the interface between the edematous host orbital fat and the unaffected graft of axillary fat.
(Fig. 8). Section of fat from the axillary region of an exophthalmic animal. Note absence of edema even in the connective-tissue band.
(Fig. 9). Section of edematous orbital fat from the host zone shown in Figure 7.
(Fig. 10). Section through the transplanted axillary fat from the donor zone shown in Figure 7. Compare this tissue with the axillary fat in situ shown in Figure 8.
(Fig. 11). Low magnification of the orbital contents of an exophthalmic guinea pig showing the edematous native orbital fat and the unaffected grafted fat taken from the axilla.
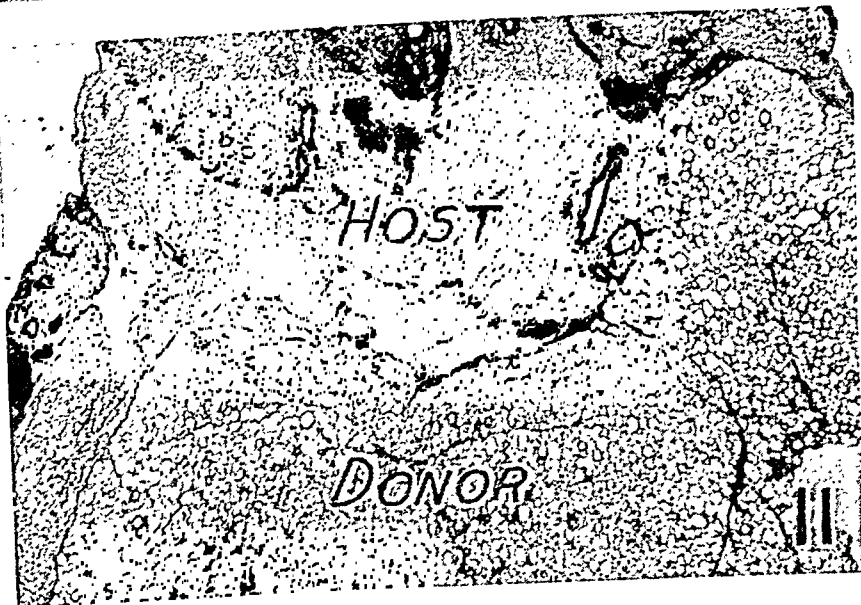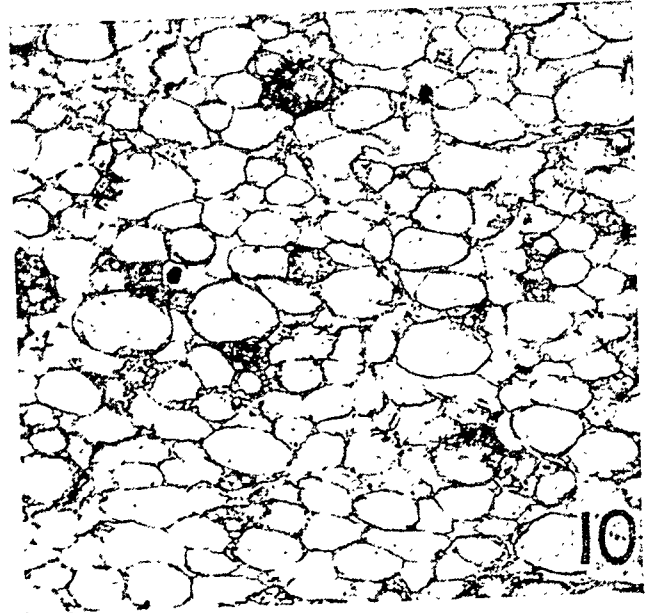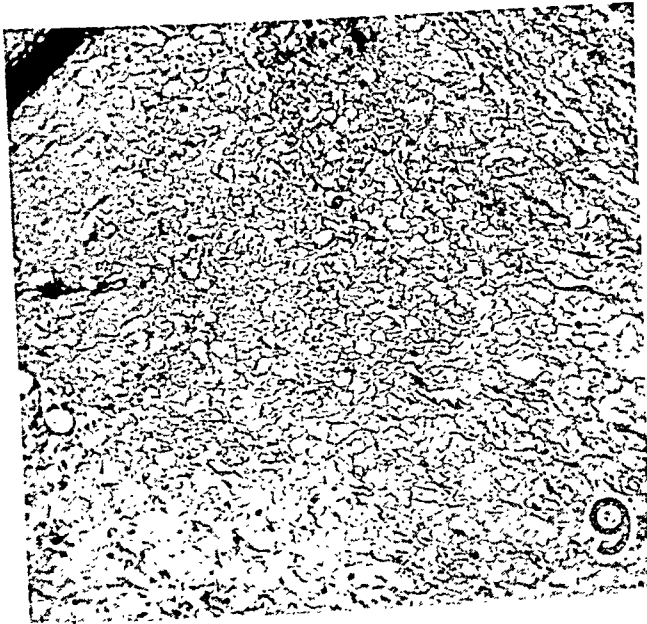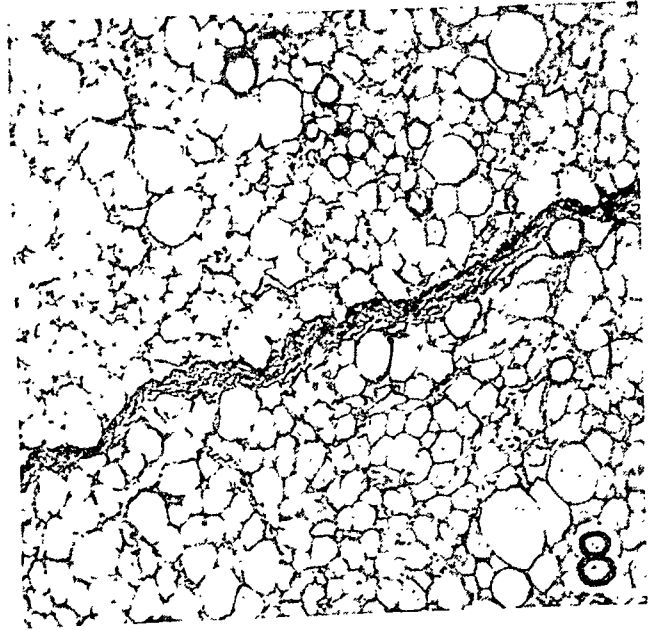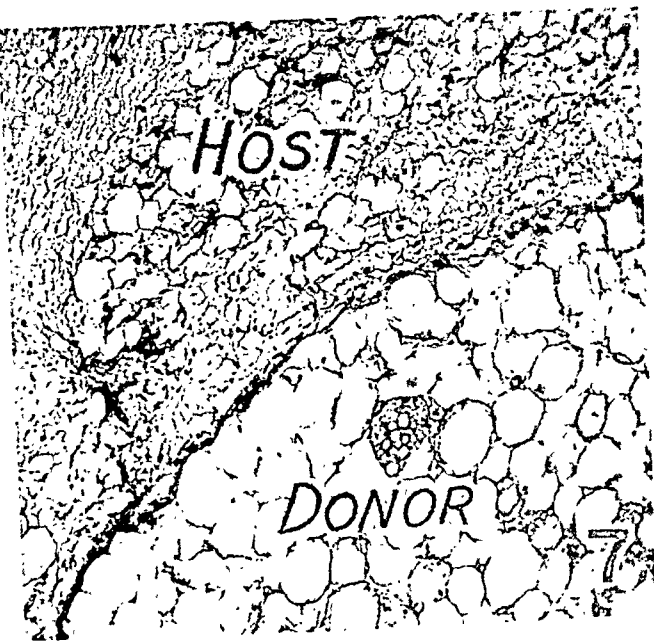
with one exception, discussed later.

The fat from one orbit of an exophthalmic animal containing a testicular fat graft was not entirely similar to the others. The transplanted portion consisted largely of solid nonedematous fat as did the others but in the center of this mass, apparently unconnected with the host orbital fat, was a group of epididymal tubules which had been taken with the transplant by accident (fig. 5). They lay in loose connective-tissue network which was distended and infiltered with a protein containing edematous material similar in texture and staining reaction to the edema of the orbital fat (fig. 6).

Sections of one testicular fat in situ of another injected guinea pig also passed, by chance, through some of the epididymal tubules. These tubules were supported by a loose connective-tissue framework which contained an edematous material similar to that seen in the orbital and in the transplanted testicular fat of the case already mentioned (fig. 4).

DISCUSSION

The data reported strongly supports the concept that the condition of the fat tissues found in exophthalmic guinea pigs is due to some basic characteristics of the tissue and/or its vessels, rather than to its location or the peculiarities of its site, such as lymphatic drainage. Since the transplants of orbital fat to the orbit reacted exactly as did native fat in both operated and intact orbits, it would appear that the act of transplantation did not interfere with the changes brought about by injection of the extracts. The transplanted tissues of all types maintained themselves and grew, rather than were replaced by growth of the host tissue, because two distinct masses of fat were found separated by a band of connective tissue.

In a few instances, not included in the reported cases, a graft of orbital fat obviously did not persist. In such cases the orbit contained some, presumably, native fat and a mass of scar tissue located in the region of the orbit where the transplant had been made. The orbital fat found was situated within the muscle cone and was traversed by the retractor bulbi muscles and ciliary nerves in the manner characteristic of the normal orbital fat.

Axillary, uterine, and testicular fats were transplanted under more favorable conditions than were the orbital fat grafts since they were autotransplants. All were well incorporated and had increased in mass in the orbit, but were unaffected by the injected extracts. They remained in a normal condition, as did the fat of their types in the normal environment. In an earlier study it was reported that fat in the axilla was not changed in a manner similar to that noted in the orbit. Fat from the region near the Fallopian tubes, however, was affected, indicating that the edema produced by injection of anterior pituitary extracts was not limited to the orbit, but was found in some other tissues and was absent, or very scant, in others. This observation was confirmed in the present experiments.

Dobyns's[9] report that testicular fat was modified in similar experiments performed by him is in essential agreement with cases reported here, for, although in most instances the sections of testicular fat studied showed no structural change from normal, they were only through that portion of the testicular fat body which contained very few connective-tissue septa and no epididymal tubules.

Obviously edema does occur in at least a restricted portion of the testicular fat of the experimental animals. This observation emphasizes the conclusion reached in the study of the other facts, namely, that transplanted tissues behave in the orbit in the same manner as they do in their native environment. Grafts of the nonreacting part of testicular fat were unaffected in the orbit by the injected extracts; whereas, that portion which became edematous in the scrotum also became edematous in the orbit.

SUMMARY

1. The injection of anterior pituitary extracts into thyroidectomized guinea pigs produces an exophthalmos and an edematous condition of the orbital and some other fat tissues.

2. Orbital fat which has been transplanted to the orbit is affected in the same manner as the native orbital fat.

3. Fat which is unaffected in its normal location by the injection of anterior pituitary extracts retains this characteristic when transplanted to the orbit, although the grafts are well incorporated and have increased in size.

4. Fat tissue which is affected in the pituitary-extract treated animals also becomes edematous when transplanted to the orbit of appropriately treated animals.

5. These data are interpreted to suggest that the edema of the orbital and other fats caused by the pituitary extracts is due to conditions peculiar to those tissues and their vascular supply, rather than to their location in the body.

630 West 168th Street (32).

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OPHTHALMIC MINIATURE

In no subject were the Greeks less independent than in the pharmacology of the eye. They took a formidable list chiefly of inorganic compounds over from the Egyptians. The list contains antimony, alum, saltpeter, lapis lazuli, and half a dozen others.

Hirschberg, Graefe-Saemisch Handbuch.

LEPTOSPIRAL UVEITIS*

HAROLD A. HANNO, M.D.
Philadelphia, Pennsylvania
and
ALBERT F. CLEVELAND, M.D.
Drexel Hill, Pennsylvania

Of the many pathologic conditions which are known to give rise to disease of the uveal tract, one of the more rarely encountered and less frequently recognized is Weil's disease or Leptospirosis icterohemorrhagica, only 222 cases of which have been reported in the United States literature.[1]

Weil's disease is an acute systemic infection. The etiologic agent is the Leptospira icterohemorrahgicae, a spirochete found commonly in rats, and less frequently in dogs, mice, cats, and other animals. Human infection usually occurs from contact with stagnant waters contaminated by murine excreta, the portal of entry usually being the abraded skin, although infection may occur by way of the gastro-intestinal tract, the nasal mucosa, or the conjunctiva. The disease is especially prevalent in those working in rat-infested environments: sewer workers, fish and poultry handlers, miners, butchers, tunnel diggers, and so forth. Clinically the disease is characterized by a sudden onset with headache, fever, prostration, and myalgia. In the more severe cases, jaundice occurs, and hemorrhagic phenomena and evidences of renal impairment are present. In the milder and anicteric cases, diagnosis may be difficult, and it is undoubted that many go unrecognized.

Diagnosis may be definitely established by the isolation of the causative organism from the blood or urine, and by the demonstration of specific lysins and agglutinins in the serum. A positive agglutination in a titer of 1:300 or above[2,3] or a complement fixation titer of two units or more[4] is considered diagnostic of Weil's disease. Death is extremely rare in the anicteric cases, but the fatality rate in some epidemics of Weil's disease has been as high as 30 to 48 percent.[2,3] Penicillin is a specific therapeutic agent. Streptomycin and aureomycin are also drugs of value in this condition.

The eyes are commonly involved in Weil's disease. Early in the course of the illness conjunctival injection is the rule.[2,3,5-8] In some cases a catarrhal conjunctivitis[6] and petechial hemorrahges in the conjunctivas[3] may be present. Patterson[9] found conjunctivitis and episcleritis in every one of a series of 37 cases of Weil's disease which he studied. A mild form of iritis or iridocyclitis frequently occurs late in the disease, appearing between the 16th and the 42nd day.[5] The frequency with which the anterior uveal tract is affected is variously reported at from 3 percent[7] to 44 percent.[5,8] Hypopyon has been noted.[7] The posterior uveal tract is rarely involved.[6] The retina may show congestion and small hemorrhages, and occasionally optic neuritis may occur.[6] Orbital pain due to involvement of the extraocular muscles is occasionally present.[10]

CASE REPORT

Because of the uncommonness of established cases of Weil's disease in this country, and the unusual features of a case which was recently seen, the following case report is presented.

History. C. S., a 26-year-old Negro, was admitted on September 27, 1947, to the ophthalmologic service of Dr. James S. Shipman at the Wills Hospital with the chief complaints of some blurring of vision and the presence of streaks and spots in the fields of vision in both eyes. He stated that he was well until a month previously, when he de-

veloped fever, sweating, chills, headache, generalized malaise, and anorexia, his temperature going up as high as 102°F. After a week of pyrexia, his fever subsided and he noted jaundice. Two weeks later, while his jaundice was still present, his eye complaints began. He was afebrile after the first week of his illness.

Physical examination on admission revealed a well-nourished, young Negro in no acute distress. There was no fever. A moderate degree of conjunctival icterus was noted. The lungs were clear, and the heart showed no abnormalities of note. The liver edge was palpable one-finger's breadth below the right costal border and the spleen was not demonstrably enlarged. No hemorrhagic phenomena were noted.

The vision was: O.D., 6/60; O.S., 6/21. Both pupils were dilated and fixed, and there were numerous keratic precipitates of various sizes on the posterior surface of both corneas. A positive flare and some small pigmentary changes on the anterior and posterior lens surfaces were noted. Because of the presence of numerous thready, floating, vitreous opacities, the details of the fundus could not be well visualized.

The hemogram revealed an erythrocyte count of 3.02 millions with a hemoglobin of 62 percent and a total leukocyte count of 7,100, with 63 percent mature polymorphonuclear leukocytes, 3 percent stab forms, 8 percent eosinophiles, and 24 percent lymphocytes. The color index was 1.0. No sickling of the red blood cells was seen. The fasting blood sugar was 71 mg. precent, and the serum bilirubin was 1.0 mg. percent with a delayed direct reaction.

The prothrombin index by the simple bedside test was 63 percent, and the cephalin flocculation was plus 2 at the end of 48 hours. The sedimentation rate by the Westergren method was 25 mm. per hour. The agglutination reaction for B. abortus was negative. The erythrocyte fragility revealed that hemolysis began at 0.42 and was incomplete at 0.28.

The Wassermann reaction and the intradermal Mantoux test were negative, and a prostatic smear showed no evidence of infection. X-ray examination of the chest revealed no evidences of any active pulmonary disease. Slight mucosal hypertrophy of the left ethmoid cells was noted on X-ray study of the nasal accessory sinuses. No evidences of dental infection were found on roentgen examination. Otorhinolaryngologic consultation revealed only deviation of the nasal septum and minimal tonsillar disease.

Course in hospital. It was felt upon admission that the patient's jaundice resulted from a subsiding infectious hepatitis and, as a consequence, fever therapy was felt to be contraindicated. He was treated conservatively for his eye disease with atropine, and for his suspected liver disease he was placed on a high carbohydrate, high protein, low fat diet with multivitamins.

He was afebrile during the course of his hospital stay except for a mild temperature rise during his first hospital day as a result of an initial dose of typhoid vaccine which was administered on admission. The jaundice gradually disappeared and satisfactory recovery of vision and clearing of the media occurred.

The patient was discharged from the hospital on October 10, 1947, with vision with pinholes of: O.D., 6/15—1; O.S., 6/12—2.

He returned to the medical clinic on October 22, 1947, at which time no icterus was discernible and the liver and spleen were not palpable. A bromsulfalein determination showed a retention of less than 5 percent with the 2 mg. dose after 30 minutes, and the serum bilirubin was 0.3 mg. percent.

Serologic studies. Questioning at this time elicited the information that until the onset of his acute febrile illness, the patient had been working as a member of a construction gang engaged in the tearing out of an old sewer and the installation of a new one. Because of this occupational history, it was suspected that the illness from which the patient had recovered might have been a leptospiral infection.

Serologic studies at the Graduate Hospital, Philadelphia, revealed a positive agglutination in a dilution of 1:1,000* and a complement fixation titer of 3.75 units for the Leptospira icterohemorrhagicae, both strongly positive reactions. The cephalin flocculation at this time was negative after 48 hours, and the hemogram revealed an erythrocyte count of 4.31 millions with a hemoglobin of 72 percent and a total leukocyte count of 10,300 with 76 percent polymorphonuclears, 5 percent eosinophiles, 2 percent basophiles, and 17 percent lymphocytes.

Iridocyclitis. The patient's ocular condition continued to improve on his periodic visits to the eye clinic, and the vision on December 26, 1947, was 6/9 + 2 in either eye. On February 10, 1948, however, an acute iridocyclitis recurred in the left eye. He was readmitted to the hospital the same day with vision of: O.D., 6/9; O.S., 5/60.

Examination revealed the presence of numerous punctate keratic deposits in the left eye. There was marked turbidity of the aqueous and numerous cells were present in the anterior chamber. The vitreous contained large varishaped opacities. Central visual fields in the left eye showed a quadrantlike cut in the upper temporal area with a 1-mm. test object.

Additional serologic studies at this time revealed a positive agglutination in a dilution of 1:1,000* and a complement fixation titer of 4.5 units for the Leptospira ictero-

hemorrhagicae. A course of penicillin therapy totalling 5,000,000 units given at 3-hour intervals over a period of 12 days was administered, and the patient's uveitis became quiescent. He was discharged from the hospital on February 23, 1948, with visual acuities of: O.D., 6/6; O.S., 6/12.

The patient's progress was followed periodically in the out-patient clinic. When he was last seen on May 28, 1948, there was no injection of either eye. Both irides were active and free of synechias. Very few keratic deposits were present. No anterior chamber abnormalities could be found, and the vision in each eye was 6/6.

COMMENT

The case reported above represents an instance of a mild case of Weil's disease complicated by a bilateral iridocyclitis with some evidence of posterior uveal involvement. The eye findings dominated the clinical picture and constituted the presenting complaint which brought the patient to seek admission in an eye hospital. It is of interest that the patient's occupational history furnished the clue to the diagnosis.

The diagnosis of Weil's disease rests upon a high index of suspicion. The possibility of Weil's disease should be thought of by the ophthalmologist in any patient with iritis or iridocyclitis accompanied by or preceded by fever or jaundice, particularly in those patients whose occupations bring them into contact with rat-infested surroundings.

1737 Chestnut Street (3)
1216 Morgan Avenue.

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* The agglutionation reaction was not carried beyond a dilution of 1:1,000.

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LIMITS OF STEREOPSIS DUE TO PHYSIOLOGIC DIPLOPIA*

PAUL W. MILES, M.D.
Saint Louis, Missouri

In the ordinary two-line tests for stereopsis, the ability of the subject to detect the difference in distance of the lines from the eyes increases indefinitely with the increasing nearness of one line. Obviously, at some point, physiologic diplopia occurs, just as a spot on the window pane appears double when one observes a tree outside, and the tree appears double when one observes the spot. One is not commonly conscious of physiologic diplopia becouse of suppression of one of the two retinal images.

Does physiologic diplopia interfere with stereopsis? There has been to date no evidence that it does. A crossed physiologic diplopia, where the left image is seen by the right eye and the right image is seen by the left eye, has been believed to produce a strong binocular clue for nearness. An uncrossed diplopia was believed to produce a clue for farness.

This paper presents experimental set-ups where more than a certain amount of difference in the distance of vertical line targets from the eyes causes a deterioration of depth judgment. The evidence suggests that imperceptible degrees of physiologic diplopia are enough to interfere with stereopsis.

This new phenomenon is interesting to ophthalmologists for several reasons: It gives evidence on the extent of Panum's fusional areas. It adds a new factor to consider in devising instruments to test steropsis. It helps to explain difficulties some patients have at first with the space eikonometer, which is a rapid test for stereopsis on line targets. It will modify the technique used in testing aniseikonic patients.

EXPERIMENTAL TECHNIQUES

EXPERIMENT I

In the summer of 1946, A. Ames, Jr., of the Dartmouth Eye Institute devised a new target for testing patients with aniseikonia which he asked me to try on patients already tested with other instruments. This target, illustrated in Figure 1, consisted of luminous
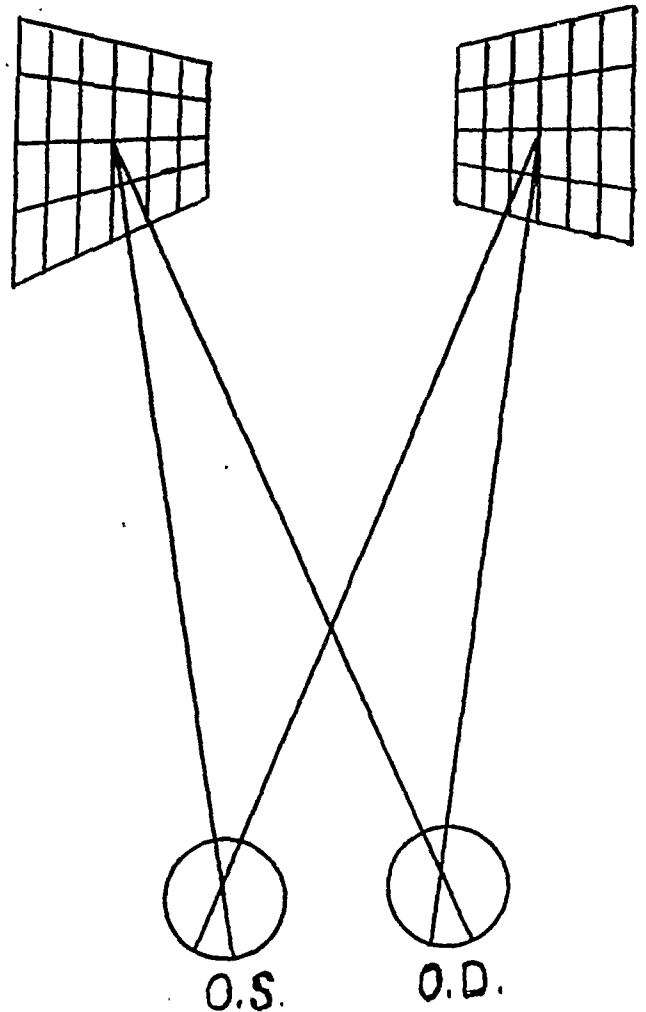
Fig. 1 (Miles). Rectilinear luminous grid targets, devised by A. Ames, Jr., for measuring aniseikonia which showed defective stereopsis with increasing physiologic diplopia.

rectilinear grids placed at eye level 14 feet from the eyes. These grids, made on black-painted glass by scratched lines, were placed on a box containing fluorescent lamps. The

grids measured 16 by 24 inches, and were mounted face to face 8 feet apart.

The patient was placed with head fixed in position as indicated in Figure 1, in complete darkness, with his refractive prescription before his eyes. He was asked to look from one of the grids to the other and report which appeared nearer. Then the two grids magnification exceeded 0.75 percent. Patients were unable to localize the targets in space until their size prescription, within about 0.75 percent, was placed before their eyes. At the time, it was believed that the difficulty was due to one grid geometrically approaching the patient's face absurdly near, causing the patient to discard binocular clues.

TABLE 1

RESULTS OF 112 JUDGMENTS AS TO POSITION OF THE TWO TARGET LINES EXPOSED IN RANDOM ORDER IN SEVEN DIFFERENT POSITIONS. NOTE THAT JUDGMENT IS BETTER WHEN THE DIFFERENCES IN TARGET LINE DISTANCE TO THE EYES ARE SMALL, AND DEFECTIVE WHEN GREATEST

Actual target line position, 64 mm. P.D. Experimental near judgments	Right 3 cm. Near −3 L. R.		Right 2 cm. Near −2 L. R.		Right 1 cm. Near −1 L. R.		Even 0 L. R.		Left 1 cm. Near +1 L. R.		Left 2 cm. Near +2 L. R.		Left 3 cm. Near +3 L. R.		Sensitivity at 75% Correct
1. M. B., stenographer, 62 P.D. (Dark adapted)	8	8	5	11	4	11	8	8	12	4	11	5	8	8	10 mm.
	11	5	5	11	6	10	9	7	12	4	10	6	12	4	18 mm.
2. J. A., maid, 60 P.D. (Dark adapted)	4	12	3	13	12	4	10	6	11	5	13	3	12	4	6 mm.
	2	14	3	13	12	4	14	2	14	2	15	1	14	2	5 mm.
3. M. M., housewife, 62 P.D.	1	15	0	16	1	15	9	7	12	4	14	2	12	4	5 mm.
4. J. S., M.D., 62 P.D.	2	14	4	12	5	11	11	5	16	0	16	0	14	2	10 mm.
5. M. L., nurse, 62 P.D.	0	16	0	16	0	16	4	12	13	3	14	2	13	3	5 mm.
6. D. F., M.D., 64 P.D.	1	15	3	13	1	15	7	9	13	3	15	1	16	0	5 mm.
7. R. R., student, 62 P.D.	1	15	2	14	2	14	4	12	9	7	15	1	11	5	7 mm.
8. R. P., M.D., 60 P.D.	3	13	2	14	3	13	13	3	14	2	16	0	15	1	8 mm.
9. E. D., M.D., 68 P.D.	0	16	0	16	2	14	10	6	15	1	16	0	16	0	5 mm.
10. E. G., M.D., 62 P.D.	7	9	7	9	6	10	7	9	10	6	10	6	7	9	?
11. U. L., M.D., 60 P.D.	0	16	1	15	2	14	2	14	7	10	15	1	16	0	6 mm.
12. K. O., M.D., 60 P.D.	5	11	5	11	7	9	8	8	10	6	13	3	16	0	20 mm.
13. B. T., M.D., 66 P.D.	10	6	10	6	9	7	10	6	8	8	12	4	13	3	?
14. Y. T., M.D., 66 P.D.	5	11	2	14	3	13	6	10	13	3	16	0	15	1	11 mm.

were equated by placing, by hand, size lenses (axis-90°, magnifying afocal lenses) before the eye on the side where the grid appeared nearer. Then, the sensitivity of the patient was determined by finding the smallest size lens which would make a perceptible difference in distance of the two grid targets.

Twenty-four known aniseikonic patients were tested in this way. Four were insensitive, and the others were highly sensitive to small size lenses, but insensitive to size lenses magnifying more than 0.75 percent. The conclusion was that the target was more sensitive than the space eikonometer target to small differences in magnification, but that something destroyed sensitivity when the

EXPERIMENT II

The present experiment began as a study of stereopsis in the dark-adapted individual. When the first subject showed excellent stereopsis on a two-line test at 2 meters with one line moved back and forth 2 cm., but none at all when the line was moved 3 cm., it was realized that the same phenomenon elicited by the luminous grid targets was occurring.

The apparatus consisted of the ophthalmoeikonometer instrument, table, and hydraulic chair, and a target consisting of two miniature ophthalmoscope lamps mounted instead of the usual two lines in stereopsis tests.

The lamps were wired in series with 7.5 volts A.C. producing constant maximum brightness. A large piece of red Maddox-rod glass was placed before both eyes about 15 mm., so that the two small points of light appeared as two bright-red thin vertical lines without ends. The ends extended up and down about 45 degrees, but changed so with vertical eye movements that they could not serve in depth judgment. Nothing else in the room was visible in the 45-degree field straight ahead. Room illumination came from a diffuse source overhead. In Subjects 1 and 2, Table 1, the light was turned on bright for the light-adaptation test, and completely off for the dark-adaptation test. In other subjects, the overhead illumination was quite. dim, so that the buff walls reflected only about 0.2 foot-candles on a light meter at eye level.

The set-up can be seen diagramatically in Figure 2. The two lamps were at "0" and "Fixation," and were 36.2 cm. apart, 192 cm. before the corneas. The usual variable axis-90° size lenses were used before each eye to introduce the disparity. The effect of separation of an afocal combination of minus and plus axis-90° cylinder to magnify the images seen by one eye is seen in Figure 2. With interpupillary diameters from 60 to 68 mm., the size lenses produced the effect of moving the luminous line at "0" back and forth at intervals of 9 to 11 mm. In the diagram, fixation is limited to the right line target, which is placed in the optical axis of the size-lens combination. The eyes were free to move from one to the other line target, in which case the disparity changes eyes but maintains equal angular space relationships. Slight movements of the head were prevented by the head holder but did not change the apparent distance of either line in any position of the size lens.

On the retina of the right eye in Figure 2 is seen the exactly corresponding point "0," and the disparate points from plus to minus 3. In the past, the diplopic images

on each side of "0" were said to produce a "near" clue to depth, if temporal, and a "far" clue, if nasal, to the corresponding point.

In Figure 2, the retinal point "0" of O.S. corresponds exactly to point "0" of O.D., but the points from minus to plus 2 in O.D., although not corresponding, may fuse with "0" producing a stereoscopic cerebral image and perception of depth. These disparate
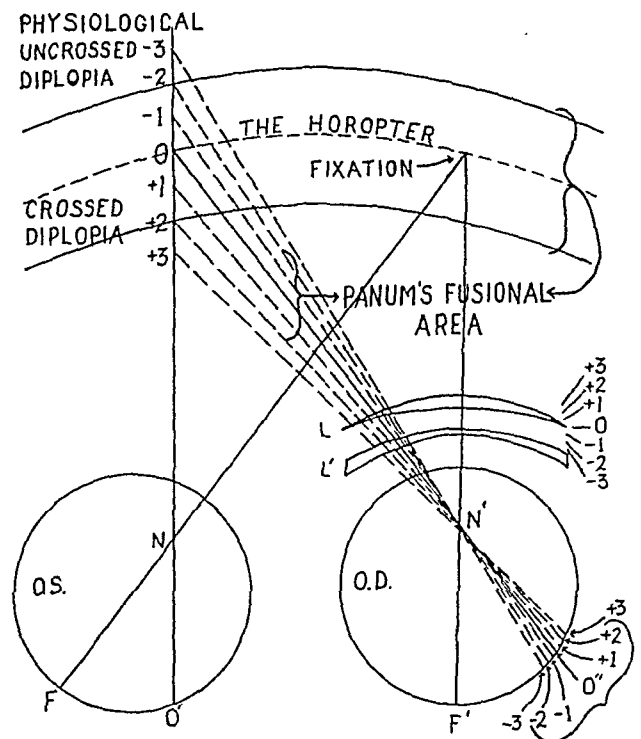
Fig. 2 (Miles). Diagram of experiment on stereopsis using luminous line targets at "0" and "Fixation." Stereopsis was found defective when the lines were placed at minus-3 or plus-3 positions.

images which fuse correspond to Panum's fusional areas, which exist before and behind the horopter, in which physiologic diplopia must be present but is imperceptible. The points minus and plus 3 outside this area may or may not appear as diplopic images, according to the attention or imagination of the observer.

The subject was seated before the apparatus, and the pupils aligned with the optical centers of the variable size lenses. The target was tested each time to insure that the subject could see both target lines equally well monocularly with each eye at all positions of the size lenses. The right size lens was set at 2 percent, and the left

was then adjusted until the subject reported the two lines appeared equidistant from the eyes.

The right eye was covered by the examiner's hand, while an adjustment of the right size lens was being made to any of

and none volunteered that the lines ever appeared blurred or doubled.

All subjects had normal vision except U. L., who had 6/7.5 in the left eye. Four wore glasses. Two subjects, E. G. and B. T., had no stereopsis by the Maddox-rod test,
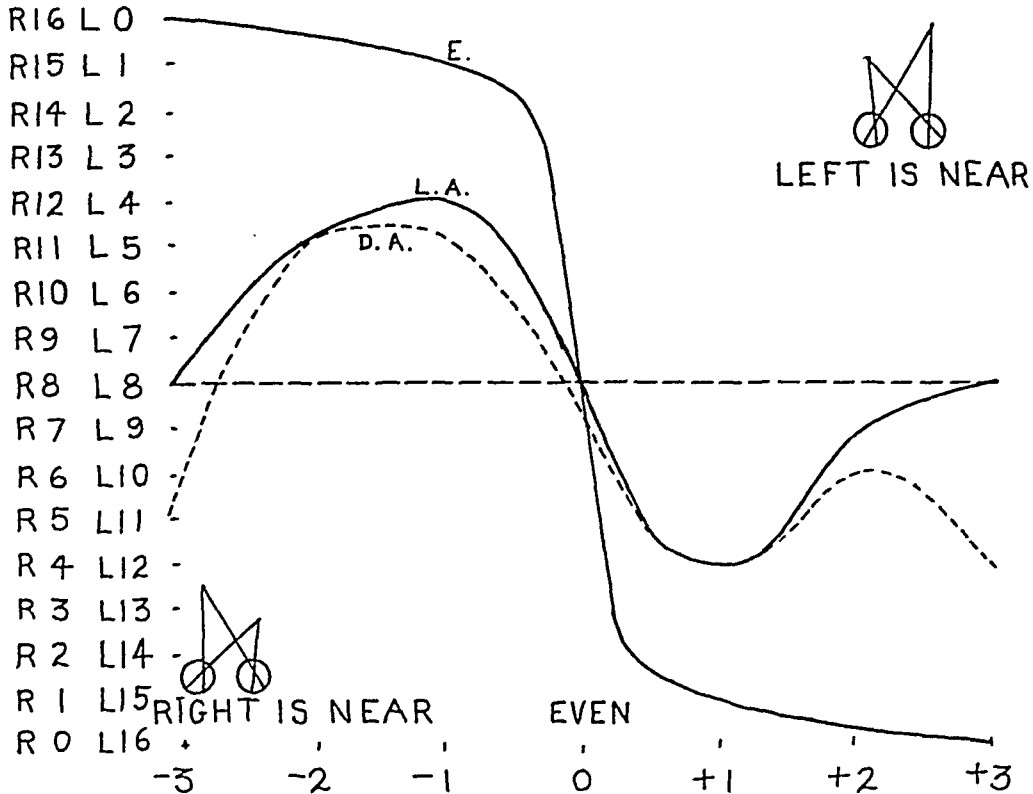
Fig. 3 (Miles). Sixteen judgments of each position presented graphically in Case 1 (M. B.). "E" represents the expected curves if stereopsis improves with distance differences of targets.

the seven different settings used. Setting intervals, to produce the target movement described, were 0.50 percent. Any change of 0.50 percent in the size lens made an apparent movement of one target about 10 mm. by calculation. The setting made, the hand was removed to let the subject see binocularly. Sixteen judgments as to which line appeared nearer were required for each of the seven settings. The settings were presented in random order, with care that the subject got no clue whatever as to which direction the size lens was changed. The subject was required to guess right or left, if the target lines appeared equal. No suggestion of diplopia was made to the subject,

although by usual tests it was normal. Results on 14 subjects are shown in Table 1. The plus- and minus-3 positions in the last eight subjects were made four times the 10-mm. interval, instead of three times. This was done in the hope of exaggerating the phenomenon and to decrease the chance that it is simply an experimental accident.

Figure 3 expresses graphically the results on Subject 1, compared to "E," the curve described previously by K. N. Ogle[1] in studies of sensitivity to changes in the space-eikonometer target position. According to "E," the nearer one target line is to the observer, the higher statistical chance there is of 100-percent correct judgments.

Figure 3 shows, in curves L.A. and D.A., that, when the two target lines were actually equidistant, the subject was declaring the right line nearer just as often as the left line nearer (R8-L8).

When the right or left line was brought 10 mm. nearer, the judgments made were 75-percent correct (R12-L4) (R4-L12) in each case, and, when brought 20 mm. nearer, the judgments were 62.5-percent correct. When the right or left line was brought still nearer, 30 mm., the judgments were again only 50-percent, which indicates no stereopsis.

In other words, M. B. had the best stereopsis when the disparity was least, and the worst when the disparity was greatest. From her horopter at 192 cm., Panum's fusional area was about 20-mm. wide. Of the 14 subjects, only four failed to show this phenomenon and, of these, two had no stereopsis with this type of test.

In Figure 3, the solid line L.A. refers to light adaptation, and the dashed line D.A., dark adaptation. Results are not conclusive, because the target background contrast is different in the two conditions, undoubtedly affecting stereopsis.

M. B. was tested again in the same equipment without the Maddox rods, without the size lenses, and using an apparatus with vertical line targets of the same separation at the same distance, introducing the same disparities mechanically. The vertical lines were aluminum wire about 3.75 mm. in diameter. A mask, 33 cm. before the eyes, obscured the ends of the wire in all positions. With the room illumination dim, and the background a painted black screen, no details were visible in the same 45-degree field as with the Maddox-rod tests. Results in the analogous positions were as follows:

-3	-2	-1	0	$+1$	$+2$	$+3$
0 16	1 15	2 14	4 12	9 7	6 10	10 6

The data are skewed, but no decrease of stereopsis occurred at the extremes.

This test was repeated with an aluminum background to decrease the contrast of the aluminum test objects, and the following resulted:

-3	-2	-1	0	$+1$	$+2$	$+3$
1 15	3 13	1 15	4 12	5 11	10 6	14 2

DISCUSSION

The Maddox-rod line target for measuring stereopsis gives different results from those of other targets. One may review all known clues to depth perception, and find no difference between the two types of test. M. B. was tested on the aluminum rods monocularly and made largely incorrect judgments, confirming Howard's finding[2] that retinal image size difference is not a sufficient clue. Neither type of test involves different illumination of the two line targets. Parallax, overlay, perspective, and haze are ruled out. There cannot be much difference in convergence upon alternating fixation on the two lines of either type of target. Even if there is, convergence has been shown to be a poor clue to depth perception.[3]

There is definitely something about vertical luminous line targets which accentuates physiologic diplopia or prevents fusion of disparate images. The Maddox-rod line has no definite breadth when the light source is small, and it is an ideal straight line. One is reminded of the comparison of resolving power using two points with resolving power using two straight lines. The lines can be distinguished with 10 times more precision. It is the principle of the vernier, which is used in all precision measuring instruments.

Conclusive evidence that the thin straight-line concept produces the phenomenon described in this paper is found in use of the frontal plane apparatus[4] for measuring aniseikonia (fig. 4). This target is the complete opposite of the straight line, since it consists of irregular ink blots. When the target plane is placed at zero on the scale and observed from the position indicated by the head holder, it appears on a true frontal plane. When axis-90° size lens is placed before one eye, the plane appears to rotate on

its central vertical axis and will continue to rotate further with increasing magnification until about 25 percent has been attained. At this point, the frontal plane has rotated about 60 degrees. This high fusional amplitude of obviously disparate images is due to the irregular ink-blot type target which, although highly distorted, the cerebral centers will fuse. The Maddox-rod straight lines

judgment were found. Results on W. H. L., M. D., vision 6/6 without glasses were:

-3	-2	-1	0	$+1$	$+2$	$+3$
11 5	12 4	9 7	14 2	14 2	13 3	16 0

With increasing nearness of the right target, judgment became worse and worse.

The possibility that stereopsis might again improve with still more increase in the binocular disparity was not studied in these
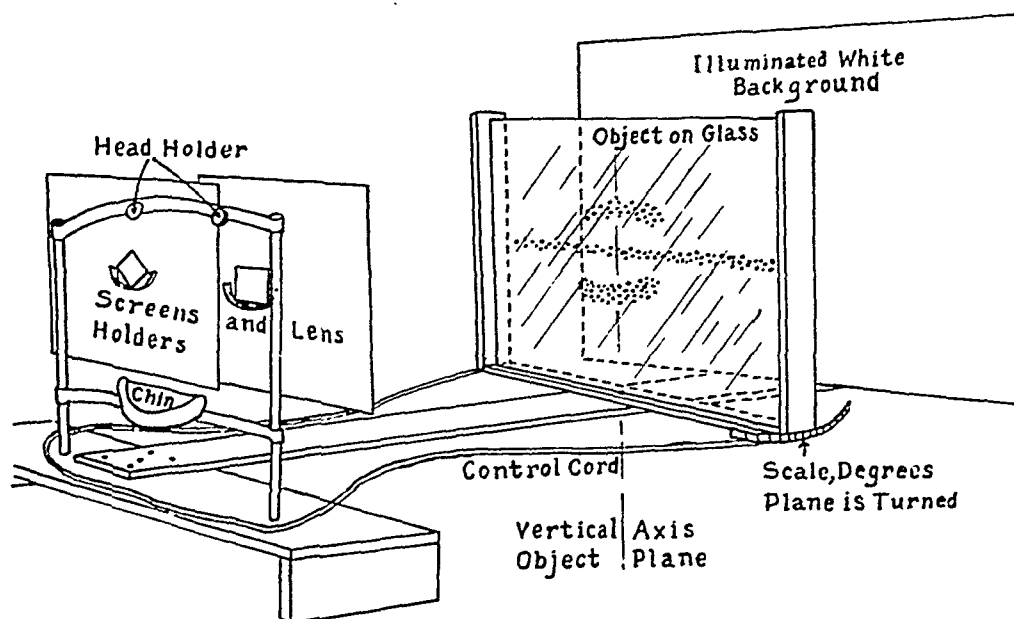
Fig. 4 (Miles). Frontal plane apparatus. The irregular ink-blot target will not accentuate physiologic diplopia like luminous vertical line tests do. The amplitude of this target is about 25-percent magnification, compared to about 1.5 percent for vertical line targets, before stereopsis deteriorates.

undergo diplopia at about 1.5 percent with loss of stereopsis.

The experimental findings described in this paper were found under conditions of artificial aniseikonia. The defects in fusion due to unequal sized images from the two eyes are well known. The artificial aniseikonia is not believed to be a factor in the present experiments because the Maddox-rod line target is of such indefinite thickness. The thickness varies constantly with the eye movements and, frequently, the line which appears slightly thicker is definitely more distant during tests.

However, to make certain, four subjects were tested with Maddox-rod targets in which the light bulbs themselves were moved mechanically. The same difficulties in depth

experiments. However, there is a suggestion of such a trend in Subjects 1 and 6, in Table 1. Theoretically, it would not be expected unless parallax, or perspective, or size clues crept into the experiment.

SUMMARY AND CONCLUSIONS

An experimental set-up is described in which more than a certain amount of difference in the distance of two vertical line targets from the eyes causes a deterioration of depth judgment. Tests were performed on 14 subjects with apparently normal eyes and normal stereopsis by the ordinary tests. Each subject was tested on a two-line target with the lines in seven different relative positions with 16 trials in random order of each position. Target distance was 192 cm., lateral

separation was 36.2 cm., and the variation of one line nearer or further was in three steps of about 10 mm. each, depending on the interpupillary distance.

This phenomenon is characteristic of thin vertical line targets and does not occur in the ordinary tests for stereopsis.

The evidence apparently modifies Hering's laws of stereopsis:[3] (1) That depth judgments are directly dependent on the magnitude of the retinal disparity, which is the deviation from strict retinal correspondence in normal binocular vision. (2) That depth judgment from noncorresponding points seen in physiologic diplopia is "far" for images falling nasally, and "near" for images falling temporally on the retina.

The extent of Panum's fusional areas at a fixation distance of 192 cm. is about 20 mm. from the horopter.

When testing patients on the space eikonometer, who do not immediately project the target properly or who do not appear sensitive to changes in the size lenses, one should consider that the stereopsis limit due to physiologic diplopia as described in this paper is being exceeded and that trial and error changes in the size lenses are advisable to pick up the target position in which the patient is sensitive.

640 South Kingshighway (10).

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A SIMPLE, MORE ACCURATE MEANS OF CHARTING VISUAL FIELDS

GEORGE ZUGSMITH, M.D., AND IRVING REHMAN, PH.D.
San Pedro, California

The first concept of perimetry was elaborated by Euclid,[1] who taught that a fluid streamed from the eye in the form of a cone with the apex in the pupil and the base on the object being looked at. The base comprised the visual field.

The field of vision was first illustrated by Ulmus of Padua in 1602. However, no further information regarding this subject appeared until the article of von Graefe in 1856.[2]

Many attempts to chart visual fields accurately have been made since the introduction of modern procedures about 50 years ago, as evidenced by the numerous articles published. The first perimetry was done with an illuminated object. In 1884, Abertotti used a "fluorescent" test object. In 1889, Bjerrum[3] stated that using one test object was like using only the 20/40 line for vision testing. He advocated multiple testing with various sized test objects. This was the method that prevailed until 1933 and to a large extent has prevailed since.

However, in 1933 Mayer,[4] seeking for a more adequate and reliable type of test, described the visual-field test done with a minimal light stimulus. In reviewing Mayer's work and the subsequent literature, it was found that his work had not been developed further, by himself or others.

In 1935, Mayer[5] described a means of

perimetry utilizing an apparatus for producing a minimal light stimulus of measured interval duration. His apparatus consisted of a condenser discharge into a neon bulb, thus producing a flash of very short duration and fixed intensity.

The apparatus was expensive and cumbersome. The flash of the neon was red and Dr. Mayer states that tubular fields were not present with this light stimulus. He also stated, "Varying slightly with the person tested," the speed of the flash, 0.033 second, is so rapid as to be lost at the 50- to 60-degree meridians. As more peripheral meridians are approached, the flash is lost at lesser speeds.

Thus, it was concluded that Dr. Mayer was endeavoring to find a much more quantitative visual-field test. He stated, however, that the advantages of this type of stimulus are that it is critical and it eliminates a moving target.

A moving target, in itself, has definite inherent disadvantages: (1) There is much poorer control of fixation however good the fixation device; (2) there are variable effects of previous exposures on the sensitivity of the retina; and (3) there is a time error which cannot be standardized.

The criticisms raised by Mayer and his attempt to remedy the disadvantages are readily apparent when one considers the apparatus he developed and its inherent difficulties.

DEVELOPMENT OF NEW APPARATUS

Our own objective was to get a simple, inexpensive, reliable machine which would render visual field taking easier and more accurate and would dispense with multiple test objects. In an effort to achieve a more reliable test object (light) for perimetry, an inexpensive apparatus was developed by the Chart-lite Instrument Company of Los Angeles. This instrument produces a pulsing light in the form of a flash of measurable duration, which can be accurately controlled and easily varied in intensity and frequency.

The usual technique may be employed in determining visual fields with slight variations. Our technique was to move the light slowly from the periphery to the fixation point, moving more slowly or stopping at the critical point in the field where the light was observed. A movement of one-half inch at this point, in most cases, eliminated the light or made it appear. There was no hesitation or indecision on the part of the patient, because the flash is clear cut and definite. This same advantage holds for central fields. These were taken on the Gruss tangent screen. The blindspots, when outlined with this apparatus, are better than textbook illustrations.

Another refinement, which we were able to introduce, was in the cases of poor central fixation. In these cases the central target for fixation could be made any size. We have used a white disc 12 inches in diameter with crossed lines. The patient fixes easily and yet the scotoma is beautifully outlined because the pulsing light passes from black on to the fixation target without disturbing the patient's fixation.

The fields were taken on the optical perimeter and on the tangent screen, using the same arm to hold the light, and the perimeter was painted black. The optical perimeter is the one mentioned previously, as constructed under the supervision of Ferree and Rand.[6] Two arcs of the same radius of curvature were constructed at right angles to each other—one, a 180-degree arc, the perimeter arm; the other, a 90-degree arc, the lamp arm, at the end of which is placed the source of light. The two arms are fastened together at the center of rotation.

A housing shields the lamp from the patient. This housing is made of black japanned iron and is painted a mat black on the inside in order that all of the light that passes to the perimeter arm will, as nearly as possible, radiate directly from the lamp filament.

Its dimensions are 4¼ by 4¼ by 5 inches. Filtering the light to daylight quality is accomplished by using as a source of light a well-seasoned, 75-watt type C_2 (blue bulb) Mazda lamp operated by ammeter and rheostat control. The surface of the bulb is acid-etched to diffuse the light.

A chin rest on a tridirectional stand is placed at a distance of 33 cm. from the central fixation point, which is the center of these intersecting arcs. The horizontal arc is marked in degrees up to 90 in two directions from the center. Fixation is controlled by sighting through the hole of the bisecting arcs. A movable ratchet allows for the eye of the observer to be regulated at the 33 cm. distance from the fixation point. Seven and a half foot-candles is the amount of light generally recommended and is controlled by the ammeter and rheostat mentioned previously.

The light test object consists of a six-volt straight filament bulb that produces a very even and efficient source of illumination. This light is mounted on an 18-inch rod that serves as a light wand. A flexible wire permits complete freedom of motion of this light source (wand) in determining the visual fields. The wand is coated with a non-reflecting black lacquer to eliminate possible reflections resulting in false readings; our perimeter being black, the same wand is used for tangent-screen work. For perimeters of a gray color, a wand of the same color may be substituted.

In order to make this procedure utilizing the light technique comparable to that employing multiple test objects, it became necessary to be able to vary the intensity of the test light. This has been incorporated into the instrument so that the light intensity may be varied from zero or no light to an intensely bright light. The intensity range is gradual from zero to bright so that extremely small increments may thus be obtained.

A means has also been included to vary the speed or frequency of pulsation or flash-ing of the light. Four speeds have been found to be optimal in the results they produce; that is, flashes occurring at intervals of one second, one-half second, one-third second, and one-quarter second. Provision has also been made for manually controlling the rate and duration of the pulse so that the intensity, frequency, and duration of the flash may be varied to any desired pattern, each one completely variable and independent of each other. The instrument is very compact, is about six-inches square, and is readily portable (fig. 1).

Comparative tests were made with this instrument on a number of cases for charting
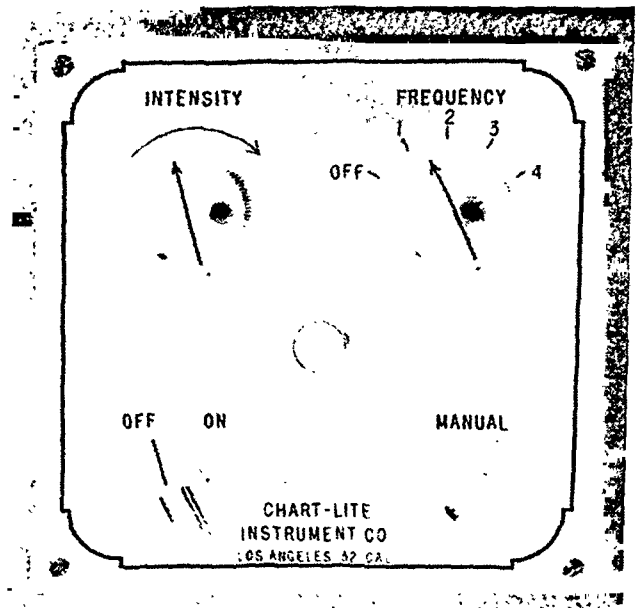
Fig. 1. (Zugsmith and Rehman). A new instrument for charting visual fields.

normal visual fields and these were plotted against the various sized test objects normally used. The technique of using a pulsing light was found to be quite simple. Since the flash is of definite intensity and duration and the target is stationary in nature, the patient error is minimized or eliminated.

The calibration was difficult since we were unable to obtain a light meter which would record the intensity of the flash in lumens or foot-candles because the duration was so

short as not to be able to overcome the lag or latent period of the various meters used. We found an arbitrary point of intensity on our machine which was comparable to the 1-mm. white test object.

Reeves[7] has estimated the least amount of radiant energy which would excite the retina sufficiently to give rise to a perception of light. This light is well above this minimal stimulus, but not high enough to produce an after-image. It has been shown that the rods are the rapid organs and the cones are the slow factor in the reaction to light[8] and a flash as rapid as the one used will not exhaust the retina.

SUMMARY

A mechanism is presented, which is inexpensive and yet more reliable and more accurate than the test objects. The patient finds this test easier and more definite than one with nonluminous test objects and the physician has, at the turn of a control, various sized objects for both perimeter and tangent-screen work.

529 West Eighth Street.

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THE LEARNING PROCESS IN ORTHOPTICS*

JULIA E. LANCASTER, M.A.
San Francisco, California

The visual act has two distinct parts. One part consists of the mechanism for receiving an image with each eye, the other part consists of the means by which the two images are coördinated and interpreted in the brain. From another point of view, binocular vision may also be considered to have two parts; an innate structural, reflex part, which matures in the normal growth process, and a more complicated part which requires use, experience, and interpretation to develop fully.

Orthoptics is concerned with developing normal binocular vision and is almost entirely limited in its applications to this second field of development; that which takes place by use and interpretation and the acquisition of binocular skill. Orthoptics cannot alter growth, it cannot change, as can the surgeon, anatomic and pathologic conditions which prevent the normal maturing of each eye. It can only work with the kind of eyes ophthalmologists have been able to obtain for the patient by occlusion, refraction, surgery, or other treatment. It is then the function of orthoptics to help the patient acquire the best binocular skill of which these eyes are capable.

If there is some insuperable obstacle to binocular vision, such as a permanent amblyopia or an uncorrectable deviation, it is beyond the possibilities of orthoptic training to obtain normal binocular vision in such cases. Fortunately, for ophthalmic progress, many conditions once thought insuperable are now correctable, and binocular vision is becoming correspondingly more frequently attainable.

BINOCULAR VISION PERFECTED BY LEARNING

The process by which binocular vision is perfected is the learning process. This is true whether it is acquired in the normal development of the child or by deliberate training in orthoptics. Learning is purposeful adaptation to environment, to the constant stimuli which the organism is receiving. Since it is innate in the organism to respond to stimuli, learning consists of making responses which are an effort to make useful adaptations.

If such adaptations are successful, they are accepted by the individual as useful learning and are repeated each time the stimulus is received. If they are unsuccessful, they tend to be discarded and something else is tried next time. Thus learning becomes a kind of trial-and-error.

The learning of visual skill is no exception. The growing infant experiments with the various aspects of the visual act. For the safety and welfare of the individual, it is highly important that he acquires a clear single image. Hence the mechanism for achieving it is mostly innate and develops at the reflex level.

Some portions of the mechanism are not mature at birth, and it takes nearly eight years before full growth and visual acuity are achieved but, as the correct age is reached, each factor in the growth pattern matures, ready for use.

If, during the growth and learning period, anything interferes with the opportunity to get normal use and experience, the visual act will not come to normal completion. It is also true that if, after normal skill is acquired, something interferes with constant practice of the skill, it will not be maintained and may decrease. It will certainly not improve.

It is, therefore, of the utmost importance that the growing child shall first get enough practice and use of each eye to permit the innate growth processes and reflexes to come to maturity; secondly, get the practice in

binocular skills necessary to learning to use both eyes correctly; and finally, have opportunity for abundant interpretive experience.

LEVELS OF LEARNING

Learning is essentially a stimulus-response mechanism. It differs from the simple reflex by the highly complicating factor of the emotions and the intellect or cortex of the brain. Strictly speaking, learning may take place at four different levels: (1) The somatic or body-growth, (2) the neuromuscular or reflex, (3) the intellectual or cortical, and (4) the emotional.

Because of the innate and hence nonmodifiable character of the somatic and neuromuscular responses, they are rarely included in the classification of learned responses. They require opportunity for experience and, as soon as experienced, are learned—that is, accepted by the organism for repetition.

It is responses that involve the mind and emotions that are highly modifiable and hence considered as learned responses. There is opportunity for choice in the response, and the chosen response is the learned response. The borderline is not sharply drawn since many reflexes are neuromuscular in character, and much neuromuscular learning is initiated at the cortical level.

The primary method by which the infant learns binocular control is through the experience of diplopia. The desire for a clear single image is innate, the dislike of diplopia is equally instinctive. The infant responds in various ways to his binocular stimuli, discards the responses that give him diplopia, and accepts the satisfactory responses that give him single vision. In this essentially simple manner he learns binocular skill.

So far as is known at present, there are only four ways in which a single image can be achieved: (1) By normal fusion of the images from the two eyes, (2) by using only one eye at a time (the other eye may be amblyopic, or it may be suppressed), (3) by developing anomalous correspondence, and

(4) by the Swan syndrome (turning one eye so that the stimulus to vision falls on the blindspot).

The two latter methods are comparatively rare. The vast majority of abnormal adaptations to binocular vision are by suppression. Any of these adaptations mean that the infant has successfully achieved a single image; he has learned how to solve the problem of binocular vision. If there is no obstacle to the development of fusion, that will be his response but, in the presence of certain obstacles, fusion will be either difficult or impossible and he learns some other way out.

OBSTACLES TO FUSION

The commonest obstacles to fusion are amblyopia of one eye (visual acuity less than 20/70), strabismus, hypermetropia, and anisometropia. Less common causes include aniseikonia, congenital defects, whether anatomical or neural, phorias, and developments of later life such as convergence insufficiencies which lead to abandonment of binocular skills previously acquired.

Strabismus is an obstacle since the deviation of the eyes makes fusion impossible. Unless the eyes can be moved so that the images fall on the foveas, fusion is impossible. Hypermetropia is an obstacle because, in order to see clearly, the patient has to overaccommodate, which leads to overconvergence and hence to loss of fusion.

Anisometropia is an obstacle because the two eyes are so different that fusion is difficult and hence frequently abandoned by the patient. Phorias also require much adjustment which the patient may give up for the easier method of single vision by suppression. The growing infant and child thus learns to adapt to his binocular stimuli in such a way that his response is a single image.

HOW LEARNING TAKES PLACE

Five steps are necessary for each tentative response, and only the satisfactory completion of each step will lead to learning.

1. Attention

The stimulus must receive attention. The organism is constantly bombarded by stimuli both from within and without. Most of them are ignored; no learning takes place in connection with them. The organism must select the stimulus to which it will respond before a response will be made.

2. Recognition or awareness

This is a cortical and emotional factor, not necessary at the reflex level, but of the utmost importance in establishing the conditions necessary for learning. It is the place at which the organism recognizes that the stimulus to which it is attending has possibilities for response. It is the point at which a decision is made to continue with the experience and not discard it as of no interest or value.

If attention is not followed by recognition, the learning process stops at once and the individual frees himself for attention to further stimuli.

3. Response

Response inevitably follows recognition. As soon as the organism recognizes a situation it becomes necessary to make a response. The response may be positive or it may be inhibitory. Inhibition is a very important type of response. Response is the keystone in the arch of learning. As soon as a response is made, learning is on the way to achievement.

4. Satisfaction

Again emotions enter the learning process. The response inevitably results in some feeling about the situation; satisfaction or dissatisfaction. This is the point at which learning succeeds or fails. If the response is satisfying, it is accepted as learned response and is ready for repetition. If it is dissatisfying, the individual avoids repeating that response and learning is blocked.

5. Repetition

It is at this point that learning is established as part of the individual. Adequate repetition is necessary to make the same response assured. It is by means of repetition that habits are established. Habits are the result of responses repeated so often that the steps involving the emotions or intellect are by-passed in the stimulus-response sequence. They become similar to reflexes. Since binocular vision should be the normal habit of the individual, adequate repetition is necessary, whether learned normally in infancy or artificially by orthoptic training.

Orthoptic training functions by taking the patient through the five steps of the learning process in binocular vision as rapidly and efficiently as possible. It does not function in any other way. It does not do anything to the patient or his eyes; it merely offers special opportunities for him to take the steps of learning under guidance. This kind of guidance is teaching. The technician teaches; the patient learns.

Teaching consists of offering selected stimuli to the patients so that the correct response will be easy and give him the satisfaction necessary for repetition, and sufficient practice in these responses so that they become habitual.

Orthoptics is not a treatment done to the patient; it is an opportunity offered to the patient. It is subject to the limitations inherent in all opportunities; they may be accepted or rejected by the patient. They may be rejected at step one; he may fail to attend to what is going on. He may fail at step two; he may reject the situation as one he does not care to recognize or take an interest in. He may fail to get satisfaction out of the response he makes, or he may not repeat it ofen enough to establish habits. The only thing he cannot fail to do is make a response of some sort while he is in the office.

This is an important fact because, if the response he makes is not the desired one, he is actually learning something different from the intended skill. Practice in faulty responses leads to bad habits. This is the reason that poorly conducted orthoptic training is worse than no orthoptics for the patient. He

may simply get a set of experiences in doing the wrong thing.

EVALUATION OF ORTHOPTICS

Orthoptics should be evaluated for the skill with which the right opportunities are offered, the wrong ones eliminated, and by the resulting satisfaction to the patient when he makes the right responses and dissatisfaction when he makes the wrong ones. This standard reduces orthoptics to its simple essential elements.

There are many factors involved in creating the right opportunities. They form the teaching triangle of the patient and his specific problem, the facilities available for his orthoptic training, and the skill of the technician in applying the facilities to the patient.

Since learning is response to stimulus, if the patient is unable to respond to a given stimulus, no learning takes place. For this reason it is of no value to expose a patient to difficult and impossible situations.

An example of this is the patient with an amblyopic eye who is asked to fuse. If he cannot see the object presented for fixation, he cannot get a second image to fuse with the better image, and he learns nothing about fusion.

If he is partially amblyopic, and can see when the image in front of his amblyopic eye is very brightly illuminated, he may then be able to fuse, and profit by this specialized experience, but when the illumination is decreased below the threshold of his perception the learning that has taken place no longer has any stimulus to start the fusion response, and there is no opportunity to continue the practice of fusion.

Another example is the patient who cannot fix steadily with both eyes. It may be because he has a habit of alternation, and changes fixation from one eye to the other at random, suppressing the nonfixing eye. Patients with a phoria often have intermittent suppression that prevents stable binocular fixation. As long as they do not fix steadily with both eyes they cannot start to learn the advanced steps of binocular vision, and it is useless to expect them to practice vergence control or stereopsis.

Suppression is the commonest cause for failure to profit by orthoptic training. Unless the patient uses both eyes he cannot fuse or develop the other skills of binocular vision.

Orthoptic learning begins with binocular fixation, and proceeds through the subsequent steps of vergence control, accommodation-convergence control, and training of the perception of color, stereopsis, and other interpretive skills.

The learning process requires not only that the anatomic mechanism for transmitting images shall function adequately, but that the individual shall be emotionally receptive to the stimuli so that the interpretive portion of the visual act shall be completed with satisfaction. If the patient does not give attention to the stimuli, or is not aware of what he perceives, or is not satisfied with his sensations, learning stops.

Anomalous correspondence functions so as to give the patient satisfaction with his adjustment at a reflex level and is usually associated with suppression. In some cases the anomalous correspondence reflex is so firmly established that it is beyond the power of the individual to inhibit it and distressing postoperative anomalous diplopia persists, despite all efforts to develop normal fusion skills. Variations in results in attempting to correct anomalous correspondence may often be traced directly to variations in sound application of the learning factors, or in the innate teachability (adaptability) of the patient.

ESTABLISHING EMOTIONAL ATTITUDES

Learning stops when the patient decides, whether justifiably or not, that the situation is too difficult. A large part of orthoptic teaching consists, not of arranging suitable optical set-ups for binocular experience but of establishing emotional attitudes on the part of the patient so that he will take the necessary steps in learning. He cannot be

forced to learn but he can be eager to learn.

A certain amount of discipline may be important in controlling attitudes, but the difference between establishing opportunities, and securing use of the opportunities (which is learning) must be clearly understood. Any portion of the visual act which is subject to either inhibition or choice-of-responses, is subject to learning.

Inhibition is itself a choice of response, but it is classed separately because of its importance in controlling reflexes. Reflexes, which, being innate, cannot be altered, can be inhibited under certain conditions. This is why orthoptics reaches down to the very fundamentals of binocular vision in developing normal habits; the abnormal adjustments previously made by the individual must be inhibited before normal responses can be established.

Inhibition is a very difficult response to make to a reflex stimulus. Because of their innate mechanism, reflexes are very strong and prompt in their control. Moreover, inhibition cannot be forced upon an individual. It is an emotional type of response that has to be exerted from within. The desire to inhibit must precede the act of inhibition.

This inhibitory control is slow to develop in the individual; it is definitely an attribute of maturity. This is a primary reason why young children cannot change their pattern of binocular control once it is established. They are not sufficiently mature in their inhibitions to inhibit the reflex patterns they have already learned, preparatory to learning new ones.

If the extent to which normal binocular vision is a learned process is clearly understood, the process of orthoptic correlation of faulty binocular vision may be more easily analyzed.

ANATOMIC AND PHYSIOLOGIC FACTORS

Normal binocular vision depends upon the slow maturing of anatomic and physiologic components involved. The first imperfect images received by the infant require only the simplest interpretation of direction and size. He does not need to make complicated interpretation of form and color since he has not sufficiently accurate data (clear images) to work with.

There are only three kinds of errors which can be made at the reflex level (1) Errors in direction, or fixing the desired object; (2) errors in accommodation, or getting a clear image; and (3) errors in fusion, or getting a single image.

Patients may fail in one of these factors or in a combination of two or more. All the time that the growing infant and child is getting practice in establishing a clear, single image of the object fixated, he is also getting a vast amount of interpretive experience in learning about what images mean. He is also building up a body of satisfactions and dissatisfactions with his results.

If his growth processes are normal, by the time he is eight years old he has developed normal binocular vision. If, during this growth period, something interferes with his ability to fixate, to accommodate, or to fuse his two images, he will develop an abnormal adjustment to binocular vision.

Due to his anatomic and physiologic immaturity during this period, such adjustment is reflex in character, with all the reflex attributes of becoming the innate responses, of by-passing the cortical-willed impulses, and of not being subject to further choice and change.

The fundamental reason that the patient makes such faulty adjustments is because of the comfort or satisfaction that results from them. Thus the emotion of satisfaction is the tool with which the child works to establish his visual habits. These emotions of satisfaction are even more innate than normal visual reflexes. The comfort of clear single vision will be achieved by abnormal reflexes when necessary.

The visual mechanism is such that it is possible for the patient to get comfort and satisfaction in several different ways. He is not limited to the normal way, by fusion. If

the condition which prevented the patient from developing normal fusion persists, he is as well adjusted as it is possible for him to be when he uses one of the alternative solutions of binocular vision, suppression, anomalous correspondence, or the Swan syndrome.

If, however, the original cause is corrected, as by refraction or surgery, then his original adaptation is no longer necessary. If the correction takes place while he is still young enough to be developing and experimenting with binocular vision, he has a good chance of accepting normal fusion but, if he has fully established his reflex adjustment in an abnormal manner, he will continue to use these reflexes and fail to take advantage of improved binocular opportunity. The mere presence of improved opportunity is no guarantee that the patient will use it.

The factors which control the learning process are the ones which will determine the use the patient will make of his opportunity, and the emotions are a predominant factor in the learning process.

PROGRESS IN ORTHOPTICS

It is the function of orthoptics to guide the patient through the steps of learning binocular vision. To find out whether it will correct a given problem—that is, develop normal binocular vision for a specific patient —it is necessary to know how fully such a patient meets the requirements of the learning process.

This is the science of prognosis in orthoptics, still one of the most uncertain fields in the orthoptic procedure. It need be uncertain only to the extent that the learning factors cannot be determined. The more such factors can be evaluated as part of the original diagnosis the more certain prognosis becomes. Many of the factors are discoverable only by a trial period. This is why orthoptics is so largely empirical. It is gradually becoming less so as the learning process is more completely understood and fully applied.

There are four obstacles to satisfactory

binocular learning. One has already been discussed; the patient who cannot fuse, who has an insuperable obstacle to normal binocular vision. There is still some uncertainty about what constitutes an insuperable obstacle, and more orthoptic research will be needed before such patients can be diagnosed conclusively. This applies especially to the "neuro" portion of neuromuscular disturbances, to patients in whom the etiology of strabismus is "unknown."

The second obstacle is the patient who does not accept the necessary steps in the learning process, who fails to give attention, to recognize the orthoptic situation, and to get satisfaction out of binocular effort. The most usual cause of failure in this group is immaturity. They may be immature due to calendar age, or for other reasons. Many adults do not take a mature attitude toward their visual problems.

The third group of patients fail because the fusion problem, while not insuperable, is too difficult for habitual use. This includes patients with insufficient surgical correction, and some of the phoria cases. It also includes some cases of anomalous correspondence. These patients are often able to learn orthoptic skill, but are unable to apply it continuously for casual seeing.

The final obstacle to orthoptic success consists of inability to learn to recognize the difference between single vision by fusion and by the previously developed reflex adjustment. Many cases of exotropia fall into this classification. They are characterized by inability to perceive diplopia when fusion fails.

All orthoptic failures fall into one of these four groups. Orthoptic progress is largely concerned with group two; the better the teaching skill the fewer failures in learning. The other groups are inevitably mostly the responsibility of the ophthalmologist who must improve his preparation of the patient for binocular vision to the limits of ophthalmic knowledge by removing all possible obstacles and making fusion easier.

Art of Orthoptic Teaching

The foundation of learning is the satisfaction resulting from a specific response to stimulus. This is why the orthoptic situation must center around the individual. No matter how scientifically sound the optical arrangements for binocular vision may be, if they do not result in satisfaction for the patient they will not result in learning. They will not meet his needs if they are beyond his capacity at either the physical or emotional level. He must be able to respond physically and to get satisfaction emotionally out of the response.

The primary response is simultaneous perception—the use of both eyes; the primary satisfaction is a clear single image.

When, by using both eyes, the patient gets a clear single image he has taken the first step toward establishing fusion as his response to binocular vision. Because of the fact that he is a patient, and not a normal individual, if he uses both eyes he will probably get either diplopia or a blurred image.

The art of orthoptic teaching is to give the patient sufficient satisfaction with his preliminary binocular experiences so that he will continue making new responses and not give up and fall back on his old reflexes.

All satisfactions may be grouped into two classes, physical and social. Orthoptics is obliged to make much use of social satisfactions to stimulate learning, since much orthoptic learning is far from physically pleasing to the individual. Hence it is easy to see that, if the patient is too young, or otherwise not amenable to social satisfactions, orthoptic learning will not be satisfactory.

There are many levels of satisfaction. A child may "hate" his orthoptic lesson, but if he hates the attitudes of his parents or technician when he has a poor lesson even more, the outcome will be satisfaction with a lesson well done. The manipulation of the lesson situation in such a way that the satisfactions for work well done outbalance the dissatisfactions of tedium, physical unpleasantness (such as diplopia), and the discipline

of inhibition is the basis of orthoptic teaching skill. The ability of the teacher to impart enthusiasm to the patient is part of good teaching.

The second corner of the teaching triangle is the selection of equipment and the creation of situations in which the correct response will be made by the patient. These are the facilities of orthoptic environment, which make binocular vision possible as it has not been possible before in the history of the patient.

It was the development of orthoptic equipment which was the first great forward step in the history of orthoptics. Failure to realize that exposure to such opportunity by means of this equipment was not the final step but only the preliminary step to binocular vision retarded orthoptic development by many years.

Nevertheless, the importance of adequate equipment is very great. At the present stage of orthoptic technique, it is still essential. Good equipment makes efficient teaching possible. Poor equipment need not prevent all efforts at orthoptic education, but it makes it unnecessarily tedious and difficult.

The technician herself is the corner that closes the teaching triangle. Her skill in adapting situations and creating attitudes is what determines how successfully the learning process will take place. The selection and application of equipment and facilities to each patient, day by day, and minute by minute, at each step in his binocular reëducation is the responsibility of the technician. It is the art of teaching. Orthoptic speed and success depend upon her ability in this field.

Summary

Binocular vision is a learned process. The mechanism for achieving it is preformed and the correct reflexes are innate. In the normal child, the development of the correct adjustments for normal fusion takes place during the first six years of growth. If some abnormality interferes with normal binocular vision 1 of 4 abnormal adjustments will be

learned instead; suppression, anomalous correspondence, the blindspot syndrome, or abandonment of single vision. This last adjustment is, of course, diplopia, rarely adopted by the child, but more frequently by the adult. If such abnormal learning takes place when the individual is sufficiently immature, it becomes the reflex adjustment of that individual.

Reflexes take precedence over other types of response, and cannot be altered, but can be inhibited. If the original need for an abnormal adjustment is corrected, the patient can learn normal responses.

There are four causes for orthoptic failure: an insuperable ophthalmological problem, failure to accept the learning process, lack of fusion comfort, and inability to recognize fusion errors.

Opportunity to learn does not necessarily result in learning. All the factors for learning must be present in order that learning will take place; attention, recognition, response, satisfaction, and repetition. Emotions, especially satisfaction, play a large part in the learning process.

Unless an orthoptic situation is created in which all the factors in learning are present in the right manner at the right time, binocular vision will not develop efficiently.

490 Post Street (2).

DISCUSSION

PETER C. KRONFELD
Chicago, Illinois

I am well aware of the fact that I am very poorly qualified to discuss Miss Lancaster's paper. One obvious reason is that I have had very little practical experience in the administration of fusion training. Another reason is that during the last few years I was engaged in a type of work in which I had to concentrate on the detection of cases of partial or complete failure of fusion training.

In 1944, I was appointed a member of a committee of the National Research Council that was to concern itself with medical problems in civilian aviation. The Civil Aeronautics Administration requested this committee specifically to include in the examinations of the applicants for pilots' licenses some test that would permit the distinction between genuinely normal binocular systems and systems that might be called patched-up ones, patched up either by surgery or surgery plus fusion training. The Civil Aeronautics Administration did not intend to bar such patched-up systems but wanted to have such systems detected and properly recorded, so as to determine whether the flying ability of the bearer of such a system differs demonstrably from that of genuinely normal systems.

At first I did not think that there was such a test that could reliably be administered by physicians without special training in ophthalmic examinations but, after extensive trials and errors, I became convinced that a modified Howard-Dolman test served the purpose of screening out inferior binocular systems very well.

In the course of this work, a great many cases of failures of fusion training have come to my attention. Nevertheless, I have tried to maintain an unbiased attitude for which I have been repaid by discovering a few cases which, as a result of fusion training, attained the highest degree of binocular coöperation, namely, an acuity of binocular depth perception of the same magnitude as that of a genuinely normal system.

Miss Lancaster's paper deals specifically with the psychology of the process of learning in orthoptics. She describes five essential

steps in the learning process—attention, awareness, response, satisfaction, and repetition. These steps seem significant and real, not only to the professional educator but also to the ophthalmologist and physiologist.

Following the terms introduced by the school of Pavlov, we often use the term "reward" instead of satisfaction. A number of years ago, I was engaged in trying to acquire a specific binocular skill, that of pseudoscopy. As you all know, pseudoscopy consists of the reversal of stereopsis by offering to a normal binocular system the "wrong" image of a three-dimensional object. A pyramid or a cube, photographed with a stereo-camera may serve as such an object. The two images are then offered to the "wrong" eye, fusion being obtained either by crossing one's visual lines in front of the images or by special pseudoscopic devices.

Such reversed images of simple three-dimensional objects very promptly and instantaneously produce the reversal of the depth effect, that is concavity, where there actually is convexity and vice versa.

If the viewed object, however, is well known to the observer, his empirical knowledge hinders the reversal of stereopsis. The stronger these empirical factors are, the more difficult it becomes to perceive reversed stereopsis. By systematic training, however, one can learn to free oneself of these empirical factors and to perceive the reversed stereopsis readily and instantaneously, despite the presence of strong empirical factors.

I subjected myself to such fusion training and, recalling my subjective sensations during that training, can very readily recognize the five steps in the training discussed by Miss Lancaster.

There are two statements in Miss Lancaster's paper that I would like to stress specifically. She advises us to distinguish carefully between fusion failure due to lack of opportunity, and fusion failure due to a specific fusion inability. I believe that this is a very important distinction.

The busy ophthalmologist in an office full of urgent major pathologic problems, is especially apt to forget that, in the case of a system with one "weaker" and one "stronger" eye, it is important to choose for the fusion test a pattern, the important parts of which can be readily perceived by the weak eye.

Most ordinary cards or slides designed for fusion tests are too difficult for an optically or perceptually inferior eye, and it is very often because of that inferiority that no fusion occurs, the examinee simply not seeing the important elements of one half of the test card. If the essential parts of the pattern offered to the weaker eye are of sufficient magnitude and impressiveness, in many such cases a true act of fusion can be demonstrated.

In her summary, Miss Lancaster states "that binocular vision is a learned process; the mechanism for achieving it is preformed and the correcting reflexes are innate."

This may seem like a radical departure from Hering's classical view of the purely innate character of binocular depth perception due to horizontal disparity. Having been an ardent admirer and follower of Hering all my life, I believe that if he could have witnessed the recent developments in our knowledge of binocular sensory coöperation, he would have worded his concept of binocular coöperation very similar to the way in which Miss Lancaster has done.

904 West Adams Street (7).

NOTES, CASES, INSTRUMENTS

ECTOPIC LACRIMAL PUNCTA

A CONGENITAL ANOMALY ASSOCIATED WITH ABSENCE OF THE LACRIMAL PAPILLAE AND CAUSING CHRONIC TEARING

ARTHUR H. KEENEY, M.D.
Louisville, Kentucky

Congenital abnormalities of the lacrimal puncta and canaliculi are usually considered in any discussion of chronic tearing, but
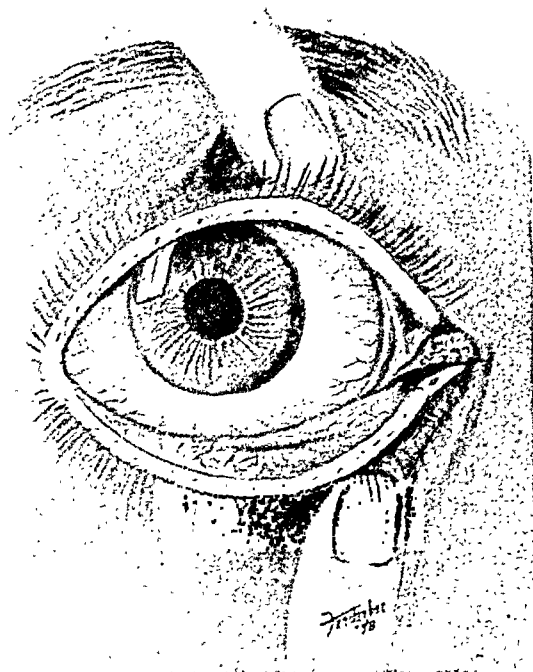
Fig. 1 (Keeney). Ectopic, inferior lacrimal punctum. The slightly ovalized and gapping point is located on the lacrimal portion of the lid border and is directed superiorily so as not to be in contact with the lacrimal lake.

practically no mention is to be found concerning the importance of small degrees of malposition of the puncta other than in cases of ectropion. It is the purpose of this report to emphasize careful study of the location of lacrimal points and to establish ectopic puncta as a rare but occasionally seen congenital anomaly responsible for epiphora.

Development of the canaliculi and papilla in solid epithelial cells occurs at the 35- to 36-mm. stage.[7] The superior canalicular segment buds directly from the sac anlage and traces its course through the upper lid.

Less simple, however, is the development of the inferior canaliculus. This buds from the advancing upper canalicular segment rather than from the sac anlage and, in the course of its lateral growth, cuts off a medial portion of lid tissue to create the caruncle.[3,6,7]

Thus, there are more opportunities for developmental faults to occur in the lower than in the upper portions of these passages, and clinically more anomalies are found in the lower portions. Canalization of these rods of cells begins in the 35-mm. embryo and is essentially complete at the 6-cm. stage, except for the puncta which open just before the lids separate in the seventh month.

Ida Mann[5] indicates the two basic mechanisms whereby faults may arise: (1) The buried epithelial buds which trace out the canaliculi and their opening may pursue abnormal courses, or (2) the structures, originally blocked out in solid epithelium, may not canalize. Miss Mann and others* have specified that by these mechanisms there may result (a) total absence of the puncta, (b) dimplelike, imperforate puncta, (c) atresia of the puncta, (d) occlusion of the puncta with epithelial plugs, (e) elongated or slit-like puncta, (f) shallow gutter openings in the canaliculi, or (g) accessory puncta.

In addition to these anomalies should be listed ectopic puncta. A review of French, German, and English literature since 1836 reveals only four such cases reported in this country[2] and three cases reported from France.[1] Another French case reported by Lempert[4] in which he described fissurelike openings 2 and 3 mm. long located medial

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* Blanchet, 1846; Cabannes, 1896; Nielsen, 1896; Fox, 1900; Lebeque, 1910; Lempert, 1920; Schaffer, 1921; Towne, 1943; Brooks, 1944; Hendricks, 1944.

to the usual site is only a slight variation of this anomaly incorporating also the characteristics of slitlike puncta. One additional case is reported herewith.

CASE REPORT

History. The patient, a 23-year-old white man, complained of moderate epiphora as long as he could remember. His parents state that he had "watery" eyes even in infancy. Temperature changes, wind, or excitement caused tearing onto the cheeks. There is no family history of this disorder. Gestation and birth were apparently normal. There have been no infections in or near the eyes and no previous illnesses other than the usual childhood diseases. He has had repeated lacrimal probings by other physicians in 1945 and again in 1947, but never with any improvement. He states that Bowman probes up to size 9 have often been passed.

Complete physical, ophthalmic, and rhinologic examinations were negative except for the lacrimal findings and a perforated left ear drum. Examination under magnification revealed no evidence of lacrimal papillae on the lower lids. Transition of the lid border between lacrimal and ciliary portions followed the usual configuration and there was no ectropion.

The superior canaliculi opened by normal appearing, round puncta directed posteriorly at the junction of the lacrimal and ciliary portions of the lid border. Each inferior canaliculus opened through the lid border at the junction of the middle and outer thirds of the lacrimal portion and formed an acute angle of about 15 degrees with this free border.

The puncta thus formed had no papillae, opened directly upward, and had no contact with the lacrimal lake. The puncta gapped slightly and were ovalized so as to measure about 0.3 by 0.8 mm. in size.

Irrigating solution was delivered with ease from any punctum into the nose. X-ray films taken after lipiodol installations through the lower puncta showed the remainder of the passages to be entirely normal.

Comment. The upper puncta were able to function by the normal processes of capillarity, but because the lower puncta were not directed against the bulbar conjunctiva, they were ineffective to drain the tears. Both lacrimal glands appeared somewhat smaller than usual.

The most logical explanation for this pathologic condition seems to be an aberration in the developmental course of the canalicular buds at the 34- to 35-mm. stage, whereby they open onto the lacrimal portion of the lid border, instead of continuing laterally to the usual site on the ciliary portion. The role of constricting amniotic bands, mentioned by van Duyse and van der Hoeve,[7] which might prevent lateral growth of the buds by direct pressure, remains speculative.

SUMMARY

A case of chronic tearing caused by congenitally ectopic puncta is presented. The inferior puncta are located on the lacrimal rather than the ciliary portion of the free border and are directed superiorly rather than posteriorly. Capillarity is hence impossible. The developmental mechanism is reviewed.

1103 Heyburn Building (2).

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BILATERAL HOMONYMOUS HEMIANOPSIA CAUSED BY VASCULAR OCCLUSIVE DISEASE

JOSEPH V. M. Ross, M.D.
Berwick, Pennsylvania

In January 1943, in the *Archives of Ophthalmology* (29:92-97), was reported a case of "Bilateral thrombosis of posterior calcarine arteries with sparing of macular vision" by P. Robb McDonald of Philadelphia, in which it is mentioned that such cases are rare. The author was able to uncover only one other case in this country and that was by Dunn, in 1895. Accordingly herewith is reported a case that I believe to be similar, although the lesions, which seem to be the same in nature, probably are slightly different in location.

In Rucker's monograph prepared for the American Academy of Ophthalmology and Otolaryngology, "The Interpretation of Visual Fields," on page 14 are illustrated fields of bilateral homonymous hemianopsia due to occlusive vascular disease which are similar to those in my case, so undoubtedly other cases have been seen and not reported.

CASE REPORT

History. This patient, H. P., aged 61 years, was first seen by me on November 29, 1947, at which time he stated that he could not get around too well because of poor and restricted vision. His history was that on November 11th at 7 P.M. he developed a pain in the left side of his head and sudden loss of vision which gradually recovered. At 11 o'clock that same night, the head pain recurred, more generalized, and vision became blurred and has remained so ever since. He

had particular difficulty in seeing to the side, so that he bumped into objects, especially those on his right side. He had been weak and bedfast until a day ago. He also stated that for several years he has been under the care of the referring physician for high blood pressure and arteriosclerosis.

Neurologic examination disclosed some spatial disorientation and some personality
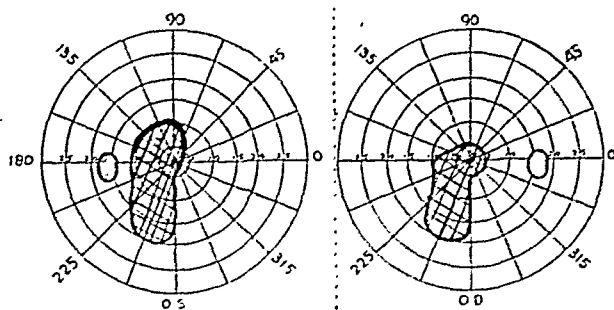
Fig. 1 (Ross). Field taken on November 29, 1947, with 6/1,000 white. Vision: O.U., 20/20.

changes. His general medical checkup revealed only an essential hypertension of 170/120 mm. Hg. All laboratory studies were normal as were skull X-ray studies.

Ophthalmoscopic examination revealed poor convergence. Relative visual acuity was: O.D., 20/200, 24-point type at 14 inches; O.S., 20/100, 18-point type at 14 inches; (correctible to normal for near and far). Refraction showed: O.D., +0.5D. sph. $\bigcirc$ −0.75D. cyl. ax. 100°; O.S., +0.5D. sph. $\bigcirc$ −0.75D. cyl. ax. 80°; (add: +2.25D. sph.).

Ophthalmoscopy revealed an angiosclerosis, Grade 2, O.U. The early visual fields were as in Figure 1. Later, June 21, 1948, small islands appeared up and to the left in each field as shown in Figure 2.

The patient had some spatial disorientation, not severe, and his wife stated some

personality changes, but no alexia. Optico-kinetic nystagmus was elicited with ease but there were no spontaneous nystagmus and no reading disabilities. There were two degrees of fusion but tests for stereopsis gave variable findings. The diagnosis entertained was bilateral occlusion of portions of the posterior cerebral arteries (calcarine?) and Dr. P. R. McDonald in a personal communication stated he believed this case might well fit into this category.

For discussion of the anatomy, physiology, and other interesting aspects of these cases, reference is made to Dr. McDonald's paper in which the subject is so clearly discussed. This case differs from McDonald's in that
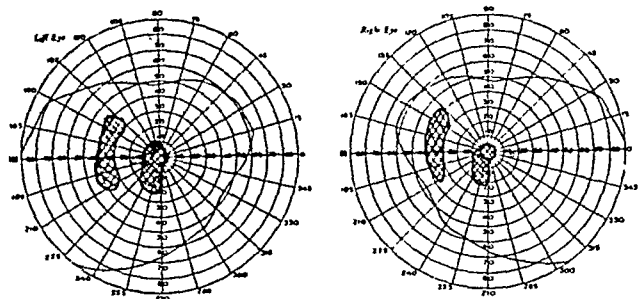
Fig. 2 (Ross). Field taken on June 21, 1948, with 6/1,000 white. Vision in both eyes was normal for far and near.

stereopsis was variable and spatial disorientation was present for a few months with recovery at the time of the last fields on June 21, 1948. The fields showed some peripheral recovery. Admittedly, as in McDonald's case, the exact anatomic diagnosis in this case can be made only at autopsy.

321 East Front Street.

DIABETIC RETROBULBAR NEURITIS

PETER SYKOWSKI, M.D.
Schenectady, New York

Recently Walsh[1] said that he had no "useful evidence to offer on the validity of diabetic retrobulbar neuritis as a diagnosis" and suspected "that it rarely is a correct one." The basis for this was the failure of Waite and Beetham[2] to record any cases of retrobulbar neuritis in 2,000 diabetic patients.

Fuchs,[3] in 1894, mentions "cases of chronic poisoning by diabetes" as leading to retrobulbar neuritis. De Schweinitz[4] writes of diabetic amblyopia as being the only symptom of diabetes, of having a central color scotoma, and of being more apt to be found in diabetics who use tobacco freely than in those who are abstaining. Also, Berens[5] points out that, since diabetics are more susceptible to tobacco amblyopia than healthy individuals, some writers have thought that it was this association which was responsible for the signs of retrobulbar neuritis in diabetics. Berens states further, however, that well-substantiated cases have been seen in patients who were not exposed to poisoning by tobacco in any form.

Duke-Elder[6] states that, although it has not always been clear that the retrobulbar neuritis is not due to poisons such as alcohol and tobacco, so many instances have occurred wherein other poisons can be excluded that the existence of the condition as a diabetic complication must be admitted.

Traquair[7] reveals that, (1) In many of the reported cases the diabetic origin of the amblyopia is not convincingly demonstrated; (2) in cases of general disease, such as diabetes, in smokers one would be correct in most cases in attributing the amblyopia to the tobacco if the scotoma is typical and, in any case, the causation of scotoma by endogenic toxins in diabetes and other diseases, although extremely rare, must be borne in mind; (3) cases of pure diabetic toxic amblyopia have not hitherto been sufficiently closely examined in sufficient number to establish the true characters of the field changes, (4) the defect due directly to the toxins of diabetes is multiform and often pericentral and varying in shape.

REPORT OF CASES

Several cases of diabetic retrobulbar optic neuritis have been observed and are being

reported. In these, toxicity from tobacco, alcohol, teeth, sinuses, tonsils middle ear, and so forth have been definitely excluded.

Case 1. S. M., a 53-year-old woman, was seen on March 20, 1948, with a complaint that three weeks previously there occurred a gradual onset of loss of vision in both eyes. At that time a blood sugar of 262 mg./cc. was discovered and diabetic treatment instituted.

At the time of the ocular examination, the blood sugar was normal. Visual acuity with and without correction was 20/80 in the right eye and 20/100—1 in the left eye. Fundus examination except for slight A.V. compression was normal. The tangent-screen visual field showed enlarged cecal areas, and with a 1-mm. white test object pericentral scotomas, one degree in circumference in the right eye and two degrees in the left eye.

Case 2. H. E. a woman, aged 62 years, was seen on June 4, 1948. Six months previously, a blood sugar of 450 mg./cc. was registered, at which time there was marked "smokiness" of vision. The blood sugar was normal at the time of the examination.

Visual acuity without correction in the right eye was 20/200 and, with correction, 20/70; in the left eye, 20/100—1 and 20/60, respectively. The fundus showed a few scattered retinal hemorrhages, the maculas being clear. The tangent-screen field showed, in the right eye, a slightly enlarged cecal area and with a 2-mm. white test object a 4-degree pericentral scotoma; in the left eye a slightly enlarged cecal area and a 1-degree pericentral scotoma with a 2-mm. white test object.

Case 3. B. W., a 47-year-old woman, was seen on April 4, 1948, in the hospital complaining of blurring of vision. Blood sugar was 385 mg./cc. One week later when the ophthalmic examination was performed, the blood sugar was 180 mg./cc.

Vision with and without correction was 20/30 in the right eye and 20/40 in the left eye. Except for several pin-point retinal hemorrhages, elsewhere than in the macular area, the fundi were normal. Fields revealed enlarged cecal areas in both eyes, and with a 1-mm. white test object pericentral scotomas in both eyes, one degree in the right eye and three degrees in the left eye.

DISCUSSION

That diabetic retrobulbar optic neuritis exists would seem to be unquestionable. Several such cases are presented; in these, other toxic elements, both endogenous and exogenous, have been eliminated.

Regarding diabetes, certain deplorable facts exist. For one, not all ophthalmic textbooks list diabetes as an etiologic factor. Secondly, referral of diabetics with early visual symptoms to an ophthalmologist occurs infrequently; there seems to be still an adherence to the old axiom of delaying until the general condition improves before an ophthalmic consultation is requested. It is likely that for the latter reason the incidence of diabetic retrobulbar neuritis lacks prominence.

Walsh[8] states that "obviously a fact of great clinical importance is that, if a patient complains of blurring of vision of recent onset, which is corrected by a change in lenses, the possibility of diabetes mellitus being causative should come to mind." Likewise, a case of blurring of vision in a diabetic should suggest retrobulbar optic neuritis.

CONCLUSION

The occurrence of diabetic retrobulbar optic neuritis as a clinical entity should not be questioned.

1330 Union Street.

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A NEW HAND-SLITLAMP*

EMANUEL KRIMSKY, M.D.
Brooklyn, New York

This new slitlamp is similar in principle to units previously reported by me.† It is not designed to replace my previous models but to show individual structural and optical features. These are: first (1) The use of a simple pencil flashlight type of battery holder to provide a flexible grasp in manipulating and in rotating the slitbeam; (2) a selective interchange of either batteries or house current with rheostat control; and (3) an improved lens-cap unit to provide a more intense and satisfactory slitbeam.

Optically, this unit consists of a straight filament lamp similar to the one used on a streak retinoscope, except that the dome of the filament was made rectangular instead of arch-shaped. Over this is fitted a condensing system consisting of a pair of plano-convex lenses, each of 11-mm. focal length. These lenses are arranged in series fashion so that the convex surface of one lens faces the plano surface of the other, and are separated by an air space amounting to

as little as 0.6 mm. The combined focal length of this condenser lens system is 5.9 mm. This lens arrangement has proved more satisfactory than the simple hemispheric condenser employed in a previous model because it provides a brighter and more clean-cut slitbeam. The slitbeam represents the image on cross section of the top of this filament when brought to the focus or conjugate focus of this condenser lens system (fig. 1).

Structurally, the lamp portion of this unit consists of a tubular battery-type handle on which is fitted a specially designed housing to hold a miniature lamp surrounded by a
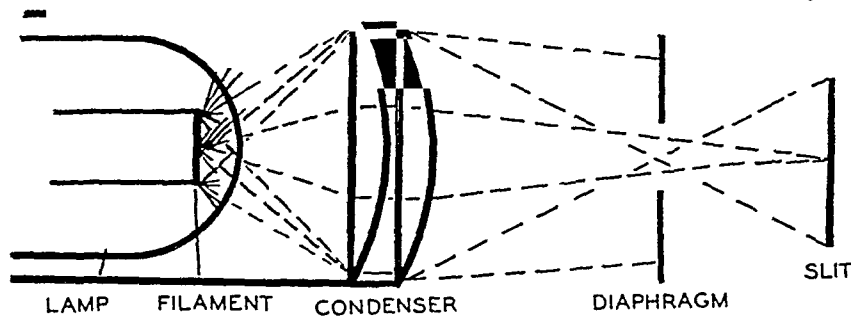
Fig. 1 (Krimsky). Optical bases for slitbeam.
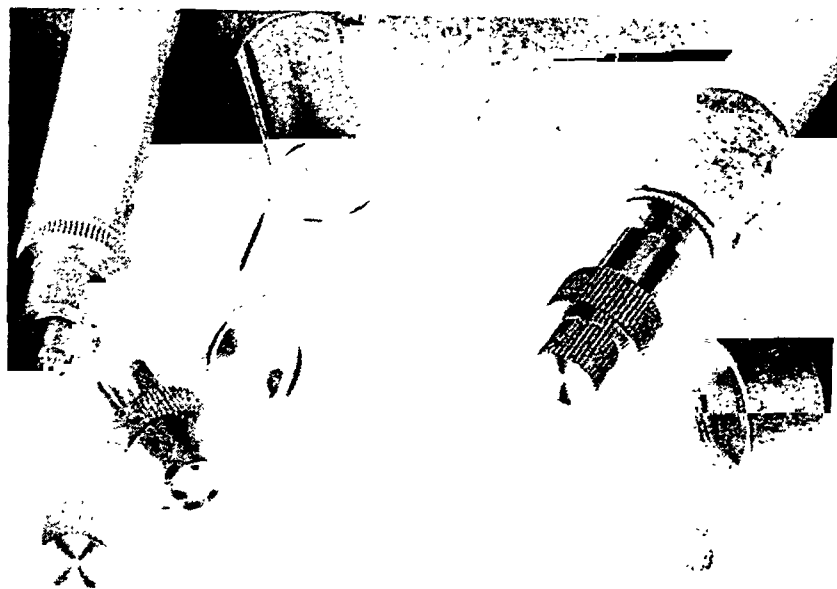
Fig. 2 (Krimsky). Hand-slitlamp disassembled to show component parts.

rotating cylindrical collar. The bulb remains fixed, whereas rotation of the collar through a helical arrangement draws it away from the handle without disturbing the fixed position of the bulb. The condenser lens cap housing fits snugly over this rotating collar so that both components rotate as a single unit. Such rotation serves to move the condenser lens system away from or toward the bulb which remains fixed during said operation. By greater separation of condenser and bulb, the size of the slitbeam becomes shorter and narrower and the operating distance is likewise correspondingly reduced (fig. 2).

Inspection of the eye is obtained selectively by means of a monocular magnifying loupe with collar which slides over the tubular handle. Also, one may operate this lighting system independently at any angle with the aid of a Beebe loupe or other type of magnifying lens system. The lens bracket is so designed and angulated that at the focal length of the viewing lens, the slitbeam is found to be in focus as well as in the center of the viewing field.

The slitbeam can be rotated to provide a vertical, an oblique, or a horizontal beam merely by rotating the lamp housing in this supporting lens bracket collar. By rotation of the lamp collar the slitbeam can be transformed to a broad or almost circular area of light. The supporting lens bracket has a spliced collar which fits over the battery holder, and can be thereby be easily slipped off and transferred to any type of flashlight holder using 915 AA small-type Eveready batteries. While the bracket here shown provides for a fixed angle between lens and light, I am having constructed a flexible bracket which will enable ready adjustment to variable angles between lens and light source.

745 Eastern Parkway (13).

HERPES ZOSTER OPHTHALMICUS

INITIATED BY KERATITIS

MARK THUMIM, M.D.
Middletown, Connecticut

This case is reported because of the rarity of the order in which the lesions appeared. Edgerton* could find only six cases in the literature in which the keratitis preceded the cutaneous eruption. Most of the cases which he found were reported many years ago. There have been, as far as we could find, no cases reported since Edgerton's paper.

CASE REPORT

History. Mrs. M. P., a 47-year-old white woman, was seen on August 11, 1948, with the complaint that, three days before, her left eye had become red, and that she had itching and a scratchy feeling in it as well as much lacrimation from it.

On examination, with oblique illumination, an area of corneal infiltration was seen at the limbus from the 1- to 3- o'clock positions. On August 12th, she began to have severe pain over the left side of her forehead and on the next day a rash appeared. When she was seen on that day, she had severe pain and she had vesicles on red bases on the lateral portion of her left upper lid, at the base of the nose to the left of the midline, and over the left part of the forehead. Corneal infiltration was still present.

She was seen again on August 18th, at which time no change was noted except that the left upper lid was swollen. On August 23rd, the pain was much relieved; the vesicles had dried; there was no change in the cornea.

On September 18th, the cornea was examined with a slitlamp and two areas of infiltration were seen. One of these was kidney-shaped and at the location of the infiltration originally noted. It was composed

of discrete opaque dots in the stroma. A second similar lesion, round, was just medial and caudad to the first. The vesicles had dried up and had been replaced by pitted areas in the skin.

COMMENT

This case is reported because of the extreme rarity in which the keratitis appears before the neuralgia or the vesicles in herpes zoster ophthalmicus. In this case the eye symptoms were present for four days before the true nature of the disease was evident. This is in contrast to the usual picture of this disease in which the neuralgia is followed by the skin vesiculation and which in turn is followed by eye symptoms and signs.

Professional Building.

THE POSSIBLE OCCURRENCE OF BACTERIUM ANITRATUM IN SEVERAL CASES OF CONJUNCTIVITIS*

W. A. MOOR
Saint Louis, Missouri

The following note is prompted by the recent publication of the description of a bacterium isolated, in most instances, from infectious conditions of the genito-urinary tract (Schaub and Hauber, 1948[†]). This bacterium is identical with a bacillus that has been found in several severe conjunctival infections, in so far as morphologic, cultural, and colonial characteristics are concerned.

SYMPTOMS

For the past seven years an occasional conjunctivitis has been encountered that has presented some rather puzzling features. These cases (there have been 15 from which the organism has been isolated) have all started in one eye as an itching sensation and have developed over a period of 3 to 4 days

to an appearance that is quite alarming. This progress has always continued at about the same rate regardless of what form of therapy has been tried (except for three cases in which streptomycin was used).

After this initial period of about a week or a little less, the other eye has usually undergone the same course. There is usually a great deal of injection of the blood vessels in the conjunctiva, a considerable edema of both the upper and lower lids, a moderate amount of irritation (however not as much as one would expect from the appearance of the eyes).

In three cases, there has been some swelling of the preauricular glands, somewhat more pronounced on the side of the eye showing the infection first. With most of the cases there has been a watery discharge but this has not been nearly as great in volume as would be expected from the appearance. There has never been any corneal involvement of any kind and, after 2 to 3 weeks, the inflammation has gradually subsided with no apparent after-effects.

It will be noted that this description could be thought to resemble very slightly the picture of a mild attack of epidemic keratoconjunctivitis; that there is a resemblance is shown by the fact that, on two occasions, tentative diagnoses of epidemic keratoconjunctivitis were made.

CULTURES

Cultures taken from these patients have always yielded a rather scanty growth (only one case showed as many as 20 colonies) of an organism that is rather slow-growing on the plate of initial isolation and on the medium that is used for routine eye cultures (2-percent tryptose, 2-percent agar, 0.5-percent sodium chloride, 0.2-percent dextrose, and 5-percent defibrinated whole rabbit blood). Subcultures on the same medium have given very good growth.

After about 20 hours' incubation at 37°C., the colonies as first isolated are quite small (about 0.1 mm. in diameter) and of a very

light grayish or white color. After 40 hours' incubation, the colonies are usually from 0.2 to 0.3 mm. in diameter and the gray-white color is more easily determined. Smears made from the conjunctiva or from the 20-hour culture will show Gram-negative bacilli, the majority of which will be so short that they may be easily mistaken for cocci. Longer incubation and subcultures bring out the true bacillary shape.

Since 1942, we have had 1 or 2 cases each year from which this organism has been isolated. There are two exceptions to this incidence. In 1944, there were six cases. However, 4 of the 6 were patients who had been examined by the same physician using the same clinical facilities for each patient. The period over which these six cases extended was about six weeks.

These facts would seem to indicate that the organism is moderately infective and that the human incubation period is in the region of 2 to 4 weeks. That the organism is only moderately infective would seem to be indicated by the fact that, during the period under discussion, this physician had been seeing a great many patients and had been using the same facilities for each.

In 1948, there were four cases from which this organism was isolated. One of these cases was a true epidemic keratoconjunctivitis and possibly represents a mixed infection, two cases were tentatively diagnosed as epidemic keratoconjunctivitis by two different physicians but did not have corneal infiltrates, the fourth case was not diagnosed.

TREATMENT

In all four of these cases, after the organism had been identified, streptomycin was administered, and they showed almost immediate improvement. The improvement in the one case of true epidemic keratoconjunctivitis was, of course, only to the degree that resulted in the elimination of the secondary infection.

TESTS WITH STREPTOMYCIN

During 1947, after streptomycin had become readily available, the organism was isolated from a case of conjunctivitis that had been resisting treatment with both sulfathiazole and penicillin ointments. This strain was tested for in-vitro susceptibility to the routine antibiotics used in the eye clinic and was found to be resistant to 5-percent sulfathiazole ophthalmic ointment, 10-percent sodium sulfacetamide ophthalmic ointment, and calcium penicillin ophthalmic ointment (1,000 u. per gm.). It was susceptible to 100 mg. streptomycin to 1 cc. saline and 10 mg. streptomycin to 1 cc. saline.

The tests were simply to supply an indication for a possible treatment and were very crude. The organism was seeded on a plate, incubated to dry the surface, and 0.1 cc. of the agent on a cotton swab was drawn lightly over the seeded surface. The plate was then incubated overnight and observed the next morning for inhibition of growth both at the site of the streak and on the adjacent areas.

The patient from whom this strain had been isolated was treated with streptomycin (100 mg. to 1 cc. saline). Drops were instilled every three hours. Improvement was noted on the second day of treatment.

In three cases treated with streptomycin in 1948, a solution of streptomycin containing 1 mg. to 1 cc. of saline was used, and the instillations were made every two hours. Improvement was more prompt.

ANIMAL EXPERIMENTS

The strain isolated in 1947 was suspended in saline and instilled into the conjunctivas of two rabbits and one cat that were prepared for the instillations by light abrasion with sandpaper. The two rabbits showed some moderate inflammation which started on the fourth day, lasted for about four days before it began to clear, and continued uneventfully for another two days. After this time, no signs of any kind could be seen. The cat showed nothing. The organism was not recovered from any of the animals.

It is hoped that serologic comparison with Bacterium anitratum will be possible.

640 South Kingshighway (10).

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW YORK SOCIETY
FOR CLINICAL
OPHTHALMOLOGY

January 3, 1949

DR. BENJAMIN ESTERMAN, *president*

RECENT DEVELOPMENTS IN TONOMETRY

DR. ADOLPH POSNER discussed this subject during the instruction period.

ORBITAL TUMORS

DR. RAYMOND G. INGALLS said that an examination of all the orbital tumors in the Pathology Laboratory of the Institute of Ophthalmology of the Presbyterian Hospital revealed the following data.

They comprise a total of 216 tumors, divisible into 27 different groups, including specific cell-type tumors, and allied pseudotumors.

Their relative frequency is as follows: (1) angioma, 35; (2) pseudotumor (lymphogranuloma), 29; (3) lymphosarcoma, 22; (4) dermoid cyst, 20; (5) carcinoma, extension from accessory nasal sinuses, 16; (6) carcinoma, lacrimal gland, 7; (7) retinoblastoma, 12; (8) meningioma, 10; (9) melanoma, 9; (10) neurofibroma, 8; (11) carcinoma, extension from lids, 6; (12) cholesteatoma, 6; (13) rhabdomyosarcoma, 4; (14) neuroblastoma, 3; (15) carcinoma, metastatic, 3; (16) hematoma, 2; (17) myoblastoma, 2; (18) fibroma, 2; (19) osteoma, 2; (20) neurinoma, 2; (21) chondrosarcoma 1; (22) embryonal myosarcoma, 1; (23) neurosarcoma, 1; (24) leiomyosarcoma, 1; (25) lipoma, 1; (26) dermolipoma, 1; glioma (astrocytoma), 1.

The following list shows the age at onset for the youngest and oldest patients:

Angioma from birth to 65 years; pseudotumor, 9 to 74 years; lymphosarcoma, 1 to 77 years; dermoid cyst, 3 to 36 years; retinoblastoma, 2 months to 4 years; meningioma, 12 to 58 years; melanoma, 47 to 65 years; neurofibroma, 1 to 39 years; cholesteatoma, 37 to 63 years; rhabdomyosarcoma, 4 to 13 years; neuroblastoma, 8 months to 3 years; hematoma, 15 to 45 years; myoblastoma, 36 to 40 years; fibroma, 17 to 75 years; osteoma, 16 to 44 years; neurinoma, 7 to 15 years; chondrosarcoma and embryonal myosarcoma, infants; neurosarcoma, 7 years; leiomyosarcoma, 34 years; lipoma, 25 years; dermolipoma, 43 years; glioma, birth.

In the carcinoma group the following ages at onset were observed: Carcinoma, extension from accessory nasal sinuses, 50 to 70 years; carcinoma, lacrimal gland, 21 to 73 years; carcinoma, extension from lids, 58 to 77 years; and carcinoma, metastatic, 52 to 63 years.

Having established a table for age at onset, we may show the incidence of new growths for each decade: second, 12; the third, 16; fourth, 21; fifth, 28; sixth, 31; seventh, 15; and eighth, 9.

The first decade shows the following incidence: first year, 19; second, 5; third, 11; fourth, 6; fifth, 2; sixth, 2; seventh, 2; eighth, 2; and the ninth, 1.

This data may now be combined in the construction of a table of some value in differential diagnosis of tumors for each decade. For instance, we may list the tumors in the order of their relative frequency in a vertical column and then place the incidence figure of each tumor for each decade in adjacent horizontal columns. To make use of the table, we consult the decade column nearest the age of the patient and read down. For example, a patient between the ages of 40 to 50 years could have 1 of 11 different

types of orbital tumor, the possibility being angioma, 8; lymphosarcoma, 3; pseudo-tumor, 3; meningioma, 5; hematoma, 1; osteoma, mixed tumor of the lacrimal gland, 4; myoblastoma, 1; cholesteatoma, 2; derm-lipoma, melanoma, 1.

Discussion. Dr. Knapp asked whether, in the presence of orbital tumors or exophthalmus, was any glaucoma noticed.

Dr. Kestenbaum said that Dr. Ingalls did not mention mucocele of the frontal bone in his very complete and comprehensive report, probably because it is not a real tumor. Dr. Kestenbaum also said that Dr. Ingalls did not mention symmetrical and asymmetrical exophthalmos, that is the eye can also be displaced to one side or the other. He felt that Dr. Ingalls's material provided a basis for study as to whether such displacements can be used in differential diagnosis. He suggested that further study might be worthwhile.

Dr. Smith asked about the apparent predilection of these tumors to the left orbit.

Dr. Ingalls replied to Dr. Knapp that glaucoma has no relationship to tumors of the orbit except in neurofibroma with infiltration of the posterior ciliary nerves with buphthalmus. To Dr. Kestenbaum he answered that mucoceles were purposely omitted from this listing. To Dr. Smith he said that it is not known why tumors of the left orbit are more frequent. Cushing had suggested that this may be because the left carotid has a direct route to the eye.

MEASUREMENT OF RELATIVE EXOPHTHALMOS BY ROENTGENOGRAPHY

DR. BENJAMIN FRIEDMAN presented a method of measuring relative exophthalmos by means of X rays. The patient lies on the X-ray table, with eyes looking straight upward; a contact lens carrying a small lead dot is placed over each eye; the X rays are directed from the foot end of the table so that the central ray passes through the lead dots at an angle of 35 degrees with the table;

the shadows of the lead dots fall upon the film. If one eye protrudes more than the other, the dot on the relatively exophthalmic eye will be projected farther back than the dot on the less protruding eye.

The chief problem is to position the eyes in space in such a manner as to eliminate sources of error, and to permit duplication of this spatial position each time an exposure is made. Steps in the procedure designed to achieve these ends were detailed.

Film measurements are made by dropping a perpendicular from the center of each dot shadow to the proximal edge of the film. The longer perpendicular belongs to the relatively exophthalmic eye. For practical purposes the difference in the length of these perpendiculars represents the relative exophthalmos, magnified four times.

The contact glasses are standard plastic lenses, with a central lead dot 1.5 mm. in diameter. The dots are placed over the pupillary centers. The lenses are handled with the usual suction grip. No fluid is needed between cornea and lens. One drop of anesthetizing solution is sufficient.

Readings in successive examinations may vary from 0.0 to 0.5 of ocular position. This, in most cases, is less than the variations found in repeated reading with the exophthalmometer.

The method measures relative, not absolute exophthalmos. For example, if both eyes were equally exophthalmic, there would be no unequal projection of the respective shadows. No dependence is placed on the distance of cornea from orbital margin. Horizontal as well as anterior deviations may be recorded.

Dr. Friedman concluded that this method cannot be expected to supplant instrumental exophthalmometry but it offers additional information. The two methods should supplement and check each other.

Discussion. Dr. Saskin asked how a norm is established.

Dr. Esterman said that, since the patient's

head is kept constant, it might be of help to place a lead dot on the brow, to give the increase of the exophthalmos on subsequent examinations.

Dr. Kestenbaum said that Dr. Friedman was using a new principle in exophthalmometry, since he uses the position of the entire head or, to be more exact, the position of the occiput and the two ear ducts as points of reference. Hertel's exophthalmometry measures the position of the cornea in relation to the two lateral orbital margins; Kestenbaum's ruler-exophthalmometry uses the two superior orbital margins as points of reference. Each of these methods is based on a different principle. The use of all three methods and comparison of the results may make us more independent of the individual variations.

Dr. Friedman replied to Dr. Saskin, that there is no need to establish a norm since each patient is his own norm. To Dr. Esterman, he replied that the lead dot was a good idea, and that he had used it. Dr. Friedman said that it acted as a center pivot from which the lateral displacement of the eyes can be measured. To Dr. Kesterbaum, he answered that any method to determine exophthalmos requires determination of what plane is to be used for measurement. In this case the plane cutting through the auditory canals is used. Overdevelopment of one part of the head can be determined by clinical examination, which should supplement the X-ray findings.

ANGIOGRAPHIC DIAGNOSIS OF ORBITAL TUMORS

DR. ANTONIO GRINO presented a paper on this subject, which was published in full in the AMERICAN JOURNAL OF OPHHTALMOLOGY, volume 32, page 897, July, 1949 (with Dr. Edwin Billet).

Discussion. Dr. Samuel Gartner said that this is an important presentation as it gives us a splendid additional technique for the study and diagnosis of orbital tumors. This is a puzzling group of diseases and we certainly need more help in their diagnosis. Exact localization in the orbit is important since a decision can then be made whether the ophthalmologist should remove the growth by the orbital route or whether a neurosurgeon should operate by the transfrontal approach.

Dr. Knapp said that he believed that the ophthalmic surgeon could deal with most cases of orbital tumor. He asked why, in the first cases presented, X-ray therapy was preferred instead of surgery.

Dr. Kestenbaum said that he had seen the first of the cases presented by Dr. Grino several years ago and again about one year ago. The latter examination revealed, in addition to the severe exophthalmos, damage to the central vision and a definite temporal hemianopic defect in the visual field of the right eye. Although the exophthalmos indicated a space-taking process in the orbit, the temporal hemianopic defect hinted at a lesion in the chiasmal region, therefore in the middle fossa of the skull.

At the Montefiore Hospital an angiography was done which demonstrated the presence of an angioma in the orbit. A renewed examination of the angiogram revealed the additional presence of an angioma in the middle fossa. This additional finding made the clinical and angiographic findings congruent.

Dr. Rizzuti asked whether stereoscopic X-ray examination was done.

Dr. Billet replied to Dr. Knapp's question, that X-ray therapy was tried first and, if it was not successful, surgery was then used. However, in this particular case X-ray therapy was very successful.

Dr. Grino replied to Dr. Rizzuti that stereoscopic X-ray examination is done routinely in all cases of this type.

Bernard Kronenberg,
Recording Secretary.

CHICAGO OPHTHALMOLOGICAL SOCIETY

November 15, 1948

DR. A. C. KRAUSE, *president*

(Presented by the Department of Ophthalmology, University of Chicago)

CLINICAL MEETING

SJØGREN'S SYNDROME

DR. T. W. ANDERSON said that D. G., a 48-year-old white woman, was first seen at the University of Chicago Eye Clinic in August, 1948. She complained of episodes of burning and reddening of the eyes for the past 25 years. This had become worse during the past four years and constant during the past year. The eyes felt dry and sticky, sensitive to light, and vision was slightly hazy.

In 1940, the patient developed polyarthritis and swelling of the small joints of the hands and feet. In 1942, she had an episode of girdle pain lasting eight months, and lost 40 pounds. At that time an enlarged spleen was noted; there was no free acid in the gastric juice. She had been slightly anemic since the age of 15 years, for which she had taken liver and iron.

About this time she developed "chronic sinusitis" with postnasal drip. A turbinectomy had been done 22 years ago to help relieve the chronic episodes of conjunctivitis. In 1942 all the teeth were removed because of their poor condition; they had always been chalky. In 1946 she developed a salivary calculus of the right parotid duct followed by infection which drained externally below the right ear. Her mouth had been dry for 10 years and was now more so. In the same year a right mastoidectomy was performed. She developed thrombophlebitis in the lower extremities at this time.

Since adolescence she had had attacks of left pleurisy and, in 1947, a severe attack, of unknown etiology, developed; chest X rays at this time were reported normal. An infection of the left parotid gland, with associated skin infection of the face, was treated with streptomycin. Cultures of the conjunctivas, nose, and throat have revealed streptococcus; bacterial vaccines have given no relief. Local medication to the eyes has given only temporary relief at times.

The patient is a gaunt, slender woman who appears chronically ill. The skin is thin and atrophic, with brown patches on the lower extremities. There is generalized atrophy of the mucous membranes of the nose and throat, dryness, hyperemia, and patchy membrane. A thick mucoid substance was expressed from the sublingual salivary duct. The left parotid gland was enlarged, nontender, with a fibrous consistency. There were scars under the right ear and over the right mastoid. The mandible was slightly limited in action, with a dry clicking sound.

Eye examination revealed vision to be: R.E., and L.E., 20/30 with a 1-mm. pinhole. The skin of the lids was atrophic and dilated vessels were visible near the margins. The palpebral conjunctivas were injected and thickened; the bulbar conjunctiva was moderately injected, with slight superficial flush at the limbus. There was a thick ropy discharge in the lower fornix. The anterior surface of the corneas had patches of adherent thick mucoid material. There was central heavy punctate staining of the epithelium with 2-percent fluorescein and the epithelium was thinned and granular appearing. There were eight filaments standing by one end from the anterior surface of the right cornea. The Schirmer test was 0 mm.

On general physical examination the liver was lightly tender and enlarged two fingers below the costal margin. The spleen was very tender and enlarged four fingers below the costal margin. There was swelling of the wrist joints and fusiform swelling of the metacarpal and metatarsal joints, and some limited motion of the elbow joints. All laboratory tests were within normal limits with the exception that histamine gastric analysis

showed no free acid and scanty secretion; culture of the conjunctivas showed Hemolytic staphylococcus and C. xerosis.

This patient will be hospitalized for further study. At this time, the clinical impression is that she has keratoconjunctivitis sicca, syndrome of Sjøgren.

HEALED LUETIC NEURORETINITIS PAPULOSA

DR. PAUL G. WOLFF said that this woman, aged 28 years, came to the clinic in October, 1946, with the complaint of poor vision in the right eye of one year's duration. One year before she had suddenly developed severe parietal headache, a generalized measlelike rash including the soles and palms, broad streaklike flashes of light, and a veil in front of the right eye. Her physician at that time told her she had secondary syphilis. Several weeks later the symptoms spontaneously subsided.

When first seen, vision was: R.E. 15/200 and could not be improved; L.E., 20/20+4, uncorrected. The optic disc of the right eye showed mild temporal pallor and an inferior temporal, dense, largely avascular connective-tissue proliferation. This tissue extended forward into the vitreous and was anchored to large retinal veins and several old chorioretinitic lesions. Peripheral fields were constricted. The left eye was normal.

The patient is still receiving antisyphilitic therapy and the Wassermann test is now negative. The eye status is the same.

This condition was first adequately described in 1926 by A. Fuchs, although previous accounts of the disease are mentioned in the literature.

SCIENTIFIC MEETING

DR. DOUGLAS BUCHANAN spoke on "Neurologic manifestations with optic-nerve atrophy in children."

DR. PAUL C. BUCY spoke on "Neurologic manifestations with optic-nerve atrophy in adults."

Richard C. Gamble,
Secretary.

OPHTHALMIC MINIATURE

Kepler's overwhelming astronomic· discoveries overshadow his important contributions to our understanding of the process of seeing. He was a strange, erratic genius and his was a most unusual mind. In the discovery of the laws of the solar system an essential step was the emancipation from mechanical models. Kepler did not proceed by thinking out possible devices by which planets might be moved across the sky. He was guided by a sense of mathematical form, an aesthetic instinct for the fitness of things. In these later days it seems less incongruous that a planet should be guided by the condition of keeping the action a minimum than that it should be pulled and pushed by concrete agencies. Many of his contemporaries must have frowned on these rash adventures of scientific thought and felt unable to accept the new kind of law without any explanation or model to show how it could possibly be worked.

After Kepler came Newton, and gradually mechanism came into predominance again. It is only in the last years that we have gone back to something like Kepler's outlook, so that the music of the spheres is no longer drowned by the roar of machinery.

A. S. Eddington in *Naturwissenschaft,* November 14, 1930

THE ACADEMY MEETING

The 54th annual session of the American Academy of Ophthalmology and Otolaryngology was held in the Palmer House, Chicago, October 9 to 14. It was one of the most successful meetings from many points of view.

The presence of Sir Stewart Duke-Elder, the guest of honor, was one of the chief attractions. He has won the hearts of his American colleagues by his scientific attainments and his many noteworthy contributions to our science. His textbook is a priceless heritage to present and future generations of English-speaking ophthalmologists everywhere. He has endeared himself to each of us by his open-handed friendship, sincerity, and great personal charm. His appearance at the meeting assured a happy and cheerful atmosphere which permeated all of the activities and dispelled for a little while the gloom of world troubles and the depression that accompanies the thought of socialized medicine.

As is usual, the multiple activities of the Academy occupied every single working hour, beginning early in the morning and extending far into the night. As one of our

witty members remarked, "the Academy meeting makes you take nembutal to sleep and benzedrine to stay awake."

The total registration topped all records; 4,848 members and guests arrived early and most of them stayed to the last minute of the last day. One-hundred-eighteen individual courses (including 12 home-study course discussion periods) and 30 continuous courses in ophthalmology, with a faculty of 175 instructors, totalling 376 hours of instruction, were eagerly attended. It would seem that every possible subject in ophthalmology was covered, with the heaviest interest and attendance in those subjects that offered clinical aids to the practicing physician. Nearly every course was sold out and the popular ones were packed to the doors.

Thirteen out of the 23 scientific exhibits were of ophthalmic interest and all were of high caliber. The exhibit, "Primary chorioretinal aberrations with night blindness," by Harold F. Falls, in collaboration with P. J. Leinfelder, David G. Cogan, Frank D. Carroll, and F. Bruce Fralick, justly received the first award; "Malignant melanoma of the uveal tract," exhibited by Helenor Campbell Wilder of the Armed Forces Institute of Pathology, with the collaboration of Lawrence P. Ambrogi, won the second award; and that of Samuel Gartner, with the collaboration of Abraham Schlossman and Edwin Billet, on "Ocular pathology in general medicine," was awarded the third ribbon. Many fruitful hours of study of these and the other exhibits amply repaid the keenly interested members and guests.

At the joint session of the scientific sections, the president, Conrad Berens of New York, spoke on "Research in otolaryngology and ophthalmology; The role of the American Academy of Ophthalmology and Otolaryngology." He pointed out the support that the academy has given to pertinent research in the past and emphasized its future influence in this field of activity. His figures showing that for every 70 dollars spent for the care of the blind, one dollar was spent

for ophthalmic research and the prevention of blindness, were startling and depressing. He urged the formation of an international institute for the prevention of blindness and the conservation of sight, whose purpose would be to coördinate the efforts of the many organizations that are dedicated to saving sight. It would be most effective if established near the permanent headquarters of the United Nations in New York City.

Sir Stewart's address was on "The physiology of the intraocular fluids and its clinical significance." He summarized the present state of our knowledge of the subject to which he has contributed so much from his own researches in the past. His fluent style, his genius for collecting the essential facts, and his masterly presentation made a most difficult subject sound easy. He quoted Goethe to the effect that "hypotheses are cradle songs which lull to sleep" and added his own thought that, while this may be true, "if you sleep perchance you dream and may even awake to write a sonnet."

He then went on to develop a working hypothesis of the subject of the formation and disposal of the intraocular fluids so logically that time and future investigation will surely bear it out.

The remainder of the scientific papers were of remarkably high quality. The annual Edward Jackson Memorial Lecture was given by William L. Benedict of Rochester, Minnesota. His subject was "Diseases of the orbit." As is customary, the lecture will be printed in the JOURNAL and each reader will have the pleasure of appreciating its excellence.

The various ophthalmic symposiums, that are becoming the most important and attractive features of the scientific sessions, were unusually good. Space does not permit a detailed description and analysis of these symposiums, but it might be mentioned that the papers by John M. Sheldon, Ann Arbor, Michigan, on the "Immunologic aspects of allergy"; the entire symposium on "Primary chorioretinal aberrations with night blind-

ness," by the groups whose exhibit on the subject won the first prize previously mentioned, and the attractive discussion of it by Sir Stewart, who pointed out that, after listening to the papers, one can readily see that the biogenic stimulator treatment of retinitis pigmentosa is "no good"; and the thrilling and outstanding contribution of Albert B. Sabin of Cincinnati to the symposium on toxoplasmosis, appeared to excite the admiration and sustained applause of the members more than has ever been experienced before in any scientific session of the academy.

A feature, introduced at the last meeting, of beginning each session with a short clinicopathologic case report by an ophthalmic pathologist, is of such value and interest that it undoubtedly will become permanent. The case report by J. Clement McCulloch on the pathology of choroideremia was particularly worthy of attention. It disposes once and for all the controversy over whether or not atrophy of the choroid is actually present in this condition.

Among the remaining papers on the program, all of merit, that of Alan C. Woods on the "Use of antibiotics and sulfones in clinical ocular tuberculosis" was preëminent. One of our many guests from all over the world at the meeting, Dr. T. a'B. Travers of Melbourne, Australia, presented an important paper on the "Practical importance of abnormal retinal correspondence," and pointed out the value of operation in this condition as early as it can be recognized.

As is customary, motion pictures of ophthalmic surgery by various surgeons were interspersed here and there in the program and were excellently received.

The social aspects of the meetings likewise were a bit overwhelming. The event of primary interest was, of course, the banquet. It was so well attended that the members, their wives, and guests, overflowed onto the large balcony surrounding the ballroom, an unheard of proceeding. After the award of 14 honor keys, Sir Stewart spoke, at the top of his form, of the machinations of socialized medicine in Great Britain in such a way that even the discussion of this gloomy and unhappy subject could not dissipate the rosy aura of good fellowship and pleasure that surrounded the dinner party. At the conclusion of the dinner, Sir Stewart was awarded the plaque of the academy, signifying his honorary membership in the organization.

The hospital reunion dinners, all crowded, occupied the attention of the members, as is usual, on one of the evenings. A dinner for the exmedical officers stationed in the E.T.O. was obviously enjoyed and was graced by the presence of the erstwhile Brigadier Sir Stewart, a former comrade in arms to all of those present.

The smoker on another evening was so crowded that the floor space became smaller and smaller as new tables were added, thus increasing the pleasurable crowding together of the dancing couples. Before and after these and other events, one·kept himself busy scurrying about from one cocktail party to another, in a sort of academy pub crawl.

The incoming president of the academy is J. Mackenzie Brown of Los Angeles, California. The following officers were elected: 1st vice-president, Edwin B. Dunphy of Boston, Massachusetts; 2nd vice-president, Kenneth L. Craft of Indianapolis, Indiana; 3rd vice-president, James Mason Baird of Atlanta, Georgia. Derrick Vail of Chicago was chosen president elect.

Derrick Vail.

RECOMMENDATIONS FOR PROTECTION OF PATIENT IN CONTACT-LENS FITTING

Under the heading "The contact lens problem," Conrad Berens, secretary of the American Committee on Optics and Visual Physiology, has written an article published in the *Journal of the American Medical Association* (*140*: 602-603, June 18, 1949), in which he discusses the fitting of contact lenses and

the recommendations made by the Committee on Optics, primarily for the protection of patients who desire contact glasses or for whom contact glasses are thought by their refractionists to be desirable.

The idea of lenses that can be worn in contact with the eyeball and the under surfaces of the lids is an old one. Dr. Berens states that it was first suggested by Sir John F. W. Herschel, a British astronomer, in 1827, and that, in the latter part of the 19th century, wearable lenses were made for pathologic conditions. In recent years much more satisfactory contact lenses have been manufactured and new modifications are continually being brought forward.

The Committee on Optics and Visual Physiology sent a questionnaire to 2,000 certified specialists of the American Board of Ophthalmology, asking their experience with contact lenses. Of 413 replying who had had experience with contact lenses, 373 preferred the molded plastic technique. The consensus was that the fitting of contact lenses was not without danger to the patient and should be performed by, or under the direct supervision of, an ophthalmologist. Corneal abrasions and corneal ulcers have resulted from the fitting and at least one case of a lost eye has been recorded.

The commonest motivation for the purchase of contact lenses is undoubtedly vanity, particularly the desire of young women with high myopia to be able to see clearly without glasses. There are, however, occupations, such as acting, dancing, war-time flying, in which the usual glasses are a serious handicap and contact lenses may be of immeasurable help. Ophthalmologists will invariably state that the great field for contact glasses is that of keratoconus. Fortunately, however, these cases are rare. Human nature being what it is, vanity will continue to influence many and the demand for contact glasses will not only continue, but will increase.

Ophthalmologists consider the fitting of contact glasses, especially the molded type in which anesthetizing drops are necessary, to be a medical procedure. Therefore, the American Committee on Optics and Visual Physiology, after a careful study of the situation in this country, has made the following recommendations which have been endorsed by the four national societies having representatives on this committee:

1. National and local ophthalmologic societies should regulate the prescribing of contact lenses and the dissemination to the public of information regarding contact lenses.

2. The prescribing and/or the fitting of contact lenses by persons not properly licensed under state or national laws should be prohibited.

3. Medical opinion should be obtained in every case before contact lenses are prescribed.

4. Ophthalmologists should establish standards for approving the qualifications of technicians who wish to engage in fitting contact lenses.

5. Competent impartial research should be initiated toward the solution of unsolved problems concerning contact lenses. The main problem at the present time, provided that the fitting of the lenses is correct, is that of hazy or cloudy vision. Blurring of vision occurs inevitably after wearing a contact lens for some hours because of the altered metabolism of the cornea.

6. The public should be warned against those who advertise the superiority of their services or of any particular type of contact lenses. It should be pointed out that the public should not patronize such advertisers because competent professional practitioners do not resort to commercial advertising.

Some of these recommendations are deserving of special comment. Recommendation 1 would require legislative action. The mere fact that ophthalmologists may consider that the prescribing of these lenses and the dissemination to the public of information on this subject should be regulated by ophthalmological societies will not necessarily bring this about. These activities will surely

not be so confined if manufacturers and dispensers of optical goods who deal directly with the public are not legally disbarred from performing these functions. In this, as in most health matters, states are essentially autonomous and there are 48 of them so that it is always difficult to pass restricting legislation, particularly if strongly opposed. Such objection would be made especially by those who advocate and dispense contact glasses that can be fitted without anesthetics, such as small corneal discs or any other form that does not require molding.

Recommendation 2 implies that the prescribing and fitting of contact lenses should be treated as a specific activity and provides that only a well-defined group be permitted to perform this function. If new legislation were to be sought, this paragraph would have to be a part of it and would encounter opposition similar to that in Recommendation 1.

Recommendation 3 emphasized the ophthalmological opinion that fitting contact glasses is a medical problem, but does not specify that medical opinion must be obtained.

Recommendation 4 would place the certificating of technicians under the control of ophthalmologists, and put the burden of determining minimum standards for technicians on the doctors.

Recommendation 5 encourages further studies for improving contact glasses.

Recommendation 6 is an application of that part of Recommendation 1 referring to the dissemination to the public of information about contact lenses and their fitting.

In summary, the committee believes that control of the prescribing and fitting of contact glasses should be in the hands of physicians and that such laws as are necessary to accomplish this should be passed. This, as stated, is a large order, but suitable procedures should be initiated to bring these laws into being. This will require much effort on the part of many ophthalmologists.

It may be that most good will be accomplished by educating the public and utilizing to the full such existing laws as apply to this problem. New legislation, as pointed out, will surely be extremely difficult to pass and, if passed, to enforce. Existing laws generally prohibit the use of drugs by others than medical doctors. In the meantime, these laws should be strictly enforced. In the case of fitting contact glasses, it is not unusual for the technician to state that the physician has delegated to him or her the right to use drugs. No physician should ever assume such a power. He certainly does not have it legally and, since it is he that is legally responsible for any injury to his patient, he not only is acting illegally, but foolishly.

Generalizing further, these recommendations of the American Committee on Optics and Visual Physiology seem excellent suggestions for regulating the prescribing and fitting of contact glasses. If their intent is carefully followed, there should be a minimum of danger to the patient and there is a good possibility of continuing improvement in the construction of these lenses through well-directed research.

Lawrence T. Post.

ERRATUM

In our article in the AMERICAN JOURNAL OF OPHTHALMOLOGY, (32: 247, Part II, June, 1949), the first two columns of the Table 6 were incorrect (due to an error in the manuscript) and should read as follows:

Major Semiaxis (a in mm.)	Minor Semiaxis (b in mm.)
0.0346	0.00289
0.0316	0.00316
0.0283	0.00354
0.0224	0.00448
0.0173	0.00577
0.0141	0.00707
0.0130	0.00769
0.0100	0.0100

Only with these figures will the cross-sectional areas of the elliptical tubes be equal

while having largely different pressure drops.

(Signed) K. W. Ascher,
Cincinnati, Ohio.

CORRESPONDENCE

NATIONAL FOUNDATION
FOR EYE RESEARCH

Editor,
American Journal of Ophthalmology:

An organization known as the National Foundation for Eye Research,* founded in Washington, D.C., proposes to raise funds for ophthalmic research. This foundation hopes to encourage public support for medical research aimed at discovering the causes for ocular diseases leading to blindness and at developing more efficacious therapies.

The National Foundation for Eye Research will differ in its operation from many organizations designed to further medical research in that its funds will not be restricted to the study of any one disease but will be used to promote research in the whole field of ophthalmic diseases.

The activities of the foundation will be limited entirely to supporting and establishing research centers for ophthalmology in various localities, leaving other approaches to the prevention of blindness and rehabilitation of the blind to existing agencies.

The need for an expanded research program is apparent when one considers that there are about 260,000 blind persons in the United States with 20,000 new cases added annually, and that the existing funds, facilities, and personnel available for ophthalmic research are pitifully inadequate to study thoroughly the basic causes of the diseases which result in blindness. For instance, there is less than $400,000 spent annually in the United States on medical research primarily designed to decrease the number of blind— less than 1 percent of that used for rehabilitation of those who have already lost their sight. Moreover, there are only about a dozen

* Shoreham Building, Washington, D.C.

trained, full-time research men working in this field in the whole country, and few practicing ophthalmologists can devote a significant amount of time to research because of the restrictions of an active practice.

Mr. George Swartz, well known for his promotion of other medical philanthropies, has been selected as national chairman. With the assistance of a board of directors composed of prominent laymen, he will be responsible for the activities related to raising the necessary funds. The allocation of funds for research purposes will be made upon the advice of a scientific advisory board consisting of Dr. V. Everett Kinsey, chairman; Dr. Francis Heed Adler, Dr. Edwin B. Dunphy, Dr. Jonas Friedenwald, and Dr. Alan C. Woods.

It is hoped that ophthalmologists through their contact with the public will add their support to the group of laymen whose interest in expanding ophthalmic research has led to the formation of the National Foundation for Eye Research.

(Signed) Edwin B. Dunphy,
Boston, Massachusetts.

NATIONAL OPHTHALMOLOGICAL SOCIETY

Editor,
American Journal of Ophthalmology:

For some years past, Dr. Louis Bothman had been discussing the matter of the organization of a national ophthalmological society which would be truly representative of the ophthalmologists of the country.

There are other organizations in ophthalmology such as the Section on Ophthalmology in the A.M.A., and the Academy, which is eye, ear, nose, and throat, and the Association for Research. However, it would seem that a national ophthalmological society, in the same sense that such a professional and scientific organization exists in other fields, one that is truly representative of the best in ophthalmology, could materially help in raising the standards of ophthalmology in the teaching, clinical, and research fields.

It might be possible for such a society to undertake annual lectureships of outstanding quality as a regular part of its program, as well as the publication of an eye journal restricted purely to original contributions. Certainly there is room for such a publication in view of the length of time it takes for articles to be published at the present time.

As a personal friend of Dr. Bothman's for more than 20 years, I should like to help make his dream of such an organization become a reality.

(Signed) Samuel V. Abraham,
Los Angeles, California.

description of aniseikonia and of contact lenses.

As is characteristic of all of Sir Stewart's work, this book is written in an extremely clear and straightforward style. It is most difficult to find any fault with the factual material. Since there is a legitimate difference of opinion regarding the best method of refraction, especially as relates to the use of cycloplegics, many will not agree with the emphasis on the manifest refraction in young adults and early presbyopes but the views expressed are conservative and represent the practices in many offices and clinics.

William A. Mann.

BOOK REVIEWS

REFRACTIONS. By Sir Stewart Duke-Elder. St. Louis, The C. V. Mosby Company, 1949. Price, $6.25.

The fifth edition of Duke-Elder's well-known textbook on refraction retains all the features which have made it one of the most popular authorities in the field and, at the same time, presents new and enlarged sections that bring the entire work up to the most modern conceptions. The introductory chapter, dealing with the philosophy of the symptoms and treatment of eyestrain, is particularly commendable for its effort to evaluate the relation of symptoms to errors of refraction. It is rightly emphasized that many errors do not require correction but that, when they do, accuracy is essential.

The discussion of the principles of physiologic optics as applied to the eye is naturally much more brief than that contained in larger works or in Duke-Elder's monumental *Textbook of Ophthalmology* but it would seem quite adequate for the purpose. Recent views on the biologic determination of myopia are discussed and material on transient changes in refraction is presented. New or amplified passages deal with anomalies of convergence, the streak retinoscope, relanoskiascopy, the mechanism of accommodation, and the effectivity and equivalence of lenses. Particularly notable is the amplified

DIE KLINIK DER LABYRINTHITIS UND PARA-LABYRINTHITIS AUF GRUND DES RÖNT-GENBEFUNDES. By Prof. Dr. Med. Horst Wullstein. Stuttgart, Georg Thieme Verlag, 1948. Imported by Grune & Stratton, New York. 150 pages, 64 figures, bibliography. Price, $8.50.

Wullstein's monograph, a culmination of 10 years of work, presents a masterly study of the labyrinth in health and disease. The exquisitely clear skiagrams, with which it is profusely illustrated, are compared with anatomic sections and artistically clarified by accompanying sketches. This volume, which should prove invaluable to the roentgenologist, otologist, and others interested in this field, reflects the best traditions of German scholarship and publishing.

James E. Lebensohn.

DERMATOLOGIE FÜR AUGENÄRZTE. By Walter Schönfeld, M.D., Professor of Dermatology of the University of Heidelberg; Director of the University Clinic of Dermatology. Stuttgart, Georg Thieme Verlag, 1947. 104 pages, illustrations, 16 color plates, and index. Price, $7.25.

The volume is well organized, and the illustrations, particularly in color, are excellent. In a general introduction, some of

the principles of diatheses are outlined. There is a brief résumé of the technique of the patch and intracutaneous tests for allergic manifestations. The chapter dealing with treatment is rather incomplete since little but modifications of zinc and mercury preparations are enumerated.

Two main chapters are devoted to the discussion of individual forms of skin afflictions. The first deals with those of an infectious nature, and is subdivided into groups of unknown origin, parasites, and fungus and bacterial infections. The second chapter discusses dermatoses, avitaminoses, malformations, congenital diseases, and tumors. In closing, anomalies of the hair, the glands of the skin, and pigmentation are described.

It should not be expected in an outline of this scope that anatomic-pathologic details would be discussed at length. However, it is disappointing that ocular changes are only mentioned rather than described in any detail. For example, the conjunctival involvement in erythema exudativum multiforme is just listed as occurring in association with the general symptoms; no details are given. Equally unsatisfactory is the discussion of Boeck's sarcoid and tularemia; syphilis is all but omitted.

Because there is a close relationship between the two specialties, this little volume is worthwhile as a refresher course in dermatology for ophthalmologists. A treatise of this nature should represent a desirable addition to the literature, and it is to be regretted that Schönfeld has accomplished this only to a limited extent.

Stefan Van Wien.

TRANSACTIONS OF THE OPHTHALMOLOGICAL SOCIETY OF PARIS (and of the Ophthalmological Societies of the East, of Lyon, and of the West). August-September, 1948, pp. 405-529; October, 1948, pp. 532-694.

The session of June 13th was opened by a famous guest speaker, D. Cordier, who discussed the role of vitamins in the physiology of vision and in the metabolism of various structures of the eye. Van Canneyt and L. DeBaets made suggestions on the marking of the cylinder axis. P. L. Drouet and C. Thomas reported a detailed biochemic and etiologic study of Sjøgren's syndrome. J. Nordman's study on the treatment of strabismus dealt especially with the timing of surgery and a comparison of early surgery, as done in the United States, with late surgery, as favored in most European countries.

Cordier reported a case of acute glaucoma after intracapsular cataract extraction. Total iridectomy controlled the tension. E. Duhamel and Umbdenstock found a reacting pupil in a case of total blindness after embolism of the central retinal artery and discussed the function and location of the optic and pupillary fibers.

Thomas, Cordier, and Algan observed a patient with tuberous sclerosis who was simultaneously affected with band-shaped keratitis, a coincidence never before described.

At the meeting of June 21st, Beauvieux read an excellent pathologic and clinical review of glaucomatous cupping which emphasized the importance of vascular disturbances and ocular hypertension. A. Mercier achieved considerable local improvement in three cases of neuroparalytic keratitis with placental implants.

Le Jamtel read a paper on lymphoblastic sarcoma of the orbit and Offret and Hervoulet saw three patients with unusual pathologic changes at the posterior pole which simulated malignant lesions and which, after enucleation, proved to be inflammatory reactions.

In the October volume, P. Toulant and A. M. Larmande described the nervous and mental disturbances of sympathetic ophthalmia, probably encephalitic and meningitic in origin. The younger patients in this group had endocrine disturbances and the older

ones a hypercholesteremia. P. Bonnet suggested that a patient with the complications of sympathetic ophthalmia should not be deprived the benefit of surgery. In his hands, an intracapsular cataract extraction was successful.

A diagnosis of bilateral tuberculous tarsitis was made by Belz and verified by biopsy. Tarsectomy and diathermy coagulation were combined with calcium therapy. He also emphasized the value of Friedenwald's ophthalmoscope in the diagnosis of central serous chorioretinitis.

P. Bonnet saw a thrombosis of the central vein, which was formed by leukocytes and an unusual segmentation of white and red blood cells in the preretinal hemorrhage, in a severe case of leukemia.

L. Paufique described a new technique for the breaking of anterior synechias before completing keratoplasty. The place of trephination is outlined with a 6-mm. trephine, overlapping the anterior synechias by 2 mm. Sutures are applied at the edge of the disc and knotted so that they are in place for the traction to be applied later on. The cornea is only partly perforated by slightly inclining the trephine. The corneal flap is carefully raised with the traction sutures and the anterior synechia is removed with an iris hook and scissors. Of 8 operations of this kind, 5 were uneventful, 1 was complicated by a mild iritis, and 2 by an increase in tension.

Alice R. Deutsch.

SITZUNGSBERICHTE DER WIENER OPHTHALMOLOGISCHEN GESELLSCHAFT. By Dr. H. Fanta. Wien, Urban & Schwarzenberg, 1947.

The proceedings of the Vienna Ophthalmological Society cover in 98 pages the 23 meetings held between January 19, 1942, and February 26, 1945. A wide range of diseases, operations, and pathologic conditions of the eye are discussed. Many of the ideas expressed are widely known now and there is very little material relating to the war. An index by subjects and authors makes any comment easily found.

J. Böck, H. Fanta, K. Heinz, J. Meller, K. Lindner, A. Pillat, and R. Rössler are prominent among the contributors.

GAIL SOPER.

IL TRACHOMA. By Giambattista Bietti. Rome, 1947. 142 pages.

In this monograph, which was contributed as part of a program financed by U.N.R.R.A. to combat social diseases, Professor Bietti systematically considers the various aspects of the trachoma problem. He presents its history, discusses etiology and epidemiology, and adequately describes the manifestations of the diseases in the various tissues that are involved, the complications, pathology, diagnosis, prognosis, prophylaxis, and treatment.

F. H. Haessler.

ABSTRACT DEPARTMENT

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1
ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Cooper S., and Daniel, P. M. **Muscle spindles in human extrinsic eye muscles.** Brain 72:1-24, Jan., 1949.

With the demonstration of neuromuscular spindles in human extraocular muscles the authors have completed the chain of evidence that establishes an anatomical basis for proprioception in ocular motility. The orbital contents were removed soon after death in 60 individuals ranging in age from 82 years to newborn. The individual extrinsic eye muscles were dissected out, pinned on cork, and fixed in 10-percent formol-saline. The muscle spindle consisted typically of a group of fine cross-striated muscle fibers with a rich nerve supply in a thin torpedo-shaped capsule of fibrous tissue. The appearance is reminiscent of human fetal muscle spindles and suggests that the human eye muscle spindle may be a rather primitive form of this neuromuscular organ. The muscle spindles were found in the proximal third and at the proximal end of the distal third of the muscles, but not in the belly. The largest number of muscle spindles were in the inferior rectus. Muscle spindles have also been found in the extrinsic eye muscles of the chimpanzee, in certain ungulates (goat, deer), but not in the macaque monkey, dog, cat, or rabbit. James E. Lebensohn.

Harms, J. W. **Transplantation of regenerative tissue into the anterior chamber.** Klin. Monatsbl. f. Augenh. 114:298-308, 1949.

Autoplastic experimental transplants of young regenerative tissue from the tail or an extremity of Triton alpestris into the anterior chamber led to a dissolution of the lens and, in some cases, of the retina. After resorption of the implant a new lens was formed from the upper border of the iris. Experiments with tadpoles raised in thiourea showed inhibition of the organs of internal secretion with a disturbed development of the eyes such as exophthalmus, smaller bulbi, and reduction in the number of rods and cones. Max Hirschfelder.

Moerike, K. **Comparative functional examination concerning the special thickness of the choroid in the macular region of the eye.** Klin. Monatsbl. f. Augenh. 114:308-319, 1949.

The choroid has greater thickness in the macular region. This is shown by the author's measurements on slides from human eyes. In birds with formation of two maculas in one eye like the tern, a particularly well developed stretch of choroid is found under each macula. The metabolism of the rods and cones in these regions requires a greater blood supply and the greater thickness of the underlying choroid corresponds to this requirement..(References.) Max Hirschfelder.

2
GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Bailliart, J. P. **The pathologic physiology of the corneal endothelium.** Ann. d'ocul. 182:509-513, July, 1949.

Corneal endothelial cells are capable of being transformed into macrophages in the aqueous humor. In the cellular examination of the aqueous large cells of approximately 50 μ. are not infrequent, with nuclei of 20 μ. and granules of 5 to 7 μ.. These cells frequently contain hematinic debris, leucocytes, iris pigment or even bacteria. The author has shown that these cells are directly derived from the corneal endothelium and considers that their phagocytic qualities are associated with senescence and inflammatory reactions.   Chas. A. Bahn.

Cogan, D. G. **Vascularization of the cornea. Its experimental induction by small lesions and a new theory of its pathogenesis.** Tr. Am. Ophth. Soc. 46: 457-471, 1948.

After small experimental lesions in the cornea of the rabbit a sequence of events leading to new bloodvessel formation occurred with remarkable regularity. After a latent period the proximal vessels, chiefly the venules and capillaries, became engorged and saccular aneurisms developed. These aneurisms burst, caused

hemorrhage into the corneal stroma and became deflated. The hemorrhagic area then became riddled with new capillaries, most of which receded in a few days, leaving loops directed toward the lesion.

Interstitial vascularization of the cornea occurs when compactness of the cornea is reduced in the region of pre-existing vessels.   David O. Harrington.

Fazakas, S. **The role of Penicillium species in fungus and bacterium cultures.** Szemészet 2:69-73, 1949.

Since 1931, the author continuously examined the fungus flora of eyes. One third of the fungi found were Penicillium species. In mixed cultures consisting of Penicillium and another species such as fission fungi, Aspergilli, Periconia keratitidis, Microsporon felineum, and Trichophyton, it was mainly the Penicillium that inhibited bacterial growth. In the mixed cultures containing Penicillium and Actinomyces the inhibiting effect was nearly equal. Many cases of symbiosis and neutrality also were observed between Penicillium and other fungi or bacteria.
                     Gyula Lugossy.

Letterer, Erich. **Ophthalmology from the viewpoint of general and experimental pathology.** Klin. Monatsbl. f. Augenh. 114:289-298, 1949.

The many and varied problems of general pathology which are illustrated by clinical or experimental findings in the eye are reviewed. Phenomena of normal and disturbed circulation can be observed at the limbus, and hemodynamic disturbances during experimental collapse in the retina. In angiospastic retinopathy, dystrophic cell damage is the result of disturbed circulation with deposit of fat and lipoids in the tissues. Storage of lipoids and phosphatids in cells is a characteristic finding in Tay-Sachs and Nieman-Pick disease. Deposit of amyloid in the ocular

tissues is rare. The avascularity of the cornea is the basis for a particular course in inflammatory processes. Hyperergic inflammatory reaction and elective sensitizing of tissues are demonstrated in interstitial keratitis as well as in sympathetic ophthalmia.   Max Hirschfelder.

Marchesani, O. **The problem of the endogenous inflammations of the eye.** Arch. f. Ophth. 149:69-94, 1949.

The frequency of keratoconjunctivitis eczematosa, endogenous uveitis and periphlebitis retinae are studied with respect to age and sex of patients afflicted with one or the other of these conditions. Keratoconjunctivitis eczematosa occurs most often in children under five years of age. Endogenous uveitis and periphlebitis retinae reach their maximums for people between 20 and 25 years of age. The keratoconjunctivitis is correlated to the so-called exudative lymphatic diathesis. Foci of lymphatic disease, especially of the glands of Waldeyer's ring of the throat, irritate the vegetative nerves of the cornea and conjunctiva and make these tissues vulnerable. A special type of endogenous uveitis is found in women during the menopause. Acute uveitis is more often seen in men, chronic uveitis somewhat more often in women. Periphlebitis prevails in young men and seems often to be combined with disturbances of the endocrine glands.   Ernst Schmerl.

Meves, H. **The elastic structure of the ocular bloodvessels.** Arch. f. Ophth. 149: 275-281, 1949.

This is a second contribution dealing with this problem. Twelve retinal gliomas were studied. In the majority of the vessels the elastica was lost. The main branches of the arteries of the glioma were often found dilated and hyperplastic. The hyperplastic parts of the bloodvessels of retinal origin showed the structural

peculiarities described before. In 8 to 12 choroidal sarcomas an elastica was present.   Ernst Schmerl.

3
VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Auricchio, G. **Permeability of the lenscapsule for glucose after paracentesis.** Boll. d'ocul. 28:161-168, March, 1949.

Rabbits' eyes were punctured three times at 48-hour intervals; 18 hours after the last paracentesis the animals were exsanguinated and the lenses examined. Some of the lenses were immersed in a 0.5-percent solution of glucose in 0.85-percent sodium chloride solution at 38°C. for two hours, before the glucose content of the lens was determined. The glucose content ascertained minus the glucose content of a lens just removed plus the glucose metabolized by a rabbit lens at 38°C. was assumed to equal the amount of glucose which passed through the lens capsule in the two hours. The other intact lenses were dialyzed against physiologic salt solution for two hours at 38°C.; the glucose content of the originally sugar-free salt solution was used as a measure of the permeability of the lens capsule. The left eyes of the rabbits were not punctured and their lenses served as control material. For determination of the glucose content the Weekers modification of Dumazert's technic was used. In four tables, 16 experiments are described; the calculations resulted in evidence of a decrease of permeability of the lens capsule after repeated paracentesis. (References.)   K. W. Ascher.

Duke-Elder, S., Davson, H., and Woodin, A. M. **Studies on the intraocular fluids.** Brit. J. Ophth. 33:452-454, July, 1949.

This is the third of a series of studies

injection of histomine. Vitamin B_2 (nicotinic acid) causes only a slight increase in ciliary permeability.   Vito La Rocca.

Swan, K. C. **Ocular effects of the choline esters.** Tr. Am. Ophth. Soc. 46:651-672, 1948.

A decade of experience in the ocular effects of the choline derivatives is reviewed. It is not possible as yet to evaluate the influence of these drugs on the intraocular vascular system but their effects on the muscles of the iris and ciliary body and upon intraocular pressure seem fairly well established. The question of corneal penetration and pharmacologic action of the choline esters is discussed with particular reference to their effect on intraocular pressure. The mydriatic cycloplegic action of Dibutoline and its range of clinical usefulness are discussed.
                    David O. Harrington.

4
PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Berens, Conrad. **The contact lens problem.** J.A.M.A. 140:602, June 18, 1949.

Considerable progress in the manufacturing and fitting of contact lenses has taken place in recent years. Nevertheless most patients can tolerate wearing the lenses for a limited time only because the solution used between the contact lens and cornea is unsatisfactory.

The American Committee on Optics and Visual Physiology recommends that the prescribing and fitting of contact lenses be restricted to properly licensed persons, that ophthalmologists establish a standard for approving the fitness of technicians, and that impartial research be initiated toward the solution of unsolved problems.   R. Grunfeld.

van Beuningen, E. G. A. **Experimental observations concerning the sensitization** of eye and ear during measurements of adaptation phenomena. Arch. f. Ophth. 149:230-239, 1949.

When the dark adaptation of several test persons was interrupted by short light stimuli, the readaptation increased in speed and intensity. Corresponding effects were observed in experiments in which the adaptation of the ear was studied. The author assumes that during the increased sensitiveness of the eye retinoneural functions prevail over photochemical processes.   Ernst Schmerl.

Cibis, P., and Huck, H. **Studies of the central color sense in normal and congenital colorblind people using stimuli of definite size and duration.** Arch. f. Ophth. 149:176-198, 1949.

The distances were determined at which the colors of small test objects on a neutral gray background were just recognized. The time was measured during which the perception of these stimuli faded. Large numbers of normal persons recognized the color of 1 by 16 mm. red and yellow objects and 1.4 by 16 mm. green and blue objects at distances of 3 m. or more. Where shorter distances were needed the color sense was doubtful or definitely pathologic. Normal persons also perceived the yellow color of test objects 5 by 5 mm. in size for a period of 2 minutes and at distances of 2 m. or more, whereas in pathologic cases the color was perceived at 1.2 m. distances or less.   Ernst Schmerl.

Cross, A. G. **Contact lenses.** Brit. J. Ophth. 33:421-445, July, 1949.

An analysis of the answers to a long, inclusive questionnaire sent to 1,850 patients who sent in 875 replies is presented. The results are most significant to all interested in the fitting and the problems of contact lenses. The most important aspect of the problem is the question of

tolerance to wear. Of those who replied to the questionnaire, one third have given up the wearing of their lenses which fact, in the light of the expense and time involved, emphasizes the great responsibility upon the fitter. The number of failures is considerably less among patients with a pathologic condition. Satisfactory fitting is still the major problem, and tolerance will increase with improvements in method.   Morris Kaplan.

Durham, D. G. **Plastic lenses in industry.** Tr. Am. Acad. Ophth. pp. 680-682, July-Aug., 1949.

The advantages of plastic lenses in industry include greater resistance to pitting from sparks of different sorts, more resistance to fogging, lightness, and greater protection. (3 figures.)

Chas. A. Bahn.

Irvine, S. R. **Amblyopia ex anopsia. Observations on retinal inhibitions, scotoma, projection, light difference discrimination and visual acuity.** Tr. Am. Ophth. Soc. 46:527-575, 1948.

This exhaustive monograph on the subject of amblyopia ex anopsia should be read in its entirety. Patients with non-paralytic strabismus fail to note apparent displacement of a fixated light during the cover test because the percipient elements of the retina that are involved because of the angle of squint have the same directional value as the macula of the fixing eye. This observation suggests that if, while one eye is fixating, prisms of varying strengths are moved before the deviating eye to displace the image less than the angle of squint, the image would not be seen or would be falsely projected. Moving prisms before an eye might be used to study projection, inhibition and scotoma in strabismus and amblyopia. Amblyopia based on organic lesions might be differentiated from amblyopia ex anopsia if

retinal inhibition and projection were more altered in amblyopia ex anopsia. The prism displacement test proved valuable in the study of retinal inhibition and projection in strabismus and amblyopia. Numerous cases were analysed singly and in groups and an attempt was made to ascertain criteria helpful in prognosticating return of vision in the amblyopic eye of an adult after loss of the other eye.

David O. Harrington

Ludvigh, E. J. **Visual acuity while one is viewing a moving object.** Arch. Ophth. 42:14-22, July, 1949.

Foveal visual acuity while one is viewing a moving object has received curiously little attention. The only reference to this subject is a note by Langmuir, who, in an effort to estimate the speed of a deer botfly, whirled above his head a piece of solder fastened to a string and noted at what speed the piece of solder appeared blurred. In view of the absence of any information, this subject was investigated.

Visual acuity was determined while the test object viewed appeared to move circularly in a plane perpendicular to the line of sight. The diameter of the circle and the velocity of the test object were varied. It is shown that when the eye is following such a moving object, acuity is reduced by reason either of the inability of the eye to move sufficiently rapidly or of the inability of the subject to adjust the relative innervation to the various ocular muscles sufficiently rapidly, or of both. It is shown that in following a moving object the extrafoveal position of the image is a negligible factor in producing the observed reduction of acuity. It is probable that imperfect pursuit movements, although maintaining the image in the immediate vicinity of the fovea, nevertheless result in a motion of the image on the retina which reduces visual acuity because the retina has less inten-

sity contrast. The hypothesis is confirmed by showing that increased illumination of the moving test object increases visual acuity. Ralph W. Danielson.

McDonald, P. R. **Evaluation of night vision.** Tr. Am. Ophth. Soc. 46:576-607, 1948.

In the experiments reported the tenfold variation in the final rod threshold of healthy young adults confirms the findings of other investigators. Two different night vision tests employed have shown good reproducibility. It has also been shown that the visual threshold in normal persons is not improved with large doses of vitamin A. Given a good instrument and an interested examiner, a test of night vision becomes an important diagnostic aid as well as a means of demonstrating the important aspects of scotopic vision. David O. Harrington.

Pacalin, G. **Physiologic diplopia in depth perception.** Ann. d'ocul. 182:617-635, Aug., 1949.

Depth perception fundamentally involves the mobility of accommodation and convergence as well as the coordination of binocular muscle balance, visual acuity and memory. Slight physiologic diplopia favors the perception of depth. Objects viewed at a closer distance than the fixation point cause crossed diplopia, and objects viewed at a greater distance than the fixation point cause homonymous diplopia. Two groups of figures are presented to illustrate that slight variations of accommodation and convergence change the apparent relative distances of objects from each other. These figures consist essentially of two larger circles with smaller eccentric circles arranged at less than the interpupillary distance. The cube of Necker is also employed to illustrate that the impression of a third dimension on the printed page is an optical illusion.

The impression is produced through perspective and memory interpretation. The author believes that these fundamentals are important in the phorias and tropias. In the former, the process is reversible. Chas. A. Bahn.

Sauter, H. **A modification of telescopic spectacles by the use of contact glasses.** Arch. f. Ophth. 149:142-155, 1949.

Contact lenses serve as oculars of these optical systems. The author considers magnification, size of the visual field and brightness of the image. Reference is made to a similar study by Bettman and McNair (Am. J. Ophth. 22:27, 1939). Ernst Schmerl.

Thomson, L. C. **Photopic luminosity curve and visual purple.** Brit. J. Ophth. 33:505-508, Aug., 1949.

The author reports his investigation of the photopic luminosity curve. The contribution of the color-perceiving mechanism to the sensitivity of the light-adapted eye is represented. Maximum sensitivity is found in the spectral regions in which modulator activity is most marked. An attempt can be made to separate the activity of the brightness mechanism from that of the color-perceiving mechanisms in the human eye. Orwyn H. Ellis.

5
DIAGNOSIS AND THERAPY

Dansey-Browning, C. **On the use of amniotic membrane.** Brit. J. Ophth. 33:-518-520, Aug., 1949.

Amniotic membrane was used to replace a defect left by the excision of a large benign melanoma of the conjunctiva. The eye healed rapidly and almost without reaction. Orwyn H. Ellis.

Eröss, S. **Therapy of scleritis.** Szemészet 2:74-76, 1949.

The etiology of scleritis is not uniform.

However, signs of oversensitivity can be found in all patterns. Therefore, the capacity of the organism to react should be transformed lest the process prove resistant to causal therapy. To this end, the author applied a specific stimulant therapy. Changes in the blood count and the sedimentation rate showed that paragen produced an adequate transformation of reactive capacity. Gyula Lugossy.

Guyton, J. S. Enucleation and allied procedures. A review and description of a new operation. Tr. Am. Ophth. Soc. 46: 472-527, 1948.

The history and technic of extirpation, enucleation and evisceration of the eyeball with or without implants is thoroughly reviewed. Ruedemann's introduction of semiburied plastic eye implants and Cutler's use of a separate attachable prosthetic section initiated technics which usually result in normal appearance and motility of artificial eyes. Infection, extrusion, or reduced motility with the semiburied implants may be potential late complications. A procedure involving the use of an exoplant with which there is no contact of inert material with any tissue except epithelium introduces a new principle which may reduce late complications. David O. Harrington.

Harms, H. Fundamentals, methods and meaning of pupillary perimetry for the physiology and pathology of the visual organ. Arch. f. Ophth. 149:1-68, 1949.

A complete study of the functions of a retinal area requires the determination of its light sense, its visual acuity, its color sense and its pupillomotor excitability. The present study compares perimetrically and under definite conditions light sense and pupillomotor excitability of the various retinal areas. A special instrument and threshold stimuli are used. The blind spot can be demonstrated by pupil-

lary perimetry. Marked differences of pupillomotor excitability in normal persons are noticed. With dark adaptation the light sense shows a central scotoma while the pupillomotor excitability of the central fovea is at its maximum. Homonymous defects of the visual fields are paralleled by pupillomotor disturbances. Changes of the pupillomotor excitability are also found with foci proximally to the lateral geniculate bodies.

Ernst Schmerl.

Koch, H. Contribution to the treatment of psychogenic amauroses. Arch. f. Ophth. 149:282-287, 1949.

In 9 cases of psychogenic amaurosis, electro-shock treatment or nitrous oxide narcosis was followed by definite improvement, Ernst Schmerl.

MacLean, A. L. Surgical procedures in retinal vascular disease. Tr. Am. Ophth. Soc. 46:348-366, 1948.

Perforating scleral diathery with aspiration of the subretinal fluid is a safe and effective procedure in the treatment of serous retinal detachment complicating diabetic retinopathy. A glass applicator with broad concave tip is used and controlled negative pressure is supplied by an electric suction pump. The procedure is safe if the scleral opening is not too large or if the retinal opening has been sealed off by previous diathermy treatment. Cervical sympathectomy was used effectively in the treatment in one case of bilateral occlusion of the central retinal artery. David O. Harrington.

Schuessler, W. W., and Steffanoff, D. N. Dermal grafts for correction of facial defects. (A series of 80 cases.) Plastic and Reconstr. Surg. 4:341-351, July, 1949.

Dermal grafts, free of subcutaneous fat, are used in various areas of the body for "fill-in material." Absorption of the der-

mal grafts show a decrease from the original volume of approximately 15 percent. A short history of the use of dermal grafts is given. This material should be used wherever there is a deficiency in the contour of the face, nose or forehead with normal skin to overlie it and a good vascular bed beneath it. It should not be used where firm structure is required, such as for protection of the brain tissue. It has the advantage over the cartilaginous graft of being soft and pliable, abundant and easy to remove and insert in the recipient area, and it seems much better than free fat-fascia graft. Various methods of obtaining dermal grafts are mentioned, and the author recommends the split-split method, introduced by Zintel. A full-thickness graft is removed with the dermatome, the dermatome reset and the desired thickness of epidermis recut on the dermatome. Sometimes the derma is inserted as a strip, or it may be cut in sections and packed up in the form of a pyramid. In 80 cases complications were present in 7.5 percent, of these 1.2 percent were due to infection, and 1.25 percent to cyst formation. Nine photographs and one drawing show this material used for repair of the atrophy of the retrotarsal fold after enucleation, for the adherent scars which form after severe trauma to the infraorbital rim, and for other regions of the face and nose.

Alston Callahan.

6
OCULAR MOTILITY

McLean, J. M. **Direct surgery of paretic oblique muscles.** Arch. Ophth. 42:50-65, July, 1949.

The author discusses seven years' experience with direct surgery of the underacting superior oblique muscle and of the weak inferior oblique muscle. There appears to be no way by which to judge

the amount of surgical correction required better than that of adjusting the tension according to the surgeon's sense of touch. The reasons for direct operative procedures to strengthen a weak oblique muscle are cited. Technics for tucking a paretic superior oblique and advancing a paretic inferior oblique muscle are described. Illustrative cases are reported. The methods of judging the amount of operation to be performed are discussed.

Ralph W. Danielson.

Murray, W. B. **A review of trachoma.** Canad. M.A.J. 60:574-580, June, 1949.

The author gives a comprehensive review of the history, etiology, differential diagnosis, pathology and treatment of trachoma and stresses the fact that early diagnosis is important for the prevention of the spread of this mildly contagious disease. The modern treatment of trachoma is efficient. The incidence of trachoma among the Indians has been reduced from 26 to 3 percent within four years after the introduction of the new treatment by the U.S. Indian Service

R. Grunfeld.

Rubino, A., and Bassi, I. **Concomitant squint and status dysraphicus.** Giorn. ital. oftal. 1:404-417, Sept.-Oct., 1948.

In a large number of patients with strabismus, the authors found a facial asymmetry very frequently. In the belief that facial asymmetry is a sign of status dysraphicus, they looked for other signs of this anomaly and found them in a large number of cases.

Vito La Rocca.

Scobee, G. **Intermittent exotropia.** Tr. Am. Acad. Ophth. pp. 658-673, July-Aug., 1949.

Anatomic abnormalities are the major factor in its causation. Complete cure is

usually possible surgically. Variations depend on mechanical obstacles to convergence, voluntary and involuntary convergence, and the strength of the fusion mechanism. Abnormalities of the intermuscular membranes, check ligaments, foot plate and other anomalies of insertion are the principal anatomic conditions involved. Exotropia is frequently greater at 20 feet than at 13 inches, unless occlusion or voluntary convergence relaxation is employed. The convergence near point is often practically normal. Generally speaking, intermittent exotropia or exophoria of 18 degrees or more can be cured only surgically. The author advocates bilateral external rectus recession performed at one time. Phorias require as much surgical correction as tropias. In the treatment of nonsurgical cases the pin-to-nose convergence exercise may decide the justification of further orthoptic training. Twenty-five cases, in 11 of which there were vertical deviations, are reported and analyzed.   Chas. A. Bahn.

Stanworth, A. **The final results of squint operations in which restoration of binocular single vision was not expected.** Brit. J. Ophth. 33:477-484, Aug., 1949.

The author presents a detailed study of the final binocular coordination in a group of patients in whom binocular single vision was not expected. In all it was concluded before surgery that orthoptic training would be unsuccessful, or it was tried and abandoned. The results showed that of the 26 percent that improved, 20 percent developed stereoscopic vision. Of the patients without binocular vision, 9 percent improved and of these 7 percent developed stereoscopic vision. Of those with simultaneous macular perception, 17 percent improved and 13 percent developed stereoscopic vision. The data suggest that if fusion will result it will

do so within 12 months after operation. Patients with vision approximately equal in the two eyes tend to develop stereoscopic vision more readily than those with unequal vision. The size of the angle of deviation before operation appeared to be of little significance. An early onset of the squint usually precludes the attainment of good binocular vision. The alternating type has less chance of improvement than the unilateral type. There was apparently no optimum relationship of age to the time of operation. The postoperative angle of squint was most important. Of the patients with simultaneous perception and a deviation of five degrees or less after operation, 49 percent developed fusion, whereas only 11 percent of those with more than five degrees of deviation developed fusion. When there was no binocular vision but the deviation was less than five degrees, 22 percent of the patients developed stereoscopic vision and when the deviation was greater, only 4 percent developed fusion.   Orwyn H. Ellis.

Wright, E. S. **Extraocular muscle paralysis from spinal injection of pantopaque.** California Med. 71:214-215, Sept., 1949.

A case report of external rectus muscle paralysis which developed five days after the spinal injection of pantopaque is presented. Three months later spontaneous recovery occurred with normal motility.   Orwyn H. Ellis.

7

CONJUNCTIVA, CORNEA, SCLERA

Bietti, G. **Antibiotic therapy of virus diseases of the eye.** Ophthalmologica 118:101-114, Aug., 1949.

Bietti and his associates have found penicillin, streptomycin and tyrothricin to be ineffective in keratitis due to herpes simplex and in epidemic keratoconjuncti-

vitis. In trachoma, however, the author reports definite, favorable response to frequent local applications of penicillin in concentrated aqueous solutions or ointments. Within a few days the secondary bacterial invaders as well as the inclusion and initial bodies disappear and the clinical picture improves correspondingly. The deeper tissue changes due to trachoma respond better to sulfonamides than to penicillin. Streptomycin and tyrothricin are ineffective in trachoma. The author considers the inclusion and initial bodies as the visible, corpuscular form of the virus. In contradistinction to its definite effect upon the trachoma virus penicillin does not alter the course of inclusion conjunctivitis. In one case of the latter disease the author observed rapid recovery under local streptomycin treatment. An extensive review of the literature is included.   Peter C. Kronfeld.

Boase, A. J. **Eyelash in the lacrimal punctum.** Brit. J. Ophth. 33:513, Aug., 1949.

A patient presented himself for treatment of an irritated right eye in 1944, and again for treatment of an irritated left eye in 1949. Each time there was an eyelash in the punctum and the root end protruded. Ulcer and granulation developed in the conjuntiva whereas keratinization is the expected change. Perhaps the rough root of the lash is more dangerous.
                                    Orwyn H. Ellis.

Buecklers, M. **A new familiar type of corneal dystrophy.** Klin. Monatsbl. f. Augenh. 114:386-397, 1949.

A complicated type of corneal dystrophy is described. The first signs appear during the childhood. There are severe defects of the epithelium with attacks of pain and inflammatory symptoms. The attacks stop after puberty and begin anew

two decades later. At times there are corneal opacities without pain. The dystrophy involves the epithelium and, especially, Bowman's membrane. The mode of inheritance seems to be dominant. (1 family tree, 10 figures, references.)
                                    Max Hirschfelder.

Cass, E. E. **Interstitial keratitis occuring in a case of Reiter's disease.** Brit. J. Ophth. 33:454-455, July, 1949.

A case of Reiter's disease in a young man who also had severe interstitial keratitis combined with keratitis profunda and iritis in both eyes is reported. The disease progressed in severity despite all treatment and vision was reduced to the counting of fingers.   Morris Kaplan.

Cima, V. **Explanation of unusual reactions after transplantation of cadaver conjunctiva.** Boll. d'ocul. 28:155-160, March, 1949.

Conjunctiva from the cadaver was first used for transplantation by Rosenzweig in 1939. In the Sassari and Pavia Eye Clinics, Bietti used this method repeatedly, preserving the cadaver conjunctiva for as short a time as possible in Ringer's solution with 5,000 units of penicillin per cc. The results were satisfactory but not better than autotransplantation of mucous membrane. In two cases of severe recurrent pterygium, however, marked reactions were observed and ascribed to tissue immunity reactions. (References.)
                                    K. W. Ascher.

Cogan, D. G. **Nonsyphilitic interstitial keratitis with vestibuloauditory symptoms.** Arch. Ophth. 42:42-49, July, 1949.

Four additional cases of the previously-described syndrome of nonsyphilitic interstitial keratitis with vestibuloauditory symptoms are reported. The interstitial keratitis was bilateral in three of the new

cases and unilateral in one. It was characterized by patchy, granular infiltrates in the deep stroma, which varied from day to day, unaccompanied by any conspicuous intraocular reaction. The vestibuloauditory symptoms were similar to those occurring in Ménière's disease and were followed by pratically complete deafness in three of the patients. The ocular and vestibuloauditory symptoms appeared within a few days in three patients but were separated by a five month interval in one. Again all four patients were young adults, all had a leukocytosis, and one a significant eosinophilia.

Ralph W. Danielson.

Coppez, L. **Partial lamellar keratoplasty.** Ann. d'ocul. 182:597-604, Aug., 1949.

This type of operation should be more extensively used because it affords better vision in eyes not adapted to total keratoplasty. Among its advantages are more rapid recovery and better nutrition of the graft, as well as its simple technique and the infrequency of surgical complications. The author reports nine cases in detail with illustrations which show the regularity of the reflecting surface of the cornea after operation. The Franceschetti technique is used. Chas. A. Bahn.

Corrado, A., and Toselli, C. **Hereditary luetic parenchymatous keratitis.** Rassegna ital. d'ottal. 18:97-111, March-April, 1949.

Eighty percent or more of luetic keratitis was found to be hereditary. Trauma was an unimportant cause in the development of the lesion. The authors studied 106 cases of the disease and have tabulated many data. Sixty-seven percent of the cases developed the keratitis under 20 years of age and 66 percent of all patients were females. The serologic tests were positive in all but four cases. Complications, such as posterior synechiae, dense corneal opacities and irregular astigmatism were more frequent when the disease appeared first in later life.

Eugene M. Blake.

Das Gupta, B. K., and Usman, M. **Bilateral symmetrical tuberculous ulcers of the bulbar conjunctiva treated with streptomycin.** Brit. J. Ophth. 33:501-505, Aug., 1949.

Bilateral tuberculous ulcer of the bulbar conjunctiva did not respond to ordinary therapy but healed promptly when streptomycin drops of high concentration were used. Acid-fast bacilli were found in the scrapings. (4 figures in color.) Orwyn H. Ellis.

ten Doesschate, J., and Fischer, F. P. **Some statistical observations on the frequency of occurrence of pterygium and pinguecula in relation to age.** Ophthalmologica 118:137-142, Aug., 1949.

The incidence of pinguecula as a function of age is expressed by an S-shaped curve which rises very slowly up to the age of 15 years. There the curve makes a sharp bend and starts to rise steeply up to the age of 50 years, where it begins to taper off. Plotted on log-log paper the incidence of pinguecula becomes a linear function of the subject's age. The incidence of pterygium follows a similar pattern but all frequencies are considerably lower than those of pinguecula. The hypothesis is offered that the persons liable to develop pterygium form a distinct group of the population. In this group also, the relationship of the incidence of the disease to age is expressed by a similar S-shaped curve.

Peter C. Kronfeld.

Drescher, E. P., and Henderson, J. W.

Senile hyaline scleral plaques. Proc. Stf. Mtgs. Mayo Clin. 24 :334-336, June 8, 1949.

Three cases of senile hyaline plaques are reported from the Mayo Clinic to clarify the diagnosis of this condition. The usual location, the clinical appearance, and the pathology are described.

Donald T. Hughson.

McGavic, J. S. Surgical treatment of recurrent pterygia. Tr. Am. Ophth. Soc. 46 :608-632, 1948.

An operative technic is described for the eradication of severe recurrent pterigium. The results were good in a series of 38 cases in which other procedures had failed to prevent recurrences. The procedure consists of lamellar peratectomy, submucous resection of all scar tissue, recession of the conjunctiva by suturing it to the sclera proper at least 5 mm. from the corneoscleral junction and allowing the denuded cornea and sclera to become epithelized. Beta radiation is used postoperatively when necessary to control vascularization. The technique is also suitable for pseudopterigia, epibulbar tumors, repair of symblepharon and removal of superficially vascularized scars. The literature is reviewed. (References.)

David Harrington.

Rosen, E. The importance of the cornea in virus diseases. Ophthalmologica 118: 81-101, Aug., 1949.

The pathogenesis of corneal lesions in systemic virus infections is discussed in the light of the newer concepts concerning the antigen-antibody relationships in such diseases. Typical clinical cases are reported to illustrate the author's views. The difference in response between the avascular center and highly vascular periphery of the cornea is stressed.

Peter C. Kronfeld.

Rubino, A., and Simonelli, M. Thymus radiation for the treatment of vernal catarrh. Giorn. ital. oftal. 1 :453-455, Sept.- Oct., 1948.

The thymus was irradiated with X rays in 15 patients, 8 to 20 years of age, with vernal catarrh, without any noticeable improvement. The findings are in contrast with those of Stanhope, who believed that the hypertrophy of the thymus was a fundamental element in pathogenesis of vernal catarrh.

Vito La Rocca.

Taussig, J. Epithelioma of the cornea following a cement burn. South African M. J. 23 :383-384, May 14, 1949.

A 35-year-old man injured his left eye with particles of cement. A slight burn of the bulbar conjunctiva and tarsus of the left eye ensued. Two years later a small tumor developed at the limbus and spread toward the pupil. The adjacent conjunctiva was injected in pterygium-like fashion and scattered through it were discrete, pinhead-sized, wart-like tumors. Two fragments of tissue were removed. One fragment consisted of simple pigmented squamous papilloma overlying a single mucous gland, the other showed squamous carcinoma.

R. Grunfeld.

Vannini, Angelo. The treatment of conjunctivitis due to Morax-Axenfeld diplobacillus. Rassegna ital. d'ottal. 18 :131-134, March-April, 1949.

In an attempt to determine whether any other medication was equal to or superior to zinc sulfate in the treatment of diplobacillary conjunctivitis Vannini administered sulfonamides, penicillin and streptomycin. While the average time of disappearance of the bacilli was 8 to 10 days with zinc, it was reduced to four days using 30-percent sulfacetamide drops every two hours. Penicillin and streptomycin were wholly ineffective.

Eugene M. Blake.

Venco, Luigi. **Disturbances at the limbus in keratoplasty.** Rassegna ital. d'ottal. 18:65-80, March-April, 1949.

The term "diseases of the limbus," employed by several French ophthalmologists, includes all of the accidents, necroses and opacification which occur at times in well executed corneal transplants. These complications may be divided into precocious necrosis, or that which occurs in the first few days, opacification developing about the third week, and delayed scarring of the transplant. Venco believes that the fundamental factor which determines the changes is trophic and vital and that necrobiotic, anaphylactic and allergic agents are not importnat.

Eugene M. Blake.

8
UVEA, SYMPATHETIC DISEASE, AQUEOUS

Alvarez, A. A. **Late syphilitic uveitis healed by penicillin in massive subconjunctival injections.** Ann. d'ocul. 182:521-524, July, 1949.

50,000 units of penicillin with 2-percent novacaine and .1 to 1,000 adrenalin was injected subconjunctivally every six hours during one day. 3,000,000 units were administered intramuscularly during eight days. Improvement promptly followed the treatment in a 42-year-old man with bilateral luetic uveitis which had responded badly to other antiluetic treatment during eight months. Vision improved from .05 to .5.   Chas. A. Bahn.

Blanchi, Guido. **Plastic uveitis in Schoenlein-Henoch disease.** Rassegna ital. d'ottal. 18:114-120, March-April, 1949.

Cutaneous hemorrhages are divided into four groups by Blanchi. They are those associated with 1. avitaminosis (scurvey), 2. hemophilia, 3. essential thrombopenia (Werlhof's disease), and 4. purpora hemorrhagica of Schoenlein-He-

noch. The latter presents a complex picture of an infection which may be acute or with recurrent attacks, and of unknown etiology. The commonest ocular complication is hemorrhage in the retina, under the conjunctiva and in the lids.

Three cases of uveitis are described, the first in a child of one year, resulting in atrophy of the globe. The disease, in the second patient, aged 12 years, ended with a shrunken globe, and in the third, aged 18 years, in a blind eye. All forms of treatment with the usual drugs and antibiotics were unavailing.

Eugene M. Blake.

Custodis, E., and Heineman, K. **Observations of retinal changes in tuberculous meningitis and in miliary tuberculosis.** Klin. Monatsbl. f. Augenh. 114:356-363, 1949.

Sixty-two children with tuberculous meningitis or miliary tuberculosis of the lungs or a combination of the two diseases were observed up to 220 days. Tuberculous infiltrates in the choroid were considerably more frequent in miliary tuberculosis of the lungs, whether it was associated with tuberculous meningitis or not. They were less frequent in patients with tuberculous meningitis who showed no involvement of other organs but even of this latter group 41 percent showed involvement of the choroid, which is a relatively high figure. It is likely that the extended observation made possible by streptomycin brought out changes in the eyegrounds which formerly had not been observed because of the early death of the patient. The authors noted the appearance of fresh tubercles in the choroid in four patients who were under active streptomycin treatment. Most tubercles in the choroid were located near the posterior pole and only very rarely were they found in the equatorial region.

Max Hirshfelder.

François, J. Contribution to the study of the heterochromia of Fuchs and its pupillary sign. (Sympathetic pathogenesis.) Ann. d'ocul. 182:585-596, Aug., 1949.

Earlier conceptions of Fuchs's heterochromia, like those of many other primary constitutional diseases require revision. The disease is not monocular, nor is the lighter eye always the first to show the degenerative changes. A study of the literature and an analysis of nine cases lead the author to believe that Fuchs's heterochromia iridis is essentially a constitutional, degenerative disease which involves especially the anterior uveal tract, and is frequently associated with degenerative changes in the superficial cervical ganglion. The discoloration of the iris is associated with abnormal pigmentation and pigment dispersion. Pigment becomes dispersed and the iris tissue absorbed because of the basic subnormality of the uveal tissue. The associated sympathetic subnormality makes eyes with this disease abnormally sensitive to parasympathetic stimulation, and insensitive to sympathetic stimulation, as is illustrated by the pupillary reactions. The effect of the following drugs, adrenalin, cocaine, acetyl-methyl-chloride, atropine and eserine, on the eyes of the nine patients, was studied. Chas. A. Bahn.

Garden, R. R., and Wear, A. R. Iridoschisis in a case of chronic primary glaucoma. Brit. J. Ophth. 33:509-511, Aug., 1949.

A case of iridoschisis with chronic primary glaucoma is reported. It appears that the basic changes are senile but that the process may be aggravated by proteolytic enzymes in the aqueous and, in this case, the product of glaucomatous metabolism. The change was chiefly in the lower half of the iris and gravity or convection currents may play a part in its development. Orwyn H. Ellis.

Malatesta, C. Rare case of conglomerate tuberculosis of the ciliary body. Boll. d'ocul. 28:223-234, April, 1949.

A 7-months-old boy developed skin eruptions of ulcerative type, swelling of numerous lymphatic nodules, and severe roentgenographic changes in his right lung. The right eyeball was atrophic and showed an almost complete destruction of the cornea and grayish-brown masses protruding from the defect. An eye specialist saw the child 3 months before the admission and found pericorneal injection, and opaque edematous cornea, fibrinous exudation in the shallow anterior chamber, and increased intraocular pressure. The eyeball was finally enucleated; the ciliary body had been replaced by tuberculous granulations. The mother had had an exudative pleuritis before the child was born. There is a discussion of the immunity factor in early life. (3 photomicrographs, references.)

K. W. Ascher.

9

GLAUCOMA AND OCULAR TENSION

Ascher, K. W. Aqueous veins and their significance for pathogenesis of glaucoma. Arch. Ophth. 42:66-76, July, 1949.

After an excellent and authoritative discussion of aqueous veins, the author concludes that the elimination of intraocular fluid can be studied biomicroscopically. Considered as a unit of clinicopathologic importance, the canal of Schlemm and the aqueous veins show parallel changes in congestion and in inflammation; in primary simple glaucoma their responses are apparently contradictory so far as blood has a tendency to overwhelm the aqueous humor and to stream back against, but not into, the canal, which in eyes with normal pressure often becomes filled with blood during gonioscopic observation. These apparent contradictions can be explained in at least

some cases of glaucoma by the assumption of a narrowing of the canal outlets.

Ralph W. Danielson.

Cristini, Giuseppe. **Cardio-aortic and sinucarotid reflexes in primary glaucoma.** Giorn. ital. oftal. 1:385-403, Sept.-Oct., 1948.

The author discusses the relation between ocular tension and blood pressure and reports his studies of the cardio-aortic and sinucarotid reflexes in primary glaucoma. The stimulation of the vasosensitive areas causes different changes of ocular tension in relation to blood pressure according to whether the patient has high or normal ocular tension at the moment of examination. He analyzes these different reactions that occur in the two stages of glaucoma and calls attention to the consequences that an exaggerated reflex of the vasosensitive area can have on the appearance of an acute attack of glaucoma, and its course.

Vito La Rocca.

D'Ombrain, Arthur. **Traumatic or "concussion" chronic glaucoma.** Brit. J. Ophth. 33:495-500, Aug., 1949.

The observations on a series of cases of monocular chronic congestive glaucoma are presented. It is suggested that there exists a type of chronic glaucoma of traumatic origin. The trauma may produce a chronic process of gradual and progressive blockage of the trabeculum by a sclerotic degeneration or proliferative lesion. The time of onset varies from a few weeks to many years after injury.

. Orwyn H. Ellis.

Galton, E. M. G. **A note on the effect of sleep on glaucoma.** Brit. J. Ophth. 33:511-512, Aug., 1949.

Observations of the effect of sleep on glaucomatous eyes is presented. The rise in tension may be due to immobility of

the lids and eyeballs with consequent lack of massage to the globe.

Orwyn H. Ellis.

Rubino, A. **Trephining and cyclodiathermy associated in the treatment of glaucoma.** Giorn. ital. oftal. 1:450-452, Sept.-Oct., 1948.

The author has associated Elliot's trephining with superficial cyclodiathermy in the treatment of 10 patients with glaucoma for whom the usual methods were not suitable, with favorable results in all. There is a lowering of the tension and a disappearance of inflammation during the year which has elapsed.

Vito La Rocca.

Sanna, M. **The reflexes of Brown-Sequard and of Tholozan in glaucomatous patients.** Boll. d'ocul. 28:193-206, April, 1949.

In order to examine the neurovegetative sympathetic medullary centers, Sanna applied thermic tests to 12 normal and 11 glaucomatous patients. While the right hand was immersed in water, the skin temperature of the left hand was registered at 5-minute intervals. To provoke vasodilatation, water at 42 to 45 degrees C. was used; for vasoconstriction, water at 10 degrees C. Skin temperatures were measured with the thermoelectric device "Thykos." A tendency to or a definite vasoconstrictive tonicity of the circulatory system was found in 8 of 11 glaucomatous patients while only 7 of the 12 now glaucomatous showed this tendency. In 10 of 11 glaucomatous patients a "lassitude of the vasoconstrictive sympathetic medullary centers" was found.

K. W. Ascher.

Stanworth, A. **The cornea in polarised light (preliminary communication).** Brit. J. Ophth. 33:485-490, Aug., 1949.

Corneal strips from cats' eyes were ex-

amined under polarised light. The birefringence of the corneal lamellæ rapidly increases with elongation of the strips. In a physiological range there should be a fairly rapid increase of birefringence with a rise in intraocular pressure. The results suggest that further studies may make the measurement of stress-birefringence available as an optical method for measuring changes in intraocular pressure. Orwyn H. Ellis.

Wolff, Eugene. **The subconjunctival ab externo approach in glaucoma.** Brit. J. Ophth. 33:514-518, Aug., 1949.

The use of a subconjunctival ab externo incision in glaucoma facilitates the performance of filtering operations. The procedure is described in detail. The conjunctival flap is retracted by the assistant with a nontoothed forceps. The operator fixes the eye with a scleral hook and makes the incision into the anterior chamber with a sharp scalpel. The safety and relative ease of performance are stressed. Orwyn H. Ellis.

10
CRYSTALLINE LENS

Davids, B. **Genesis of the complicated cataract.** Arch. f. Ophth. 149:156-175, 1949.

The cataracta complicata as well as the X-ray cataract are interpreted as sequelae of an injury to the lense epithelium which results in a necrobiosis of cells and fibers and the development of generations of pathologic cells. Other types of cataract also show epithelial changes. Quantum processes are considered as genetic factors of these pathologic processes.
Ernst Schmerl.

Gasteiger, H. **Cataract extraction in trephined eyes.** Klin. Monatsbl. f. Augenh. 114:370-385, 1949.

The result of cataract extraction in 44

eyes which had had trephine surgery for glaucoma are reported. It is estimated that cataract follows 10 percent of all trephine surgery, but is not more frequent after trephining than after any other glaucoma operation. Eyes which require multiple glaucoma surgery more frequently develop lens opacities. The author favors intracapsular extraction. His section is usually a Graefe incision without conjunctival flap and avoids the filtering bleb. Cataract extraction did not influence the ocular tension and the visual field unfavorably, and normal intraocular pressure previously established by the trephine operation was usually maintained. (1 figure, references.)
Max Hirschfelder.

Harrington, D. O. **Mechanics of intracapsular cataract extraction.** Arch. Ophth. 42:23-41, July, 1949.

In order to acquire the greatest proficiency in intracapsular cataract extraction the surgeon should have an understanding of the physical principles underlying the dislocation and delivery of the lens. It can be demonstrated by slit lamp microscopy and by gonioscopic observation during actual intracapsular cataract extraction in the eye of a living animal and a human cadaver that the rupture of the zonular lamella of the lens is accomplished primarily by the production by external pressure of a wedge of vitreous, which is made to insert itself between the equator of the lens and the ciliary processes. This deformity of the vitreous can be produced by choosing the method and the point of application of the external pressure at whatever site is desired so that one may tumble or slide the lens from its position in the hyaloid fossa. The normal vitreous is a tissue and cannot be considered as a fluid in which pressure at one point is transmitted equally to all other parts. Capsular trac-

tion facilitates dislocation of the lens by stretching the zonule, but does not normally produce its rupture.

Ralph W. Danielson.

Kuhn, H. A., and Kuhn, H. S. **Monocular cataracts: industrial implications.** Tr. Am. Acad. Ophth. pp. 682-686, July-Aug., 1949.

Should a monocular cataract in an industrial patient be extracted if vision in the other eye is normal? Eighty-two such lens extractions are analyzed to show that the risks, cost and discomforts of operation are justified in some cases. Among the potential advantages are better vision for positions requiring binocular vision, a favorable time for cataract extraction and relative infrequency of postoperative discomfort. Chas. A. Bahn.

11
RETINA AND VITREOUS

Campos, R. **Vitreous-body detachment and its relation to retinal detachment.** Boll. d'ocul. 28:12-154, March, 19949.

Detachment of the vitreous body was first described anatomically by H. Müller in 1856 and ophthalmoscopically by L. Weiss 41 years later; in 1922 the first biomicroscopic description was made by Pillat. Campos summarizes previous classifications distinguishing prebasal and retrobasal detachments; the latter may begin in the upper or in the posterior part of the vitreous body. According to the distance between retina and hyaloid membrane the posterior detachment may be incomplete or complete. Lateral detachments are questionable. Etiologic factors are inflammation, senile changes and degeneration of the colloids constituting the vitreous-body framework. Subjective symptoms are scarce: phosphenes of short or longer duration occur. The first to assume a possible connection between traction of the vitreous body and retinal de-

tachment was Iwanoff (1869). Leber and Nordenson described preretinal fibrous threads formed by proliferating cells; Gonin (1918) concluded, from the shape of most of the retinal holes, that vitreous traction on the retina was responsible for retinal detachment. This theory found numerous defenders but Vogt doubted the importance of traction and stressed peripheral and macular cystic degeneration of the retina as the main etiologic factor in detachment. Campos studied 60 eyes with retinal detachment, using Lindner's angular corneal microscope with arc light and the −55.0-diopter lens of Hruby. In 66 to 93 percent of eyes with retinal detachment, vitreous detachment was present. The highest precentage occurred in the aged and those with high myopia. The fellow eyes showed vitreous detachments in more than 60 percent of the eyes. (51 references.) K. W. Ascher.

Delaney, A. J., and Rhoades, A. L. **Angioid streaks of the retina: case report.** U.S. Naval Med. Bull. 49:572-574, May-June, 1949.

Angioid streaks of the retina occurred in a patient who had pseudoxanthoma elasticum. Donald T. Hughson.

Gandolfi, C. **Pathogenesis of retinitis circinata.** Giorn. ital. oftal. 1:425-431, Sept.-Oct., 1948.

A case of retinitis circinata with senile macular degeneration and numerous scattered spots at the periphery is reported. The author believes that retinitis circinata, like macular degeneration and scattered retinitis, is a manifestation of angiopathy of the retina. Vito La Rocca.

Herson, R. N., and Sampson, R. **Ocular manifestations of polyarteritis nodosa.** Quart. J. Med. 18:123-132, April, 1949.

The authors report the ophthalmoscopic findings in four patients with polyarteritis

nodosa who later came to autopsy. The ophthalmoscopic signs began with blurring of the edges of the disc and with one or two small hemorrhages adjacent to it. Soon wide areas of retinal edema appeared and detachments of the retina of various sizes occurred with spontaneous recovery sometimes in less than three weeks. In three cases nodules of choroiditis were found which rapidly progressed to the formation of pigmented scars. In one case the retinal arteries were directly affected by the polyarteritic process. Arteritis, obstruction of lumen, aneurysmal dilatation, and scar formation could be observed in succession. The ocular findings have a grave prognostic significance. The average duration of life in all four cases was about six weeks after the discovery of the first eye signs.   R. Grunfeld.

Jahnke, W. Treatment of retinitis diabetica with insulin. Arch. f. Ophth. 149: 240-247, 1949.

Vasodilatation and increased capillary permeability are considered the dangers in the treatment with insulin. The author recommends that a blood sugar level of from 130 to 160 mg. percent be maintained.   Ernst Schmerl.

McLean, M., and Solanes, M. Anticoagulant therapy in retinal vascular occlusion. Tr. Am. Acad. Ophth. pp. 644-657, July-Aug., 1949.

The pharmacology of heparin and dicumarol are briefly discussed. The former is administered only intravenously and preferably in 50 to 100-mg. doses at 4 to 6-hour intervals. The latter, which is slower in action, is preferably administered orally as capsules. The initial dose is 200 to 300 mg. and the maintenance dose is 50 to 200 mg. If complications ensue the drugs are discontinued and whole blood or vitamin K are administered intravenously. Forty-one patients treated with anticoagulants are reported. In venous occlusions a subendothelial and endothelial proliferation apparently occurs with the formation of a canalized thrombus. Anticoagulants apparently act by decreasing or slowing the accelerated rate of blood clotting and thus inhibit the formation of additional clots. Anticoagulant therapy should be started soon after the condition occurs and should be continued until the prognosis is determined. Although visual improvement occurred in a number of the cases treated with anticoagulant therapy, its specific indications have not yet been accurately determined.   Chas. A. Bahn.

Rosengren, Bengt. Pathogenesis of fundus changes in arterial hypertension. Klin. Monatsbl. f. Augenh. 114:328-333, 1949.

The vascular changes in the retina in benign hypertension are similar to those found in other organs, mainly those in the region of the splanchnic nerve. In malignant hypertension the process is exudative with edema and hemorrhages superimposed on very constricted arteries. Proliferation of the intima, hyaline degeneration of the media, fibrinoid degeneration of the adventitia are found. The author doubts that the retinal changes are a result of mere ischemia and points to cases of complete ischemia due to arterial occlusion which in no way resembled the picture of malignant hypertension. Renal insufficiency does not in itself explain the fundus changes. The possibility of a toxic substance as well as a purely mechanically damaging effect in hypertension must be considered.
          Max Hirschfelder.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.

601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

DEATHS

Dr. Lloyd Glenn Dack, St. Paul, Minnesota, died July 9, 1949, aged 59 years.

Dr. Clyde Elliott McDannald, New York, New York, died August 13, 1949, aged 73 years.

Dr. William Denton Rowland, Boston, Massachusetts, died July 1, 1949, aged 69 years.

ANNOUNCEMENTS

SCHOENBERG MEMORIAL LECTURE

The Mark J. Schoenberg Memorial Lecture will be held at the New York Academy of Medicine at 8:30 p.m., Monday, December 5th, under the joint sponsorship of the New York Society for Clinical Ophthalmology and the National Society for the Prevention of Blindness. Dr. Jonas S. Friedenwald, Baltimore, Maryland, will discuss "Some problems in the diagnosis and treatment of glaucoma."

This lectureship was established as a memorial to Dr. Schoenberg's interest and original work in the control of glaucoma.

On the committee in charge of arrangements for the meeting are Dr. Willis S. Knighton, chairman; Dr. Isadore Givner, Dr. James W. Smith, and Dr. Franklin M. Foote.

TEMPLE FACULTY PROMOTIONS

The following promotions have been made on the faculty of the Temple University School of Medicine: Dr. Robison D. Harley from associate to assistant professor of ophthalmology; Dr. William Hart from associate to assistant professor of ophthalmology; and Dr. Louis Hinman from instructor to associate of ophthalmology.

WILDER MEMORIAL LECTURE

The William Hamlin Wilder Memorial Lecture, "Medical ophthalmology: A Kodachrome demonstration of fundus photographs of diabetes, hypertension, nephritis, optic neuritis and choked disc," was delivered by Dr. Arthur·J. Bedell, Albany, New York, at a joint meeting of the Institute of Medicine of Chicago and the Chicago Ophthalmological Society on October 14th in Chicago.

SOCIETIES

READING SOCIETY

The 96th meeting of the Reading Eye, Ear, Nose, and Throat Society and the sixth joint meeting with the Berks County Medical Society was held on September 13th. It was a symposium on diabetes. Dr. Milton P. Adel, New York City, discussed "What can the internist tell us?" and Dr. Irving H. Leopold, Philadelphia, "How does the ophthalmologist help?"

Officers of the Reading Society for the year 1949 to 1950 are: President, Dr. William J. Hertz, Allentown; 1st vice-president, Dr. John M. Wotring, Reading; 2nd vice-president and president-elect, Dr. Roy Deck, Lancaster; treasurer, Dr. Philip R. Wiest, Reading; secretary, Dr. Paul C. Craig, Reading; program chairman, Dr. C. Fremont Hall, Phoenixville.

PERSONALS

MADE HONORARY MEMBER

On Friday, October 21st, at the annual convocation of the American College of Surgeons, Sir Stewart Duke-Elder was installed as an honorary member of the organization in a colorful ceremony.

AWARDED LESLIE DANA MEDAL

Dr. Conrad Berens, New York, was awarded the Leslie Dana Medal for the Prevention of Blindness in recognition of his outstanding contributions to ophthalmology at a dinner in his honor at the Chase Hotel, Saint Louis, Missouri, on October 15th. The medal is presented by the Saint Louis Society for the Blind in coöperation with the National Society for the Prevention of Blindness and the Association for Research in Ophthalmology.

GIVES LECTURE IN CUBA

Capt. Arthur Alexander Knapp (MC) U.S.N.R., has recently returned from Havana, Cuba, where he conducted a course in "Plastic surgery of the eye," at the university and presented a paper on "Highlights of eye surgery," before the Cuban Ophthalmological Society.

LECTURES IN TENNESSEE

Dr. Arthur J. Bedell, Albany, New York, delivered a lecture entitled, "The ophthalmoscopic signs of constitutional disease," before the Nashville Academy of Medicine and Davidson County Medical Society on October 5th in Nashville, Tennessee.

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CONTENTS

RETROLENTAL FIBROPLASIA IN PREMATURE INFANTS*

II. STUDIES ON THE PROPHYLAXIS OF THE DISEASE: THE USE OF ALPHA TOCOPHERYL ACETATE

WILLIAM COUNCILMAN OWENS, M.D., AND ELLA UHLER OWENS, M.D.

Baltimore, Maryland

A new concept of retrolental fibroplasia was introduced by our previously reported observations on the early stages and development of the disease.[1] These observations demonstrated that retrolental fibroplasia starts in the retina with an acute onset in postnatal life and runs an active course, which gradually subsides. The final picture depends upon the severity of the acute phase and the extent of contracture of the fibrous tissue formed during the active stage of the disease.

Retrolental fibroplasia was first brought to attention by Terry,[2] who described the appearance of the fully developed disease and pointed out the relationship of the disease to prematurity. Reese and Payne,[3] Krause,[4] and Klien[5] made further reports on cases they had observed in the late stages of the disease.

In the earlier literature there was considerable difference of opinion as to the nature and origin of the membrane behind the lens. Various hypotheses had been proposed relating the disease to the persistence and overgrowth of the hyaloid artery or primary vitreous, or to a generalized maldevelopment of both the cerebral and ocular neuroectoderm occurring during the early stages of fetal life. In addition the question of whether or not the disease was present at birth remained unsettled.

The main reason for these differences in opinion arose from the fact that the earlier reports had been limited almost entirely to clinical and pathologic examinations made when the disease was well advanced. None of the earlier observers had seen where the disease started, when it first began, or how it progressed. It therefore seemed logical that the first step in the investigation of the pathogenesis should be the observation of the onset and course of the disease. To do this, it was necessary to make observations on prematurely born children shortly after birth and to continue the observations periodically until the disease had reached the end stages described by the previous investigators.

The observations made on this plan showed that retrolental fibroplasia was not present at birth. No differences were found on early examinations between the eyes that subsequently developed retrolental fibroplasia and those that did not. The earliest detectable change, occurring about 3 to 5 weeks after birth, was a dilatation of the retinal veins and an increased tortuosity of the retinal arteries. Localized or generalized swelling of the retina soon followed, and the retina developed a grayish-green color. Often the retina became so swollen that the course of the retinal vessels could not be traced in the areas of greatest retinal edema. The vitreous became cloudy and proliferating fibrous bands extended forward from the elevated retina into the vitreous. The retrolental membrane was formed by the

fusion of the vitreous bands and the peripheral folds of swollen elevated retina. These findings have been confirmed by Falls,[6] Unsworth,[7] and Gilger.[8]

The active phase of the disease usually stops between the 4th and 5th month of the infant's life, and the changes that occur after this time are due to contracture of previously formed fibrous tissue. If the membrane behind the lens is complete, all vision is lost. Occasionally the disease is not so extensive and, when it subsides, only a partial membrane or a band resembling a retinal fold is formed. These eyes are often myopic and may show disseminated areas of irregular pigmentation. Some vision is retained and children with this less severe involvement see well enough to walk alone and play with toys. In premature infants both eyes are affected by the disease, but often to various degrees. The membrane may be complete in one eye and only partial in the other.

The main problem in retrolental fibroplasia is the prophylaxis of the disease rather than treatment in the late stages when irreversible damage has been done to the retina. No treatment has yet been found which is of value when the disease is well established. Operations to remove the membrane have been unsuccessful, for a portion of the retina itself is excised in the attempt to clear the retrolental space. The description of the onset and course of retrolental fibroplasia has redirected most of the thinking about the disease. Formerly, emphasis was placed on factors which might have been effective in the prenatal life of the infants[9] or to an abnormal persistence of various fetal structures. It is now evident that the most fruitful investigation is to be found in a study of factors which are active in postnatal life.

ETIOLOGIC CONSIDERATIONS

In our first report the idea was proposed that the disease might be related to a metabolic disturbance produced by some of the newer methods used in the care of premature infants to compensate for their physiologic immaturity. The close correlation between the incidence of retrolental fibroplasia and the birth weight of the infant adds support to the theory that a metabolic abnormality may be the cause of the disease.

One of the main physiologic differences between the premature and the full-term infant is the defective fat metabolism of the premature infant.[10] Because of this defect, premature infants have been given diets low in fat and high in protein as they apparently can utilize protein efficiently.[11]

Shortly after the high protein diets were introduced it was found that a disturbance was created in the metabolism of the aromatic amino acids. Phenylalanine and tyrosine were found to be incompletely oxidized and the intermediary products p-hydroxyphenyl pyruvic and p-hydroxyphenyl lactic acid appeared in the urine. This abnormal metabolism of aromatic amino acids could be prevented by increasing the amount of vitamin C in the diet.[12] It seemed possible that some similar metabolic disturbance might be the basis for the occurrence of retrolental fibroplasia.

The low fat diet recommended for premature infants contains very little of the fat-soluble vitamins. In view of this fact and the poor absorption of fats by the premature infant, a minimal supply of fat-soluble vitamins would be available to the premature infant were they not supplemented. It seems probable that the premature infant might have a marginal prenatal storage of a necessary fat-soluble substance. As this substance is depleted or the need for it increased in postnatal life, the infant might be unable to replenish it from the diet. This hypothesis can be correlated with the clinical observation that the earliest detectable changes of retrolental fibroplasia are noted about one month after birth. Of the fat-soluble vitamins, A, D, K, and E, the vitamins A and D have been provided routinely in large doses in the vitamin supplements currently used. Vitamin K is usually given shortly after birth. Vitamin E alone of the fat-soluble vitamins has not routinely been in-

cluded in the vitamin supplements of premature infants. It is known that regardless of how high the maternal intake of vitamin E may be, the newborn rat begins life with a negligible supply of this vitamin.[13]

In addition to the low vitamin E available in the reduced fat diets, and the poor absorption of fat-soluble substances by the premature infant, the amount of vitamin E available might be further reduced by two factors in the current care of premature infants. The first factor is the use of large amounts of vitamin A given to supplement the diet. The vitamin-A supplements are given usually either in the form of natural fish-liver oils which contain large quantities of unsaturated fats, or as vitamin A in water-miscible preparations. It has been shown that the requirement of vitamin E in experimental animals is increased when vitamin A[14] or when unsaturated fats[15] are administered. This is thought to be due to the role of vitamin E as an antioxidant in protecting the unsaturated carbon bonds in these compounds.[16] Therefore the supplements of large amounts of vitamin A, or of fish-liver oils containing unsaturated fats, might serve to increase the needs for vitamin E in the diet of the premature infant. The use of iron to overcome the anemia which premature infants develop in postnatal life might serve to decrease even further any small amount of vitamin E available to the premature infant. It is well known that ferric salts destroy vitamin E. One of the methods of producing a vitamin-E deficient diet for experimental animals is to treat the ingredients of a full diet with ferric chloride to destroy the vitamin E present.[17]

Kinsey and Zacharias found a positive correlation between the rise in incidence of retrolental fibroplasia and the increased use of water-miscible preparations of vitamins and of iron.[18] The relationship of large supplements of vitamin A and iron to the occurrence of retrolental fibroplasia is still under study. In the premature nursery of The Johns Hopkins Hospital retrolental fibroplasia developed in two infants who had not received vitamin A or iron. Two other children have been seen here with retrolental fibroplasia in the late stages of the disease who had also never received either vitamin A or iron supplements. Kinsey and Zacharias have reported similar cases, and it is likely, as they point out, that the administration of large amounts of vitamin A and iron are not primary factors in the etiology of the disease.

From these considerations, it is apparent that numerous factors in their dietary regime would allow premature infants to have only marginal amounts of vitamin E available. Among these factors are the low fat diet, the poor absorption of fats by the premature infants, the lack of vitamin-E supplements, and the use of such substances as vitamin A, unsaturated fats, and iron, all of which might increase the need for vitamin E.

In addition, the relative importance of fat metabolism in the immediate neonatal period, plus the predominant absorption of unsaturated fatty acids by the premature infant might further increase the vitamin-E requirements in this critical period.[10] Soon after birth, newborn infants have a sudden increase in the metabolism of lipoid substances. The fetus probably uses little fat for its heat production but stores considerable for later emergencies. After the newborn infant has fairly well depleted its glycogen stores, it begins to depend largely upon reserves of fat for energy. There is a greatly increased transport of fat substances in the blood so that the concentration of most types of blood fat are roughly doubled between birth and the second week of life.[19] Recent studies on the biochemical function of vitamin E indicate that many of its physiologic effects are related to its antioxidant properties, especially in relation to fat metabolism. Vitamin E functioning as an antioxidant plays an important role in protecting or stabilizing unsaturated fats during their mobilization, metabolism, and storage within tissue cells.[20]

The immature organism is particularly

susceptible to vitamin-E deficiency. Nursing rats born of vitamin-E depleted mothers develop acute muscular dystrophy 17 to 19 days after birth.[21] Young chickens, placed on a vitamin-E deficient diet at the time of hatching, suddenly develop nutritional encephalomalacia at 3 to 4 weeks of age.[22] This disease is characterized by areas of edema, hemorrhage, necrosis, and glial proliferation in the central nervous system. In each of these diseases, there is an age limit to the susceptibility of the animals to the nutritional derangement. As they grow older the incidence of the disease steadily decreases.[23] This susceptibility of immature animals to vitamin-E deficiency might be paralleled by the susceptibility of premature infants to retrolental fibroplasia.

A further function of vitamin E is to control excessive tissue oxidation. The lowering of the oxygen consumption of brain homogenates of vitamin-E deficient animals by alpha tocopheryl phosphate appears to be due to the prevention of the reduction of cytochrome-C wherever the cytochrome system comes into play; whether in carbohydrate, fat, or protein metabolism.[24] Since the retina has a higher rate of respiration than that of almost any other tissue,[25] and since the premature infant is characteristically in a marginal status of anoxia[10] vitamin-E supplements might be expected to play a role in the prevention of retrolental fibroplasia through this function.

These considerations immediately raised the question whether supplements of vitamin E might prove to be a factor in the prevention of retrolental fibroplasia. In an effort to study the problem of retrolental fibroplasia from this standpoint, a series of laboratory and clinical investigations have been undertaken. These investigations are still in progress, and this report covers only the observations on the clinical aspects. The results of the laboratory studies will be reported in another paper.

CLINICAL STUDY

The clinical study on the use of dl alpha

tocopheryl acetate was begun in June, 1948. At that time the only available preparation suitable for premature infants was a mixture of natural tocopherols of low potency. Vitamin-E activity is possessed by three higher alcohols known as alpha, beta, and gamma tocopherol. Alpha tocopherol has the greatest biologic activity of these three forms. Tocopherols are widely distributed in vegetable oils and in lesser concentration in animal fats. Their esters are much more stable than the free forms.[26] Synthetic dl alpha tocopheryl acetate has been accepted as the international standard of vitamin E.[27] In July, 1948, a special preparation of synthetic dl alpha tocopheryl acetate in a water-miscible menstrum was obtained.*

For a period of 10 months, alternate infants admitted to the premature nursery of The Johns Hopkins Hospital with birth weights of three pounds (1,360 gm.) or less were given supplements of this preparation. The dose used was 150 mg. daily, given orally in 50 mg. doses every eight hours between feedings. This was started as soon after birth as the infant was able to take feedings by gavage or by mouth. Most of the infants in each group received 9,000 units of vitamin A and 900 units of vitamin D daily in a water-miscible preparation. About one third of the infants in each group received 4 cc. of a 10-percent solution of ferric ammonium citrate daily. This iron supplement was begun when the infants were six weeks of age.

During this 10-month period, 11 infants received vitamin-E supplements and none developed retrolental fibroplasia. Fifteen infants in the control group did not receive vitamin E, and five of these developed retrolental fibroplasia.

These results were so encouraging that in May, 1949, the plan was changed and vitamin-E supplements were given to all premature infants weighing three pounds (1,360 gm.) or less at birth. The routine ad-

ministration of vitamin A and iron was discontinued. Each infant was given 500 units of vitamin D daily in a water-miscible preparation. Since this time 12 infants have received alpha tocopherol supplements.

One of them has developed retrolental fibroplasia, showing massive retinal folds extending from the disc to the periphery of the fundus in each eye. The neonatal course of this infant was unusual. The birth weight of the infant was 1,110 gm. This fell to 880 gm. by the second week of life. The infant was apneic and cyanotic, and not expected to survive. Because of its poor condition, the only nourishment it received for 11 days after birth was parenteral glucose and amigen. From the 11th to the 15th day, feedings by gavage could be given, but only glucose solution was tolerated. On the 15th day, milk feedings could be substituted for the glucose solution. It was necessary to continue feedings by gavage until the infant was six weeks of age. The alpha tocopherol could not be started until the 11th day when feedings by gavage were begun.

Before the time alpha tocopheryl acetate was used, a total of 63 infants weighing less than three pounds at birth were followed routinely. Of these, 12 developed retrolental fibroplasia.

In summary the experience with the entire group of infants followed routinely from birth can be divided into three periods: (1) The period before the use of alpha tocopheryl acetate supplements, (2) the period during which alternate infants were given alpha tocopheryl acetate supplements, and (3) the period during which all infants were given the supplements. All of these infants had a birth weight of three pounds (1,360 gm.) or less. A total of 101 infants was observed. Seventy-eight of these did not receive alpha tocopheryl acetate supplements. Seventeen of these (21.8 percent) developed retrolental fibroplasia. In contrast, 23 infants received alpha tocopheryl acetate supplements. Only one of these (4.4 percent) developed retrolental fibroplasia (table 1).

As mentioned before, during the period when alternate infants with birth weights of 1,360 gm. (three pounds) or less were given tocopherol supplements, five infants in the unsupplemented group developed the early stages of retrolental fibroplasia. In addition four infants in the group weighing over 1,360 grams who did not receive vitamin E prophylactically showed the early stages of the disease. The preparation of dl alpha tocopheryl acetate was used in these nine babies to determine whether vitamin-E supplements would alter the course of the disease in its early stages. Vitamin A and iron preparations were withheld from these infants when the vitamin-E supplements were begun. Under this regime, progress of the lesions was arrested in five cases. In the other four cases, the course of the disease was unaffected by the supplement. Spontaneous regression of the disease after the stage of diffuse retinal exudation is unusual.

In our experience thus far, vitamin-E supplements are of no value if not started at least before the baby is six weeks of age, since by that time irreversible retinal changes have occurred. The supplement must be started early before the retina has become detached and visible as a partial or complete membrane behind the lens. It is of no value when the disease is recognized grossly by the parents or doctor by external examination.

No serum levels of vitamin E in prema-

TABLE 1

EFFECT OF VITAMIN E SUPPLEMENTS ON THE INCIDENCE OF RETROLENTAL FIBROPLASIA IN PREMATURE INFANTS WITH BIRTH WEIGHTS OF THREE POUNDS (1,360 GM.) OR LESS

Diet	Number of Infants	Number with Retrolental Fibroplasia	Percent Retrolental Fibroplasia
Supplemented with Vitamin E	23	1	4.4
Not Supplemented with Vitamin E	78	17	21.8

ture infants have been reported in the literature. The normal level in adults has been found to vary from 1.0 to 1.2 mg. percent.[30] Only a few determinations have been reported on full-term newborn infants. These levels were significantly lower than the maternal levels, and varied from 0.2 to 0.5 mg. percent.[31, 32]

Determinations of the vitamin-E levels of the serum have been made in the course of this study. At first the determinations were made by a method[28] which required 5 cc. of blood—an amount which was not feasible to obtain frequently from small premature infants. It became evident that a micromethod for determining vitamin E was essential. Dr. V. E. Kinsey solved this problem for us by adapting a method devised by M. L. Quaife which requires only 0.2 cc. of serum.[29] The vitamin-E determinations on the sera are being made at present under Dr. Kinsey's direction at the Harvard Medical School. Forty-six determinations of the vitamin-E level were made on sera of premature infants who were receiving no vitamin-E supplements. The average level in these determinations was 0.25 mg. percent. When dl alpha tocopheryl acetate was given, the serum level rose with increasing supplements. The average vitamin-E level was 4.12 mg. percent in 103 determinations made on sera of infants receiving 150 mg. dl alpha tocopheryl acetate daily. Most of these infants had birth weights of three pounds or less, and the sera were obtained from 2 to 8 weeks after birth.

It is important to follow the serum level of tocopherol for, in a few of our cases, the serum tocopherol level did not rise even though the infants were receiving large oral supplements of dl alpha tocopheryl acetate. The problem of parenteral administration of alpha tocopherol to premature infants who show evidence of inadequate absorption by the oral route is now being investigated.

COMMENT

In evaluating our experience with tocopherol supplements, there are several observations for which an explanation is not readily available. There appears to be no constant correlation between the serum tocopherol level and the occurrence of retrolental fibroplasia. Some of the infants in the unsupplemented group who developed retrolental fibroplasia did not have lower tocopherol levels than some infants in the same group who did not develop the disease. In addition the one infant in the supplemented group who developed retrolental fibroplasia showed progression of the disease even though the serum tocopherol level was adequate from the time the first retinal changes were observed at six weeks of life. As stated before the exact mechanism whereby vitamin E functions in the body is not known. It seems apparent, however, that at the high serum tocopherol levels we have obtained, the tocopherol is not exerting a true vitamin function but rather a pharmacologic action as suggested by Harris.[33]

The material presented in this paper is the report of studies still in progress. It must be remembered that, as yet, no claims for the role of vitamin E in human nutrition have been substantiated, although its role in animal nutrition has been well established. So far the results in the prophylaxis of retrolental fibroplasia have been encouraging, and it is planned to continue these studies until sufficient data have been accumulated to evaluate critically the role of vitamin E in relation to this disease. It seems certain that the solution to the etiology of retrolental fibroplasia will be found from such a metabolic study.

CONCLUSIONS

1. A total of 101 premature infants with birth weights of 1,360 gm. (three pounds) or less have been observed at routine intervals since birth. Twenty-three of these infants received supplements of dl alpha tocopheryl acetate. One of these (4.4 percent) developed retrolental fibroplasia. Seventy-eight infants did not receive supplements of dl alpha tocopheryl acetate. Seventeen of these (21.8 percent) developed retrolental fibroplasia.

2. The average serum tocopherol level in the unsupplemented group of premature infants was 0.25 mg. percent. On a dosage of 50 mg. of dl alpha tocopheryl acetate every eight hours, the average serum tocopherol level rose to 4.12 mg. percent.

The Johns Hopkins Hospital (5).

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THE PHYSIOLOGY OF THE INTRAOCULAR FLUIDS
AND ITS CLINICAL SIGNIFICANCE*

STEWART DUKE-ELDER,† M.D.
London, England

I find it impossible to proceed with this lecture without a preface recording my great appreciation of the fact that this academy has made me its guest of honor. I know that on an occasion such as this it is the usual and graceful habit of the lecturer to express such thanks; but in this case I would wish you to believe that my thanks are more than usually sincere and from the heart. Before the war on more than one occasion I was a guest in this great country and drank deep of American hospitality. During the war one of the good things—and there are some good things even in war—was the close association which I and my British colleagues had with Americans, particularly American ophthalmologists. After the war one of the sorrows of peace was the departure of our American friends from England; but I, for my part, having grown used to your company, have made up for my loss by recurrent invasions of your country. In 1946, I was made the guest of honor of the select company of the American Ophthalmological Society and also of the Association for Research; in 1947, I was again the guest of honor of the wider company of the ophthalmologic section of the American Medical Association; and today I am overwhelmed by a similar courtesy from what must certainly be the largest convention of ophthalmologists in this world. I have to thank you, Mr. President, and your council —and you all—for thus filling my cup to overflowing; and I hope you will believe me when I assure you that to come and be with you is to me not to come amongst strangers to a foreign land, but to meet again very

old and very dear friends—to go, as it were, from one room to another in my own home through a door which is never locked.

Some of you may remember that about a quarter of a century ago I summarized my early work on the problem of the mechanism of the formation of the intraocular fluids in a monograph wherein I stated, unequivocally and with all the assurance of youth, that the aqueous humor was a dialysate of the capillary blood. Fortunately I had the wisdom, even in those days, to end the monograph thus: "This is to be accepted in the light of a working hypothesis which may, or may not, aid after the manner of a temporary scaffolding in the erection of a building of whose very design we are ignorant, and as such it is to be treated. For the whole progress of knowledge is strewn with the wrecks of such systems." However much or little the formulation of this hypothesis stimulated work on this problem, the fact remains that today such a theory can no longer stand alone: it is to explore what must take its place and what practical lessons must follow that is the purpose of this address.

This necessity to discard a hypothesis, of course, is not at all uncommon in the advance of any science and is essentially a sign of progress. The methods of investigation available 25 years ago were crude in comparison with those of today: they produced results with a large margin of error which could be synthesized into broad and apparently satisfying generalizations. But today the introduction and evolution of improved and novel techniques have changed all this. The accuracy of chemical analyses, particularly of minute quantities of fluids, has improved enormously; but what is of much greater importance, to the chemistry of molecules there has been added the physics

of radioactive tracer elements whereby we can follow metabolic processes throughout all their intricacies without, so far as we know, upsetting the normal metabolism. By these electronic techniques it is relatively easy to determine the rate of penetration of a given element from the blood stream into the uvea, the aqueous humor, the vitreous, the lens, or the cornea in quantities so minute as to be quite outside the range of chemical analysis. With this technique we have gained immeasurably in refinement of accuracy, ease in manipulation, and—a very important point—in lack of disturbance of the natural conditions.

It is not surprising that with these new weapons at our disposal, with all their refinement of accuracy, we are getting results differing from the old and we have been confronted with many new awkward facts which will not fit in with a picture so simple as that of a dialysate. It follows that the conception of a dialysate must be abandoned and something else must take its place. It frequently occurs, however, that in the evolution of science from a relatively simple to a more complex stage, the transference is a period of considerable confusion and complexity. To a large extent we are at present in the confusion of this interim period, and so, if I choose this opportunity to put forward a new theory, I would hasten to deprive it of any proved or pragmatic significance. If it merely serves as another temporary scaffolding whereon to build and eventually has to be discarded on the discovery of further new facts, it may have served its purpose of ordering our present knowledge and stimulating new avenues for research.

I like to think it is often valuable and frequently stimulating not to make our science too rigid and pontifical, but to anticipate that which is wholly verifiable. Those who refuse to go beyond fact rarely get as far as fact; they will miss much of the fun of life. Goethe may have been right when he said that hypotheses are cradle songs which lull to sleep; but if one sleeps one may dream dreams, and perhaps awake to write a sonnet. And if for a few days I have escaped from the factual fetters of nationalized medicine in Britain into a community where medicine is still—if perhaps only temporarily—free, I hope to make the most of my liberty and take you along with me on a journey in the hope that, even if we do not reach the end with certainty, we may find some illumination by the way. In any event the journeying is always more pleasant than reaching the goal.

Here then are some facts.

I do not think there is any doubt but that the essential blood-aqueous barrier is the capillary walls, as in fact they are the blood-tissue barrier elsewhere in the body. It is true that in the ciliary region the further barrier of the ciliary epithelium is interposed, which, as we shall see presently, exerts a considerable influence on the composition of the intraocular fluid; but on the anterior surface of the iris there is no other barrier, for there the capillaries are naked to the aqueous, and posteriorly the tenuous internal limiting membrane of the retina can have little physiologic significance. A multitude of experiments on the transfer of materials both naturally occurring and artificially injected, both in the normal state and in conditions of increased capillary permeability, as well as clinical facts such as the possibility of the maintenance of a relatively normal physiology when the eye is divided into compartments by a seclusion of the pupil, leave little doubt that an exchange between blood and intraocular fluid throughout the vascularized tissues of the eye constitutes the background of the metabolic interchange.

With this premise I want to examine for a moment the transfer of material across the walls of the ocular capillaries. Table 1 indicates the rate of transfer both into the aqueous humor and into the vitreous body of certain substances. These substances are chosen from many on which we have ex-

perimented as being typical examples of classes, and for comparative purposes their respective rates are expressed in terms of a constant which has a relative but no absolute significance.

TABLE 1

RATE OF TRANSFER: BLOOD→EYE

Substance (and molecular weight)		Aqueous K_{Aq}	Vitreous K_V
Water	(18)	600	—
Lipoid Soluble Substances:			
Ethyl alcohol	(46)	250	150
Sulfapyridine	(249)	100	30
Thiourea	(76)	70	—
Sugars:			
Glucose	(180)	34	11
Sucrose	(342)	5	0.29
Inulin	(5000)	nil	nil
Ions:			
Sodium	(23)	40	7.5
Chloride	(35)	40	6
Thiocyanate	(58)	46	7.5
Nitrogenous Substances:			
Urea	(60)	14	1
Amino acids	(75)	14	0.3
Penicillin	(334)	1.3	nil
Proteins: (70,000–140,000)		nil	nil

In this table several things are of significance. In the first place, water gets through from the blood into the anterior chamber with the greatest of ease; proteins, with their gigantic molecules, hardly at all. In the second place, all the other diffusible substances get through comparatively slowly into the anterior segment, and with much greater difficulty and much more selectively into the posterior segment. In general terms the rate of entry is governed not by molecular size, as in physical diffusion, but by the chemical nature. Thus lipoid-soluble substances get through most readily, nitrogenous substances with the greatest difficulty. That some physical basis exists is suggested by the fact that within each group of substances the retardation varies to some extent with the molecular size—ethyl alcohol passes more quickly than the sulfa drugs, the monosaccharides more quickly than the di-

saccharides, urea than penicillin, and so on. But by and large, a physical differentiation does not apply. Here we see an unusual delay in the passage of all molecules; an equality of the rate of passage of molecules of different size (when sodium and glucose enter at much the same rate); a block to the passage of nitrogen-containing molecules (whereby amino acids enter more slowly than glucose, the molecule of which is twice the size—or penicillin lags behind sucrose); and a facilitation of lipoid-soluble molecules (whereby the rate of penetration of sulfapyridine is over 20 times that of sucrose although the molecule is only slightly smaller, or the translation of urea to the larger molecule of thiourea increases its ease of passage five times). Clearly the passage is not on a physical basis but to a large extent is determined chemically. It is important also that synthetic substances, such as trimethyl glucose, which do not participate in metabolic activity in vivo, enter at the same rate as corresponding natural substances so that the process of transfer in their regard, at any rate, does not seem to be a secretion.

In the posterior segment of the eye this tendency is more accentuated. The chemical differentiation is greater and, what is more interesting, a regional differentiation exists. Thus we have found that sugars and thiocyanate enter throughout the whole of the circumference of the posterior segment while sodium and chloride enter in significant quantity only from the ciliary region. This, as we shall see presently, is important, but in the meantime we may note that in the posterior segment not only is the barrier less permeable and more selective, but for some substances, such as salt, is regionally selective.

Let us compare this with what happens in the body generally. As a working concept the capillaries may be considered as a meshwork of thin, platelike endothelial cells placed edge to edge to form a mosaic, the opposing edges being made tight by an intercellular cement substance of calcium protein-

ate, except for the presence of pores. In the extremities the tissue fluids contain some 0.5-percent protein; in the liver and intestines, 50 percent of the plasma proteins escape; in the intraocular fluid (and in cerebrospinal fluid) there is only a trace (0.02 percent). We may take it, therefore, that there are some pores in the intercellular spaces of the capillaries of the extremities of a diameter up to 38 Ångstrom units (the equatorial diameter of the plasma proteins); a large number in the liver and intestine; and only an exceptional one of this size in the capillaries of the eye. In the body generally, however, molecules smaller than this pass through the intercellular spaces of the capillary walls with ease—sodium, potassium, chloride, nitrate, and urea almost as easily as water, calcium, magnesium, and glucose with only slight delay—and even such large molecules as inulin comparatively easily. That is a physical passage by diffusion mainly through inactive intracellular spaces. The delay experienced by all molecules in traversing the ocular capillary walls and the differential retardation of molecules on a chemical basis can only, I think, be reasonably explained by a transference essentially through cell bodies instead of through their interspaces. This, of course, is not dialysis but something more subtle, discriminating, and apparently purposive.

A word now as to the regional differentiation. The blood-aqueous barrier in the anterior segment must be the uveal capillaries. In the posterior segment of the eye we have seen that there is a greater over-all difficulty in transit, more chemical differentiation, and in particular the block to sodium and chloride is very effective. We know that, when the retinal arteries are blocked, the inner layers of the retina behind the equator die, but anterior to the equator the entire thickness of the retina can be nourished and maintained in health from the anterior ciliary vessels. The deduction we may tentatively draw from this is that in the posterior segment of the eye, transudate from the choroi-

dal capillaries does not reach the inner retinal layers, in quantity at any rate, so that fluid traffic into the vitreous in this region is essentially from the retina; in the pre-equatorial part of the vitreous chamber, on the other hand, traffic will be from the retina and choroid; and in the most anterior part, from the ciliary body. Posteriorly, therefore, where only the tenuous internal limiting membrane of the retina separates the tissues from the ocular cavity, the nature of the fluid bathing the vitreous will be determined essentially by the retinal capillaries.

This opens up a very interesting analogy between the permeability of the capillaries of the retina and those of the central nervous system. We know that all the capillaries of the body except those of the central nervous system are stained by acid dyestuffs such as trypan blue and allow their passage freely through their walls. Palm has recently shown that the same peculiarity applies to the retinal capillaries, for neither the endothelium of these capillaries nor the tissues of the inner retinal layers take on such a stain. It is obvious that the block here is the capillary walls. It is also interesting that the same deficiency of sodium chloride is found in the cerebral tissue-fluid as we have found in the vitreous. It would seem that the retinal capillaries have the marked peculiarities of the capillaries of the central nervous system which have been shown to differ widely from those of the rest of the body.

Let us turn now for a moment to the concentration of the various constituents of the intraocular fluid. It is interesting that all its constituents are in deficit in comparison with the plasma with four major exceptions: (1) hyaluronic acid, which must be synthesized locally and secreted into the eye; (2) ascorbic acid, which in some species (including man) seems to be actively transferred from the blood to reach a high concentration in the aqueous; (3) lactic acid in the presence of the lens, presumably a metabolic product; and (4) salts. The excess of salt (sodium and chloride) in the aqueous in comparison

with the blood is, I think, real. I am aware that this has been questioned, but our chemical analysis has received confirmation from another point of view. By every method we have employed we find constantly that the osmotic pressure of the aqueous is higher than that of the blood plasma; and if the two are dialyzed across a collodion membrane, chemical and physical measurements show a transference of salt from the former to the latter. It seems, therefore, that while all other freely diffusible substances with the specific exceptions just mentioned are in deficit, the concentration of osmotically active salts in the aqueous humor is in excess of that in the blood: in its transfer energy must therefore be expended, that is, it must be secreted.

Studies of the most varied nature in other organs of the body have consistently failed to produce any evidence that the capillary walls act otherwise than as a simple filter; they may block substances but they have not, so far, been detected in the act of secreting any substance. We know that, in the posterior segment, salt enters essentially in the ciliary region, and the work of Friedenwald, so ably summarized in his recent Proctor lecture, suggests a mechanism which might form the basis of such an active process occurring in the ciliary epithelium.

In the formation of the intraocular fluid we are therefore led to the suggestion that throughout the vascularized tissues of the eye there is a peculiar and controlled transfer of materials through the cell bodies of the capillaries instead of through their interspaces as in the body generally, and superimposed upon this, presumably in the ciliary region, a secretion of osmotically active salt. It is quite possible and indeed probable that the ciliary secretion may embrace other substances than salts, but I know of no conclusive evidence as yet to prove this.

If the integrity of the capillary walls is impaired, of course, these conditions are immediately and fundamentally altered. This change, which occurs universally throughout the capillaries of the body, can be accom-

plished by toxic or chemical influences but is most easily seen in alterations of the pressure relationships. This property of capillary fragility (as opposed to permeability) can be seen if a capillary is closed at both ends and is injected under pressure with India ink by means of a micropipet; as the pressure is increased the India ink will spurt out through a few isolated spots between the epithelial cells even though no tears in the endothelium can be seen. When the pressure is reduced and the circulation allowed to resume, these particles remain as localized collections outside the capillary walls and flow is resumed with permeability unimpaired. On paracentesis of the eye the reverse pressure relationship is seen, for the sudden lowering of pressure outside the capillary walls allows the passage of a protein-rich fluid wherein all the diffusible constituents approximate those of the plasma to form the plasmoid aqueous humor which is a simple filtrate from the blood; the proteins and all the diffusible substances increase, except the chlorides which diminish. In this case the ocular capillaries revert to the mechanism of the capillaries generally, and about this mechanism, which is universal throughout the body, we need not concern ourselves further.

Let us turn now to the drainage of these fluids. From experiments with heavy water, first carried out by Kinsey, Grant, and Cogan in Boston, we know that there is a full and free transfer of water in both directions across the capillary walls, just as occurs throughout all the bodily tissues, determined by the kinetic energy of the molecules involved; half the aqueous of the rabbit, for example, is replaced every 2.7 minutes—that is, there is a transference into and out of the anterior chamber of about 50 cu. mm. per minute. In addition to this there is a through-and-through circulation by way of the canal of Schlemm and the aqueous veins. This, unlike the general metabolic interchange, is not a process of diffusion but an undifferentiated flow in bulk allowing free mechanical exit to com-

paratively large molecules. This has been shown experimentally in my laboratory and also by a number of investigators using various techniques, and has been confirmed by the observation of the exit-flow through the aqueous veins in the human eye; the unanimity obtained by these results is striking. It would appear that in the normal eye approximately one percent of the fluid in the anterior chamber drains away per minute, a flow amounting in the normal human being to some two cu. mm. per minute.

We have now come to the point when we might venture to clothe these facts with some integrative philosophy. It may be asked, what is the purpose of this relatively complicated mechanism which we are postulating? Presumably it is concerned with making the eye a useful optical organ for which purpose two desiderata are necessary— optically clear media and an internal pressure sufficiently high to keep the globe a relatively rigid optical system. The peculiar impermeability of the ocular capillaries can be construed as a teleologic adaptation to maintain the ocular media optically clear and homogeneous. Transparency is maintained by excluding substances from the aqueous, but the deficiency of sugar, urea, creatinine, amino acids, and proteins amounts to about 4.5 millimols per liter. This has to be made up. An essential function of salts in the body is to maintain osmotic flow and equilibrium throughout the tissues. By a secretion, containing among, perhaps, other constituents, salts, this is made up and more than made up, so that the pressure in the eye is determined as a hydrodynamic steady-state by the capillary pressure plus an excess of osmotic pressure. And a slow outflow is provided, allowing a leak at the angle of the anterior chamber, so that the actual pressure in the eye is less than this pressure-head; and a safety-valve mechanism is provided so that the pressure does not get out of hand.

Finally it may be useful to consider what may be the practical bearing of this on the variations of the intraocular pressure found

clinically. Obviously it may be disturbed by at least four factors: (1) An upset of the secretory activity involving in the first place osmotic changes; (2) a change in the permeability of the capillaries allowing the formation of a filtrate; (3) a change in the hydrostatic blood pressure, becoming effective either at the arterial ends of the capillaries when a rise in blood pressure will involve a rise in ocular tension or in the venous capillaries when an increased flow will encourage reabsorption of fluid and bring about a fall of ocular tension; and, finally, (4) by a blockage of the drainage channels which, by embarrassing the safety valve, will lead sometimes to a cumulative rise of pressure, sometimes to a strangulating crisis depending on other events in the eye.

About the effects of an upset of the secretory mechanism we know nothing; that is a problem full of enticement but equally full of difficulty. About the effects of vascular disturbances we know more. So far as local events are concerned, the effects of a rise in the capillary pressure on the tension of the eye have been elucidated. We also know that local stimuli have a generalized vasodilatory effect throughout the entire uveal tract through the mediation of axon reflexes so that dramatic results may follow insignificant stimuli. The massive and widespread vasodilatation, associated with increased permeability and edema, that may result therefrom constitutes the picture of acute congestive glaucoma. We also know that an increase of flow through the venous capillaries tends to lower the intraocular pressure; this action of eserine and pilocarpine, which cause such a dilatation and even open out new functional capillary districts, I think accounts for their hypotensive action often as much or sometimes more than their mechanical miotic effect. But about the central control of the local vascular system we know much less. Clinical observations with, it must be admitted, a slender experimental background suggest that neurovegetative, endocrine, and psychosomatic influences play an important part in its regulation; and

clinical and experimental facts relating to the diurnal pressure variation, the existence of a regulating mechanism, and the interdependence of the circulatory events in one eye with those in the other, whether determined by chemical or mechanical stimuli, strongly suggest the presence of a controlling center in the central nervous system, presumably in the upper brain stem or hypothalamic region; but the whole of this subject awaits experimental exploration.

About the effects of deficiencies or difficulties of drainage we are more fully aware; and probably because they are more obvious and amenable than the others to dramatic relief by treatment, I think we often attach undue importance to them. We know that a blockage of the angle of the anterior chamber seems frequently to be a precipitating cause of an acute congestive glaucoma. But it is equally important that a similar crisis may occur with the angle open as is seen, for example, in acute hypertensive uveitis. In this condition, if the accompanying vasodilatation and edema can be mitigated by control of the inflammation, the tension may fall. And after operation the tension may fall even though the angle, both in the operative area and elsewhere, is still gonioscopically blocked, suggesting that in some cases the hypotensive action of surgery may act by cutting short a vascular crisis rather than by opening up new drainage channels.

Similarly, in simple glaucoma we suspect that in a large number of cases there is some subtle hindrance to the exit channels of the intraocular fluid. But at the same time, in this disease, the outflow through the aqueous veins may be apparently at approximately the normal rate. Moreover, our everyday experience, that the normalization of pressure, either pharmaceutically or surgically, frequently does not prevent the evolution of the symptoms of this disease in their characteristic remorseless course, points to the fact that the whole philosophy of such cases cannot lie within the confines of the angle of the anterior chamber. Blockage of the drainage channels is certainly an adjuvant factor, but other mechanisms are as certainly operative; and these still require much exploration. For example, the state of capillary instability, found so commonly in cases of simple chronic glaucoma, and the lack of vascular compensation in conditions of stress, as seen in some provocative tests, are suggestive of an underlying fault in the capillary circulation, perhaps the same underlying fault which at the angle and the optic nervehead determines sclerotic changes.

The danger, of course, in studying so vast a problem is that in trying to unravel its intricacies we tend to become so specialized, each in our particular pursuit, that a broad and comprehensive view of the whole becomes increasingly difficult. Vascular events monopolize the attention of this investigator, the angle of the anterior chamber of that other. Such indeed is the tendency with the ever accelerating growth of ophthalmology in all its aspects—and indeed of all knowledge. Twenty-five years ago life was easy; today the physiologist, the chemist, the physicist, the mathematician, and the clinician all jostle each other in the market place, each advertising his own wares in his own peculiar language. To make advances in knowledge, specialization on minutiae is undoubtedly necessary; but we must beware lest, in the expanding sphere of thought, each individual discipline moves steadily away not only from a unifying and coördinating philosophy but from cognizance of each other, so that the value of each is vitiated by the exaggeration of its devotees, and its contribution to the solution of the problem as a whole is lost. For the subject of this lecture a comprehensive solution is yet far away, but insofar as it is an attempt to integrate some aspects of the problems concerned, it may perhaps be not without some value.

63 Harley Street (W.1).

CIRCULATORY ASPECTS OF THE GLAUCOMA PROBLEM*

The Second Mark J. Schoenberg Memorial Lecture

JOHN N. EVANS, M.D.
Brooklyn, New York

The opportunity to deliver the second Mark J. Schoenberg Memorial Lecture brings to me a double honor. First, is the privilege to pay his memory respect; second, the privilege of associating my name through all time, not only with his, but also with all those who by these lectures perpetuate his accomplishments. His greatness of character has touched with stimulating effect all who knew him.

It is my purpose to discuss certain mechanical aspects of ocular circulation, which it seems to me can be brought together at this time not only because they include phases of our work in which Dr. Schoenberg was interested, but also because an effort is now in progress, through national and local committees[†] to assemble many of the loose ends which may help us to a clearer view of the symptom complex which we call glaucoma.

It is proposed to discuss phases of problems which have come to my attention through my own and my colleagues' ordered studies.

One must not lose sight of the fact that the word "circulation" may not refer solely to that of the blood-vessel system. It has been employed in referring to lymphatic channels and by Cushing,[1] under the heading of "the third circulation," to describe the cerebrospinal-fluid system.

There is a similarity between the cerebral and intraocular-fluid circulations. The word "circulation" in this sense is, of course, used broadly and was thought by some to be more comparable perhaps to the ebb and flow of a tide, its movements varied by depletions and excesses through tissue demands. Modern studies were necessary to prove a continuous flow from source to outlet.

The intraocular fluid has, to my mind, a major and a minor circulation. The lesser circulation is that of the aqueous chamber, the greater that of the vitreous. Combined they may be called "the fourth circulation."

I suspect the aqueous metabolic interchanges are less massive, although there may possibly be a greater rate of flow than there is in the greater circulation. I believe we should think of the vitreous as dynamically active. We might call it the liver of the eye because of its diverse storage of metabolites.

Perhaps the physiologic course of the fourth circulation would be: arteries through capillary endothelium, to aqueous and vitreous chambers, then posteriorly through the perivascular drainage spaces[‡] and anteriorly through the escape exit of the canal of Schlemm, both to mix with venous blood.[¶]

It is conceivable that the posterior perivascular drainage may mingle with the cerebrospinal fluid of the vaginal space but our data for this idea seem to be insecure. There is evidence that certain bodies are

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† The work of the committee on standardization of tonometers; the work of the committee on the classification of the glaucomas; various tonometer testing stations; establishment of numerous glaucoma clinics.

‡ Priestly Smith[2] established that 2 percent of the outflow was by the posterior route. It would seem to me that 75 percent would be more reasonable in view of our modern ideas of vitreous function as a storehouse for retinal fuel and possibly waste products.

¶ It would seem probable that the vitreous may even receive certain of its constituents from the choroid. This is obviously so in pathologic studies, when we note opacities of the vitreous associated with the appearance of choroidal lesions.

passed from vitreous to orbital tissue. The question of the ultimate avenues of posterior drainage is definitely controversial. The metabolic constitution of fluid at any point in the fourth circulation would, of course, show local variations as it does in blood in accordance with local supply and demand.

Such an apparently static nutrient and waste concentration might indicate that the fourth circulation is designed only as an accessory for tissues of a low metabolic rate but we know that this is, in an overall sense, not so.

The interrelation of glucose interchange of vitreous and retina alone indicates that it may function as part of the retinal nutritive activity.[3] We realize that the actual volume of retina having a high metabolic rate is supplied on its outer face by the active blood bed of the choriocapillaris and that its inner face is also in contact with a relatively greater volume of vitreous.

The characteristics of a reversible elastic gell permit fluid transfer. This indicates that material amounts of nutrient and waste can be interchanged between retina and vitreous. The posterior drainage could thus be more active than past workers have indicated.[4] We need not discuss the properties of the vitreous as a gell and its many metabolic functions. Such studies have not been included in my own investigations.*

If we ask ourselves what are the metabolic demands placed upon the aqueous humor, we must admit that our answer is hypothetical. The cornea receives some benefits in a nutritive sense but the circumcorneal vessels must be a major supply source and there is a material absorption of oxygen through its exposure to the air. The iris, having its own vascular system, is relatively independent in maintaining its own support. All points considered, it would seem that the vitreous

or greater portion of the fourth circulation should receive more attention. I should like to refer to a feature of vitreous structure which may even be quite active physiologically, and more active when pathologic conditions arise, I refer to fluid interchange.

The embryonic system of vessels, which is normally observed before birth, leaves behind infinitely fine fiber strands, that may be looked upon as cleavage planes or avenues of interrupted vitreous continuity. Experiments conducted by me in 1931[5] were suggestive that certain stains injected into the retrolental space were carried from the eye through the perivascular space† regions of the optic nerve and that they passed through the vitreous along lines strongly suggestive of the idea of fiber strands, cleavage planes or channels.‡ This impression is also gained in those cases of rupture of retinal veins when we see an irregular funnel-shaped formation of the escaped blood from an apex at the disc outflaring toward the lens. Active hyalitis sometimes shows a similar arrangement of inflammatory products and also is suggestive of orderly escape paths.

Mere cleavage planes of lessened resistance through the vitreous would suffice for the flow of fluid, the migration of mobile tissue cells, or even for the direction of growth of newly formed vessels.

Our present interest lies in the possibility that under pathologic conditions, the aqueous element of the vitreous might be gradually increased in the deeper parts of the gell, to be released by relatively sudden gushes

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* The gell properties of the vitreous, particularly its changes in volume in response to fluctuations of the acid-base balance, have, in spite of elaborate studies, not advanced our understanding of the mechanism of intraocular pressure changes.

† My studies were made on animals[6] and human beings.[6] The literature dealing with our understanding of posterior drainage was published in 1930.[23] It gave credit to other workers for ideas similar to those presented at this time.

‡ I appreciate that when the acid-base balance of the vitreous is artificially disturbed, fibrillar micella[7] appear, with their long axes at right angles to the posterior lens capsule. We can confine our consideration to vitreous of undisturbed chemical balance, however, and still find evidence of retinal vessel strands. All other experimental methods of studying posterior drainage flow would seem to lead to false conclusions.[8]

through the cleavage planes to the perivascular lymph spaces which drain through the optic nerve.

This condition, with high pressure, can arise in the presence of relatively normal appearing vitreous which is relieved by a gushing forth of fluid and has been seen by all of us when performing a posterior scleral trephination.

As the opening is completed, a very considerable amount of fluid may eventually spurt from the vitreous chamber followed by the appearance of the apparently healthy gell. One can assume that, when the posterior drainage mechanism is obstructed, the iris-lens diaphragm advances, giving rise to the picture of shallow-chamber glaucoma.

The fact that the vitreous vessel remains sagged downward in adult life, would add to, rather than detract from the idea. The influence of gravity on the dependent regions of the vitreous would encourage a pool of the aqueous element below and would require a more elaborate system of escape than would the superior regions of the vitreous.

The vitreous is, according to Duke-Elder,[9] normally in its maximum stage of turgescence in healthy eyes and we must realize that gells act relatively slowly in transmitting water from one region to another. If this is so, acquisition of aqueous must be balanced by an equal escape and, since capillary dilation means increased permeability, we realize that the entire mechanism must be in constant activity.

Large nutritive demands upon the vitreous, although intimately related to similar demands upon the retina, are exceedingly difficult to study or demonstrate. The possible relation of vitreous volume to choroidal volume may seem more obvious.

The choroidal blood bed, representing as it does a much greater volume than the retinal, projects its dynamics into the problem of glaucoma. Moreover, we think of the choroid as a loosely woven mesh of thin-walled vessels in a pialike reticulum which

is so designed that there is little structional restraint on active dilation and contraction of the vessels. It is even possible that the scattered muscle fibers of the choroid may be able to modify the gross thickness of the choroid as a whole. On the other hand, blood volume in the choroid may be varied by systemic changes or by a locally acting mechanism.[10]

It has long seemed to me that we gain a very artificial picture of the form, and hence the functions, of the choroid by the study of the usual histologic preparations. An uncompleted investigation into this question has lent evidence to indicate that the relatively thin appearance of the choroid, which we study microscopically, is in part due to the fact that the standard techniques of enucleation drain most of the blood from the eye.

To demonstrate this, a study was performed on a number of cats and monkeys.*[11] One eye of each animal was enucleated by obstructing the escape of blood of all vessels by the use of the actual cautery or by ligation. The technique was so successful that the orbits after enucleation were perfectly dry and there was no evidence of escaped blood on the globe. The fellow eye, used as a control, was enucleated by the usual technique of dividing tissue and vessels with scissors and scalpel. Both eyes were immediately placed in formalin for fixing and the usual and identical technique was applied to each eye in preparation for histologic study.

The thickness of choroid was measured in cauterized and control eyes only in the region where the macula was visible in the section and where the structures had not been torn or disarranged by the microtome. This precaution was taken in order to be sure that comparable regions of the choroid were measured for thickness.

To cite one example, the eye of a Sooty Mangabey monkey was studied. The average

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* Rhesus and Sooty Mangabey monkeys.

measurements of the thickness of the choroid at the macula in four sections of the control eye, as measured with an ocular micrometer were 0.18, while the average thickness of four cautery-enucleated eyes was 0.273.* Thus, the choroid of the eyes removed without blood loss was 50 percent thicker. Moreover, the larger choroidal vessels were more rounded in cross section than oval, as is usually seen.

It is obvious that such a study is far from flawless in many respects. Yet its implications seem significant. In the living eye, the choroid must be much thicker than indicated in any of our preparations. A relatively drained choroid, as compared to a turgescent choroid, would represent a very great difference in the volume of the intrascleral chamber between these extremes.

A sudden depletion of the choroidal blood bed would be accompanied by a compensatory increase in volume of the vitreous through acquisition of the aqueous element. If this compensatory effect were over-sufficient, a rise of ocular tension would result but only if there was a derangement of the posterior drainage system. We must consider whether such violent variations of choroidal thickness can occur.

The interrelation of the clinically plotted[24] angioscotoma and the mechanism of the perivascular-perineural space has been a help in directing the management of glaucoma cases. Plotting the macula wedge as an index to prognosis and time of operation has been particularly helpful. It would seem reasonable, therefore, to conclude that there is modern evidence for the presence of a posterior drainage exit to support the incomplete evidence of the past.

After considering these features relative to the major division of the fourth circulation, it might seem reasonable to concentrate, in the future, on its physiology as an approach to the many problems of glaucoma.

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* These are units of the ocular micrometer and do not refer to millimeters.

It would be well to accept the idea of a "posterior" and an "anterior" glaucoma rather than to rely on a foreign differentiation of deep- and shallow-chamber glaucoma. We would do well to consider a specific and separate pharmacology for the posterior-chamber type; especially would it be well to consider those agents which modify, the caliber of the uveal and retinal blood vessels.

A logical surgical technique for this type of glaucoma should be devised.[†] Surgical measures may involve the production of a minute area of choroidal atrophy by the application of beta rays, radium, or the thermophore, followed by a small scleral trephination with conjunctival flap over the atrophic area.

The blanching of the skin capillaries and the cerebral vascular changes occurring with emotional shock might conceivably be associated with similar changes of the choroidal vessels. In fact, Cholst[12] has presented experimental evidence of violent circulatory changes in the eye under shock conditions. These alterations provide a possible explanation for volume changes in the vitreous chamber. They might conceivably give rise to those attacks of acute glaucoma which are often associated with acute nervous shock.

Such ideas, of course, are highly speculative in spite of the oft-used phrase "sympathetic hormonal mechanism" and our generally accepted recognition of the fact that nervous shock often precipitates acute attacks. Repeated minor disturbances of sudden choroidal thickening with an inadequate posterior drainage might conceivably be the background for a chronic glaucomatous state.[‡]

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† It is interesting to note that the first successful effort toward the permanent surgical relief of hypertension was made by William Mackenzie (1830), who believed that vitreous changes influenced the site of increased pressure.

‡ The fact that appropriate fluids, deposited experimentally in the anterior vitreous, pass out of the eye through the posterior drainage system in 3 to 4 minutes (my own studies) may possibly have significance.

More detailed study of the choroidal vessels may shed more light on how this turgescence and depletion are brought about. In a group of studies conducted for a different purpose, a so-called capillary sphincter muscle was described.[10] Other workers[13, 14] have shown that like muscles in a number of tissues relax and contract under the effects of therapeutic agents.

We have shown histologic surface preparations suggesting that spasm of such capillary sphincters, when maintained over a long period of time, results in the formation of permanent strictures with greatly distended capillaries. These capillary sphincters have no relation to the hypothetical Rouget cells studied by Krogh.[15] In fact, many modern authors contend that Krogh's work cannot be duplicated. Moreover, the endothelial cells of vessels of the order of capillaries probably cannot swell and shrink[16] enough to modify greatly the volume of the capillary bed.

The passive injection and depletion of the immense choroidal capillary bed is thought by some to be controlled entirely from the arterial side in conjunction with venous activity of similar nature. In any event, the crux of the mechanism deals with the nature and force of capillary blood flow. The difference in the pressure gradient is sometimes accepted as an adequate explanation of capillary blood flow.

This question of forcing a fluid of relatively high viscosity through tubes as small as the capillaries* is not only debated by students of human physiology but also by students of plant physiology who are still trying to explain the origin of the terrific force which causes the sap to rise hundreds of feet to the tops of trees. It would seem, therefore, that a local mechanism is present which could conceivably give rise to sudden or gradual capillary distention and result in increased thickness of the choroid.

The history of efforts to define the form

and functions of the perivascular spaces of the retina and optic nerve has been outlined elsewhere.[5] One is impressed with the similarity of these early studies to the efforts of the neuro-anatomists to investigate the cerebral perivascular spaces. At first, all was a confusion of artefacts created by techniques which were little understood.

The simple definition of the retinal perivascular spaces was, to my mind, first accomplished by the reliable technique of Wegefarth, one of Harvey Cushing's associates. He used a Prussian-blue method[17] which was radically different from the Prussian-blue methods previously employed.[†18]

Held[19] succeeded in devising a special stain and technique whereby he was able to study the minute histology of the cerebral perivascular spaces, and Kruckmann,[20] working in association with him, apparently accomplished the same result for the retinal spaces. As far as I know, however, Kruckmann's work has not been duplicated. In spite of this lack of corroboration, it is likely that his interpretations are correct. It has been pointed out elsewhere[22, 23] that there is other clinical and pathologic evidence of the existence of retinal perivascular spaces, and for other aspects of vitreous function.

Plotting of angioscotomas in all their physiologic and pathologic manifestations[22] has now been repeatedly duplicated by many workers all over the world. It would, therefore, seem justifiable to accept the hypothesis by which the studies were interpreted as reasonable. That hypothesis postulated primarily a perivascular space relation and an ultimate interruption of the retinal synapse.

CONCLUSIONS

1. The intraocular-fluid system may be looked upon as a fourth circulation (1. vas-

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* On occasion so small as to permit only a single red cell to pass.

† I attempted to duplicate the technique of all earlier workers but my own studies of the retinal perivascular spaces confirmed the findings of Wegefarth.[17] Moreover, other workers (Magitot, Bailliart) have found obstruction to the retinal flow due to periphlebitis.[21]

cular; 2. lymphatic; 3. cerebrospinal fluid [Cushing]).

2. The vitreous may take a much more active part in the nutrition and in the pressure regulation of the eye than has heretofore been realized. There may be a large variation in the amount of the aqueous element of the vitreous during emotional shock and in general physical states.

3. The rapid passage of the aqueous element of the vitreous is probably greatly facilitated by "cleavage planes" within the substance of the vitreous. These cleavage planes or channels are the remnants of the embryonic vitreous vascular system.

4. There is considerable evidence to support the idea of a highly efficient and active posterior drainage system.

5. Marked variations in the volume (thickness-cross section) of the choroid can take place under a wide variety of conditions of systemic and local origin. Such variations, in the presence of obstructed posterior drainage, are capable of causing violent and rapid rises of intraocular pressure.

6. The capillary sphincter "muscle" of the uveal blood vessels provides a local mechanism which may be responsible for rapid changes in choroidal volume under general physical and psychologic stimulation.

7. These conceptions, supported by a great mass of experimental evidence, help to explain posterior (shallow-chamber) glaucoma and indicate the need for especially designed pharmacologic and surgical measures.

23 Schermerhorn Street (2).

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GLOMUS CELLS IN THE HUMAN CHOROID AS THE BASIS
OF ARTERIOVENOUS ANASTOMOSES*

Arnold Loewenstein, M.D.
Glasgow, Scotland

Harvey's thesis that the blood circulates from artery through capillaries into the veins is still the basis of our knowledge, although the last decades have shown that this truth is not without important exceptions. It has been known for 70 years at least (1877) that local short circuits may exist between artery and vein, which eliminate (more or less) the capillary system. So strange did this appear at first, that such an authority in the sphere of vessels as Thoma of Dorpat declared, in 1892, permanent arteriovenous anastomoses to be theoretically impossible, and Mall (1906) added that they would mean catastrophe if they should exist.

The careful investigations of Hoyer (1877), Grosser (1902), and Von Schuhmacher (1904), however, have proved that arteriovenous anastomoses exist physiologically in certain animal tissues, and that they can be opened and closed. Thus the blood stream takes the capillary path when the short circuit is closed, or runs through the opened arteriovenous anastomoses directly from the artery into the vein (figs. 1a and 1b). As a rule, the lumen of the arteriovenous anastomoses is changed quantitatively but efficiently, and a complete closure does not occur.

These arteriovenous anastomoses at first were virtually ignored by anatomists, physiologists, pathologists, and clinicians. Then, interest was aroused by the initiative of Hans Hawlicek, a surgeon, who realized the great importance of this double blood circulation.

Arteriovenous anastomoses were soon the object of careful research, the classical papers being by Clara (1927), Spanner (1932), Clarke and Clarke (1934), Masson

(1935). Only the most important papers by these authors are quoted.

Arteriovenous anastomoses were found in many animals.
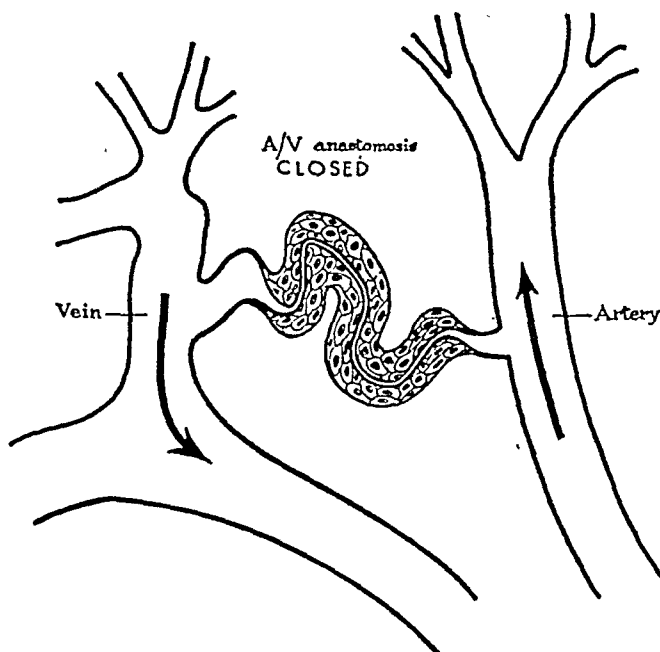
Fig. 1a (Loewenstein). The blood stream takes the capillary path when the short circuit is closed.
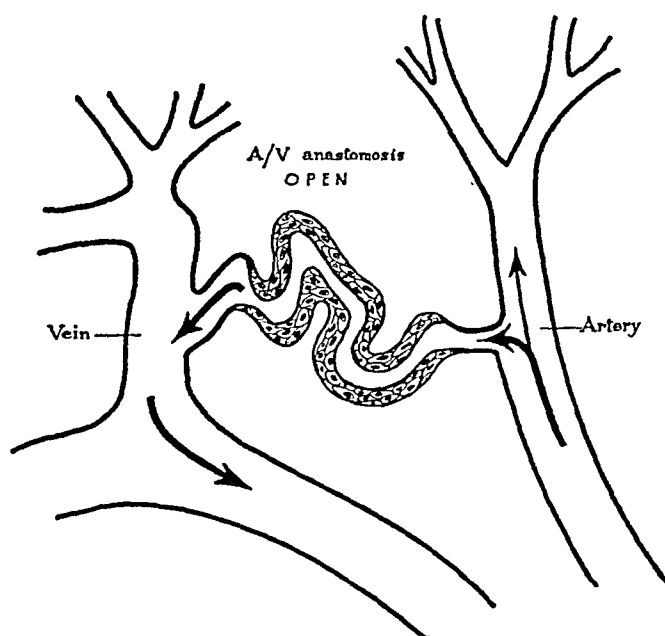
Fig. 1b (Loewenstein). When the anastomosis is open, the blood stream runs directly from the artery into the vein.

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Fig. 2 (Loewenstein). Glomus cells in the arterial walls of a normal choroid. (Hematoxylin-eosin. ×300.)

In man, they were discovered in the pulp of the fingers and toes, the nailbed, the corpus cavernosum of the penis, in the glomus coccygeum, the villi of the intestine, and in other tissues. Masson associated the normally present arteriovenous anastomoses of the fingers with painful small tumors, enveloped in a rich muff of myelinated and nonmyelinated nerve fibers, which he called "glomus neurovasculaires" (1937).

The cells which are responsible for the mechanism of arteriovenous occlusion are of an epithelial character, and are placed external to the endothelium. They are found frequently in 4 to 5 layers, and are of very characteristic microscopic appearance. They are sharply outlined, the cytoplasm is clear, the nucleus is round and central. No membrana elastica interna is seen in the arteriovenous anastomoses.
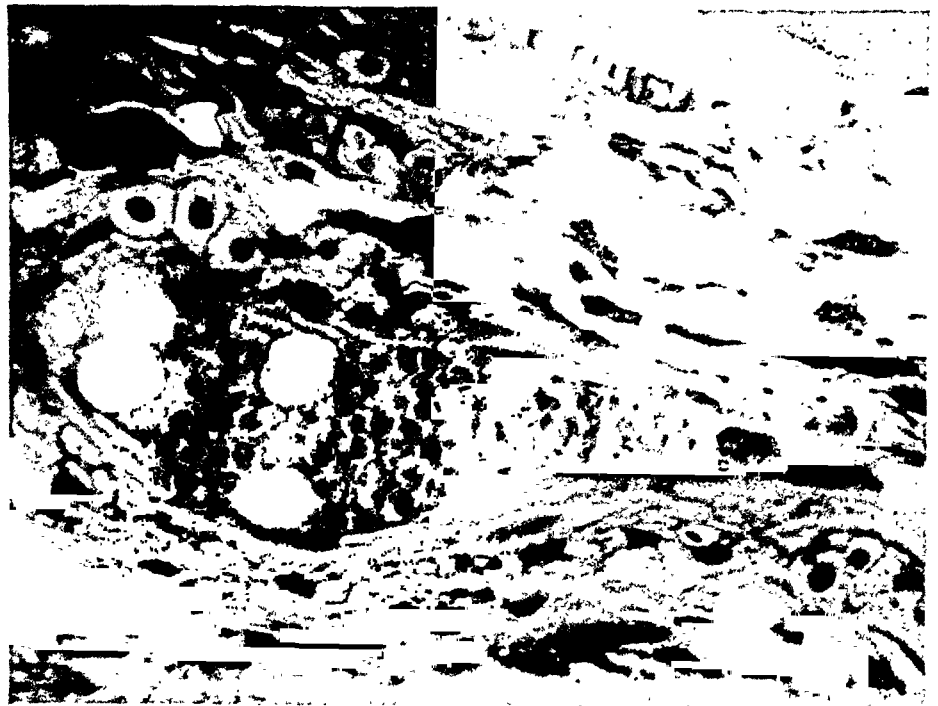
Fig. 3 (Loewenstein). Glomus cells in arterial wall of the choroid in a hypertensive case. (Hematoxylin-eosin. ×300.)

Although the arteriovenous anastomoses are more frequent in old people, Masson has found them in the fetus of 4 to 5 months, and in the newborn.

We are indebted to Clarke for the introduction of a technique permitting continuous observation of the living arteriovenous anastomoses under high magnification by a glass chamber implanted in the rabbit's ear. The Clarkes thus discovered independent

in the middle and outer choroidal layers.

These cells (fig. 2) are polyhedric or round. In diameter they are between 10 to 20 μ. sharply delineated, with a smooth, evenly dark-stained cellular membrane. They have a strikingly clear cytoplasm. The nucleus is central, darkly stained by hematoxylin, and without a visible nucleolus. Where these cells are found in groups they appear closely attached to each other, divided by the sharp

Fig. 4 (Loewenstein). Fatty, swollen endothelial cells in an atheromatous choroidal artery. Here the nuclei are granular, pale, and most eccentric. Note the granular cytoplasm. (Hematoxylin-eosin. ×300.) (A) Hexagonal cells. (B) Bruch's membrane. (C) Choriocapillaris.

spontaneous contraction and dilatation of the arteriovenous anastomoses, which is faster than the arterial. The rate of contraction is different in arteriovenous anastomoses of close vicinity. Dilatation is as rapid as contraction.

Their autonomy is apparent and places the arteriovenous anastomoses into a special category in the whole circulatory system. Masson compares them anatomically and physiologically with the heart.

So far, arteriovenous anastomoses have been discovered in a restricted number of tissues only. I have observed, in the choroid of both normal and pathologic eyes, large clear cells of a certain uniformity. They were present in groups of medium- and large-sized choroidal arteries, and therefore

cellular membrane. Their whole appearance is reminiscent, in fact, of epithelial cells (fig. 3).

I have found them in choroidal routine, celloidin sections stained with hematoxylin-eosin, in Van Gieson, Masson, and Mallory stained slides. They are invisible in Weigert's elastica staining. They are located in the posterior pole area, and are absent in the anterior choroid.

I have also seen them in the intrascleral part of the posterior ciliary arteries of normal eyes. Their frequency is greater in hypertensive cases (fig. 3). They were especially rich in the posterior part of the choroid of an eye in which a metastatic malignant growth in the orbit pressed on the posterior portion of the sclera.

This histologic picture is very striking. The only pitfall might be the presence of huge swollen endothelial cells in choroidal arteries, the so-called pseudoxanthoma cells, in cases of malignant hypertension. But this "clear" cytoplasm is granular, the nucleus is pale and eccentric. Fat staining makes the differentiation complete (fig. 4).

The cells described correspond to those depicted by Clara, Spanner, Masson and others, and are called "glomus cells" or "epithelial muscle cells." I am unable so far,

Some of these vessels with epithelial muscle cells have an inner elastic membrane; others have none.

Epithelial muscle cells are found at a
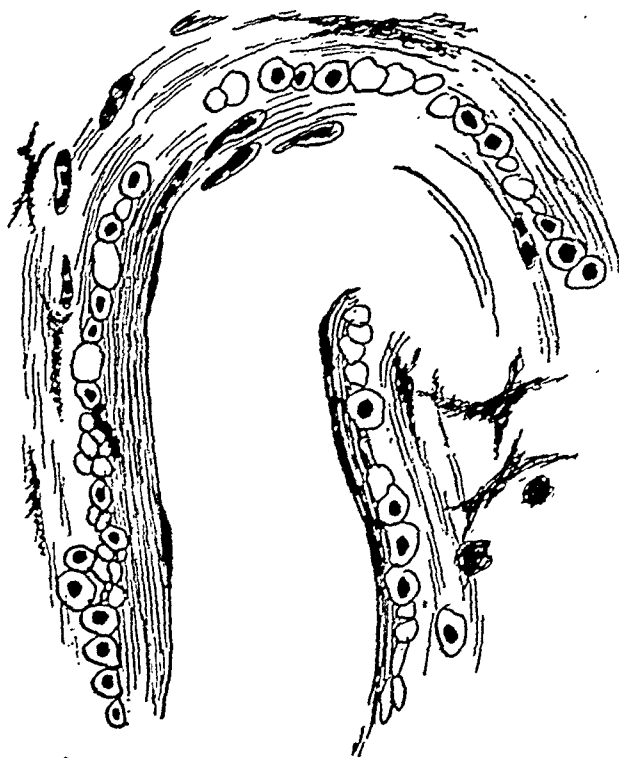
Fig. 6a (Loewenstein). Choroid in flat, Mallory stain, oil immersion. A rich mass of glomus cells in the wall of an artery. Difficult to distinguish between small, smooth muscle cells and epithelioid muscle cells.

Fig. 5 (Loewenstein). Flat section of the choroid, posterior pole. Epithelioid muscle cells in the wall of a huge vessel. Note isthmus narrowing. (Hematoxylin-eosin. ×300.)

however, to reconstruct a complete picture of a clear-cut arteriovenous anastomosis with its arterial source, with the short circuit and the vein, like many of the other investigators of arteriovenous anastomoses. Technical difficulties vary in different tissues.

The glomus cells, both single and grouped, are visible in the sagittal sections of the choroid of the macular area, which has been embedded as flat as possible in celloidin, and sectioned in this way. The glomus cells are especially frequent where the arteries are tortuous and change the breadth of the lumen abruptly, sometimes from 1 to 4 μ (fig. 5).

Fig. 6b (Loewenstein). Choroid in flat, hemalum, oil immersion. Epithelioid cells.

certain distance from the endothelium, which itself is lined with the empty shells of cells (figs. 6a and 6b). These cells might be the circular smooth muscle fibers, cut eccentric to the nucleus. On the other hand, I am not sure whether these shells do not belong to eccentrically sectioned epithelial muscle cells.

The exact relationship between glomus and smooth muscle cells has not been determined so far. In the choroid both cell types might occur intermixed.

I have tried to find the structure of the arteriovenous anastomoses in choroid in bulk. For this purpose, the macular area of the choroid is first depigmented with potassium permanganate and oxalic acid; then the specimen is stained with a dilute hemalum solution for 24 hours and cleared in glycerin. The rich mass of nuclei is rather disconcerting and no counter staining therefore appears indicated.

In this way I was able to discover several groups of epithelial muscle cells (figs. 7a and 7b). They are grouped round a cystic empty space. The cells are of varying size, mostly polyhedric, sharply outlined; the cell membrane is sharp. Delineation between the single cells is well marked. The nuclei are dark, round, and generally central. These epithelial muscle cells stand out distinctly against the background of the smooth muscle fibers of the arterial wall. In a few instances only, there are more nuclei of the type described in a big cytoplasm, without being separated by cellular membranes.

These cells are at various depths—therefore the prospects of photomicrographic reproduction are poor. The dense background of nuclei adds to the photographic difficulties. These cell groups are similar, indeed, to all that has been demonstrated of arteriovenous anastomoses previously.

Generally, we must expect to recognize histologically the large dilated glomus cells only, while the contracted ones are oblong or spindle-shaped. There is little hope of identifying the latter two shapes in a stained
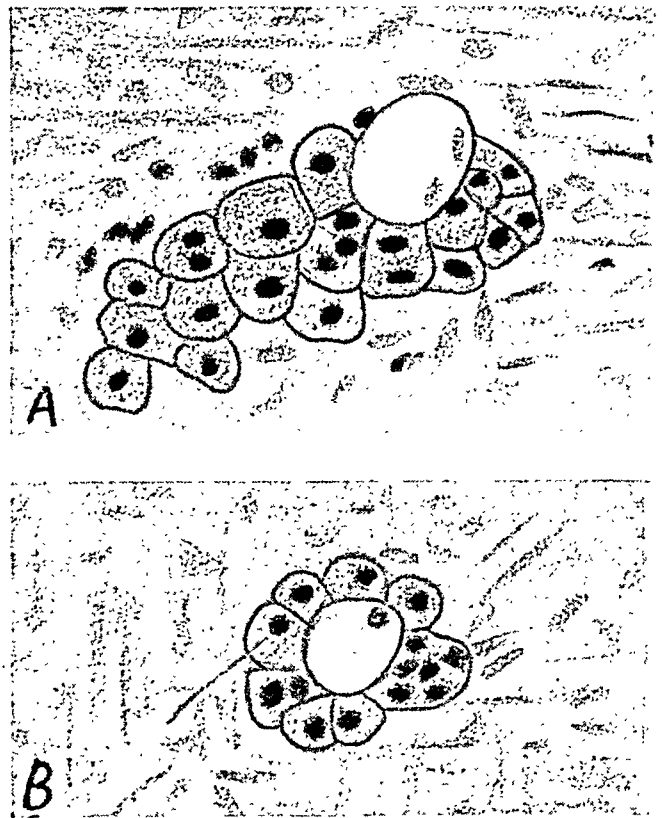
Fig. 7 (Loewenstein). Choroid in bulk, macular area, depigmented, hemalum, 24 hours, ×300, seen from scleral side. (A) Epithelioid muscle cells surrounding a cystic space. (B) Smooth muscle fibers of a middle-sized choroidal artery.

bulk specimen. But even in sections, I was unable to discover anything apart from the epithelial form of the glomus cell. We have found, therefore, a part only, and possibly a small part, of the motive mechanism of the
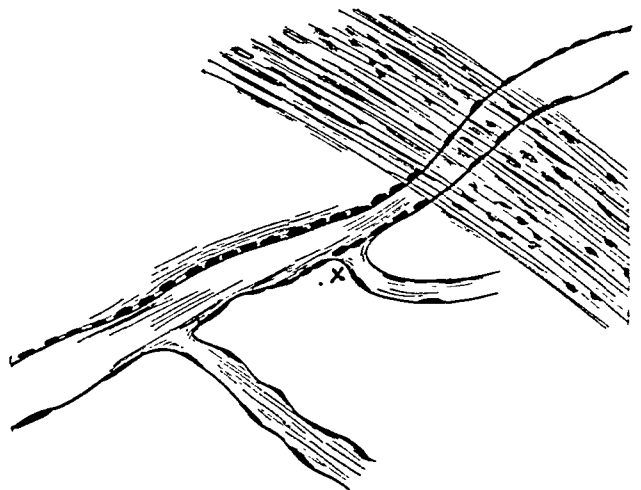
Fig. 8 (Loewenstein). Choroid in bulk, depigmented, teased, hemalum, 24 hours, ×300. One middle-sized choroidal artery shows narrowing at X. The muscle cells are dense, bigger, and darker at the place of contraction. A broad ciliary nerve branch crosses the vessel.
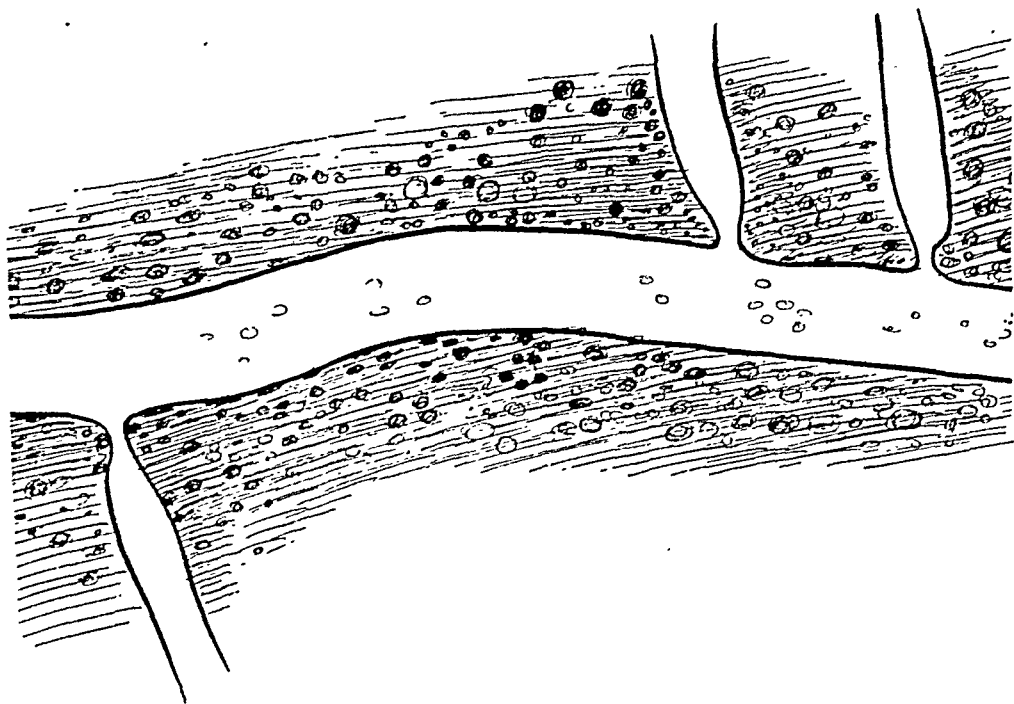
Fig. 9a (Loewenstein). Retina in bulk. Hemalum overstained and cleared. ×300. Sphincter contraction of branches. Note ganglion and glial cells in the superficial retinal layers.

choroidal blood circulation. That includes all previous research as well.

The investigation of the bulk choroid was continued by teasing the stained choroidal tissue with two needles, and clearing the shreds with glycerin.

I found, while following the course of a middle-sized artery, that the lumen 45 to

Fig. 9b (Loewenstein). Hypertensive retinopathy. Bulk specimen, hemalum, 24 hours, ×150. Sphincter contraction at the branching place of arterioles. Note retinal ganglion and glial cells.

50 μ diameter, narrowed down for a short distance to 15 μ and dilated again to the same width of 50 μ, that is a considerable contraction (fig. 8). It is interesting to observe that the muscle cells in the contracted area are denser, bigger, and appear darker than in the dilated part. We conclude that contracted smooth muscle cells in an arterial wall appear different histologically from the unstimulated ones.

Spastic changes in retinal arteries are supposed to exist and have even been observed in progress ophthalmoscopically. But no contraction of such degree has ever been seen ophthalmoscopically.

On the other hand, sphincter contraction has been described by Evans (1947) as an abrupt narrowing of certain retinal capillaries where they joined the vessel of the next order. I have shown this phenomenon at the Oxford Congress (figs. 9a and 9b) in retinal bulk specimens stained with hemalum.

The same sphincteric contraction is visible in the choroid (fig. 10) in bulk specimens. Blood transport in the district of arterioles,
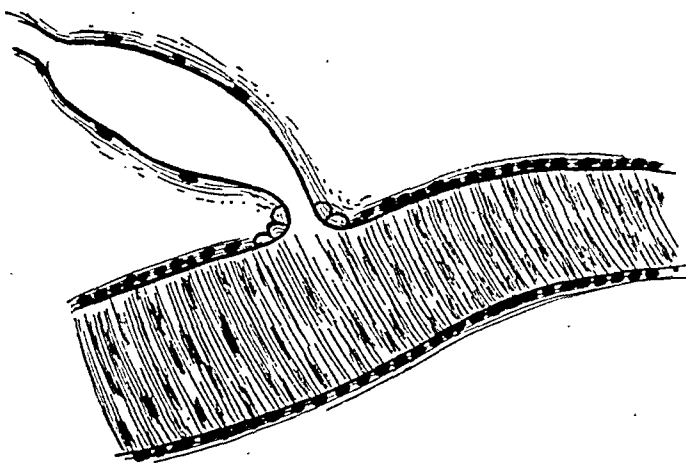
Fig. 10 (Loewenstein). Choroid in bulk, hemalum, 24 hours, overstained, ×300. Ring muscle fibers, no glomus cells, sphincter contraction.

metarterioles, and capillaries is far more complicated than was supposed. The brilliant investigations of Chambers and Zweifach (1946) have proved that a sphincter muscle is present at the union of a metarteriole and

an "anastomosis" (not our arteriovenous anastomoses).

I have shown at the same meeting in Oxford (1946) swollen, granular, endothelial cells in capillaries, precapillaries, and ves-

Cushion cells in Retinal Arteriole

675×
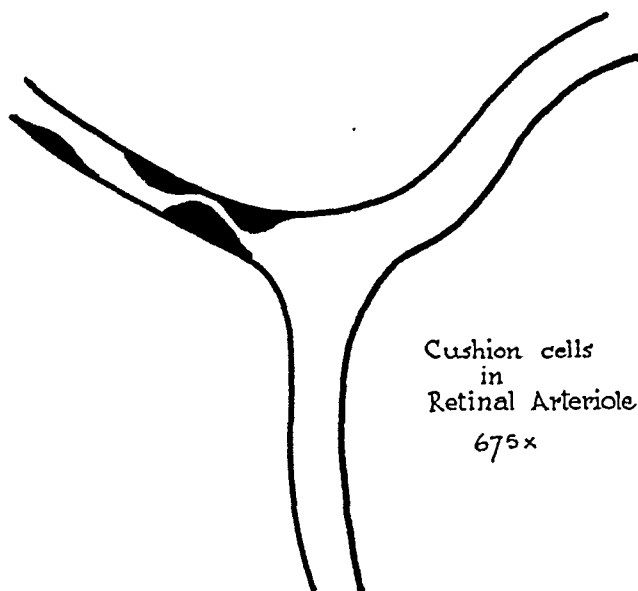
Fig. 11 (Loewenstein). Cushion cells in retinal arteriole. (×675.)

sels of unstained cleared retina in bulk at the point of branching arterioles and confluent vessels. I have suggested that these cells (fig. 11) swell and decrease, and regulate the local retinal blood supply according to need. I have not seen anything like arteriovenous anastomoses in the retina, so far.

We have seen, therefore, in the retina, two kinds of appliances to control the blood stream—the sphincter muscle and the swell or cushion cells, while we have found in the choroid epithelial muscle cells, the most probable base of arteriovenous anastomoses. The sphincter muscles of the choroidal arteries are similar to those found in the retina.

I am confident that further investigation will reveal other refinements in the regulation of the bloodstream.

It has been repeatedly stated that the choroidal structure is reminiscent of a corpus cavernosum. Filling and emptying of the biggest corpus cavernosum of man, that of the penis, is linked with existent arteriovenous of the arteriæ helicinæ.

The normal choroid is found sometimes histologically to be reduced to a thin tissue of 20 μ, while I have recorded not infrequently in the macular area of other equally normal eyes, a thickness of 200 μ.

We conclude that a regulator mechanism is able to dam up the blood and to fill the huge choroidal cavernous spaces, so impressive in flat sections or depigmented bulk specimens. It is credible, on the other hand, that arrangements are provided to evacuate this accumulation of blood in an emergency. Adaptation of the degree of filling of the cavernous system to the influx of blood and the outflow of intraocular fluid is necessary to keep the intraocular pressure at a certain level with inconsiderable and mostly regular oscillations.

One must not overlook that the most delicate tissues of the body are embedded in the hard, unyielding scleral capsule. These delicate tissues are exposed to the danger of being damaged by the increased tissue pressure, unknown mostly to soft body areas, unless a safety valve is provided. It seems that the arteriovenous anastomoses in the choroid offer sufficient possibilities to render innocuous a momentary influx of blood into the cavity of the globe. Quick reaction is therefore strictly indicated.

Such a regulation is very likely to be subject to nervous influence. Masson has, indeed, shown the highly developed and nervous muff enveloping the arteriovenous anastomoses. A similar network was shown recently by Nonidez (1942) in arteriovenous anastomoses of the sympathetic ganglion of the dog.

The nerve fiber system spread through the choroid appears very dense when studied in depigmented bulk specimens. So far, no histologic distribution of nerve fibers in epithelial muscle cells has been demonstrated successfully in the choroid. It is most probable that the function of the choroidal arteriovenous anastomoses opening and closing of the short circuits, are acting under nerve influence as are the other arteriovenous anastomoses (Clarke).

It seems different with vascular new growth in the choroid; for example, an angioma. This blastoma is seemingly not included in and subject to the free play of filling and evacuating of the blood spaces under nervous direction. We often find, therefore, increased intraocular pressure in such cases of angiomatous choroidal growth (Sturge-Weber syndrome).

It would be of great interest to observe a pulsation of the choroidal arteriovenous anastomoses resembling the spontaneous autonomous contraction found by Clarke in the rabbit's ear. I rather doubt whether the enlargement of slitlamp microscopy of the fundus will suffice. Clarke used high-power microscopy. But an eventual success will depend on the size of the pulsating area and on the intensity of the pulsation if it really exists.

There is a highly developed switchover system of the blood circulation in the tissues of the eye, basically different in conjunctiva, choroid, and retina. I have not studied so far ciliary body and iris.

The reserve vessel system in the conjunctiva has about 20 times the volume of that normally visible (Loewenstein, 1944), and will form the subject of a further paper by me. The retina, an infinitely more delicate and vulnerable tissue, has a proportionately delicate capillary mechanism in the form of endothelial swell cells, reinforced by the action of sphincters (Evans). The choroidal switchover system seems to be the most extensive.

I suspect that other devices for this purpose exist besides those described here.

Many puzzles remain unsolved and invite the investigators to continue their research in this direction. Last, but not least, it is possible that a pathologic finding might give a lead to the anatomist and physiologist. Arteriovenous anastomoses, glomus cells, respectively, are undoubtedly more frequent

in old people than in younger ones. They are found more often in hypertensive eyes than in normal ones. The process of causation remains obscure until now. It may be that their presence in the retrobulbar tumor case throws some light into the dark. More material must be collected.

I was unable, so far, to reconstruct the course of arteriovenous anastomoses from artery to vein, but I am hopeful that continued series of sections of depigmented choroidal tissue from the macular area will make it possible.

At present the first steps only have been made in this direction.

SUMMARY

Large polyhedric cells are described in the periphery of large and medium sized choroidal arteries, with a central, round, dark nucleus, a clear cytoplasm, and a smooth cell membrane. These correspond to the epithelial muscle cells or glomus cells which are the basic elements of the arteriovenous anastomoses found in several tissues of animals and man. They are present in the posterior segment of the human choroid. They occur singly as a rule, in sagittal sections, but are found linked in flat sections and are present in epithelioid units in choroidal bulk specimens.

The choroidal glomus cells were found more frequently in hypertensive cases, and were numerous in a case of retrobulbar tumor with pressure folds.

The cells form part of the ocular tissue mechanism to direct the bloodstream to the areas of need, as do sphincter muscles at the branching place of arterioles in retina and choroid and the endothelial swell cells in the retina.

Arteriovenous anastomoses appear to be the basis of the choroidal corpus cavernosum. Rapid opening and closing of these short circuits is essential for the maintenance of the intraocular pressure and is dependent on the rich nerve fiber plexus demonstrated in other glomus growth.

The University, Glasgow.

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PANOPHTHALMITIS CAUSED BY ESCHERICHIA COLI COMMUNIOR*

RUSSELL J. NICHOLL, M.D.
Cleveland, Ohio

AND

D. LOCATCHER-KHORAZO, M.D.
New York

Escherichia coli is rarely the cause of ocular infections. Its presence in conjunctival cultures is in most instances a contamination. Eyre[1] (1897) found this organism in about two percent of cultures of normal conjunctival sacs, but in more recent studies by Khorazo and Thompson[2] (1935) it was present only three times in 1,122 cases. In rare instances it does produce inflammatory changes as evidenced by severe suppurative inflammation.

Français[3] (1935) reported two cases in which the organism was pathogenic. His first patient was a man aged 71 years, who, as a result of prostatic obstruction, developed an Escherichia coli cystitis three days following cataract extraction. A panophthalmitis occurred and the enucleated eye showed Escherichia coli. The second case was in a two-month-old child with a congenital dacryocystitis. The purulent exudate was filled with Escherichia coli. Catheterization of the nasolacrimal duct resulted in cure. The same author experimentally produced corneal abscesses, iridocyclitis, and panophthalmitis in rabbits and guinea pigs by the injection of Escherichia coli.

Sanyal[4] (1929) reported a form of conjunctivitis caused by Escherichia coli which was not uncommon in young men laborers of Calcutta. The infection appeared to be transmitted directly from the fingers. The typical attack began as an ordinary conjunctivitis and in a day or two assumed a moderately severe character. The lids became red, swollen, and tense, the upper overhanging the lower. The bulbar conjunctiva was swollen and infiltrated and there was intense injection of the palpebral conjunctiva which had a velvety appearance. There was a copious discharge from the eyes, at first mucopurulent but later of a purulent character. There was little pain except for a dull browache. Corneal ulceration occasionally followed.

Owens[5] (1946) recently reported a case of a severe corneal abscess caused by Escherichia coli which responded to local treatment by streptomycin.

The following is the report of a case of unilateral panophthalmitis caused by Escherichia coli communior and unsuccessfully treated with penicillin and sulfadiazine.

REPORT OF CASE

History. The patient was a 48-year-old housewife who had always enjoyed good health and had never had any previous ocular complaints. Twelve days before her first visit to the out-patient department, she experienced a stabbing pain in the right eye. The following day, the eye became inflamed. Two days after the onset of the illness, she consulted a local ophthalmologist.

His report stated that the lids of the right eye were swollen and red. The globe was under tension. The anterior chamber was shallow and the pupillary area was obstructed by an opaque hemorrhagic mass. The pupil did not react to light. Vision was limited to light perception. The temperature was 99.2°F.

Two hundred thousand units of penicillin in beeswax were administered twice daily

and she also took 4 to 5 gm. of sulfadiazine by mouth each day. Urinalysis revealed a three plus reaction for sugar and injections of protamin zinc insulin were given. The eye gradually improved and she became able to distinguish form and color.

A sudden, sharp pain was again experienced in the eye eight days after the treatment was instituted and the lids became ▄▄▄▄ ▄▄▄▄▄▄ On the following day there was fluctuation of the upper lid at the orbital ridge. Following an incision made into this area, there was escape of sero-sanguinous fluid and relief of pain. On the 12th day of the infection, she was referred to the clinic and admitted to the Institute of Ophthalmology.

Examination. On admission to the hospital, the vision in the *right eye* was limited to light perception with questionably accurate projection. The lids were greatly swollen, tense, and red. The upper lid was involved more than the lower. There was a slight sero-sanguinous drainage from the incision over the upper temporal orbital margin and a small amount of purulent bloody discharge on the lid margins. The lids could not be satisfactorily opened during examination because of the intense edema and pain.

The conjunctiva was deeply congested and chemotic. The cornea was steamy and of a grayish color. About 0.5 mm. of the peripheral cornea was relatively clear. The anterior chamber appeared shallow but no details could be seen. The intraocular pressure could not be estimated.

The vision of the left eye was 20/20. The globe and adnexa were normal.

General examination was noncontributory. At this time the fasting blood sugar was 86 mg. percent. Subsequent examinations and four-part glucose, acetone, and diacetic acid urine examinations were compatible with mild diabetes.

A gynecologic examination failed to reveal any evidence of a focus of inflammation in the pelvis.

X-ray studies showed some cloudiness of the right frontal and right ethmoid sinuses and some thickening of the lining membranes of the antra. An ear, nose, and throat examination showed no definite focus of infection. The chest X-ray film was negative. The mouth was edentulous.

Frei, Brucellergin, and tuberculin (1:1,000) skin tests and the blood Klein test were negative. The complete blood count was within normal limits.

Direct smears and cultures (blood-agar medium) were taken from each eye at the time of admission.

Treatment consisted of the instillation of 2-percent atropine sulfate solution to the right eye three times a day. Penicillin ointment (1,000 Oxford units per gm.) was applied to the conjunctiva and hot compresses were used three times daily. Twenty thousand units of penicillin, intramuscularly, one gm. of sulfadiazine, and one gm. of sodium bicarbonate were given every four hours. A sulfadiazine blood level of 10 to 12 mg. percent was obtained.

Three days after admission to the hospital there was no essential change in the appearance of the lids or globe except that a small white necrotic-appearing area about two mm. in diameter was noted in the sclera and conjunctiva in the four-o'clock meridian about three mm. from the limbus. On the sixth hospital day the lens had disintegrated and the anterior chamber was very deep. Evisceration of the right eye was performed on that day.

LABORATORY STUDIES

Morphologic characteristics. A moderate number of polymorphonuclear cells and Gram-negative bacilli were present in direct smears from the right lower cul-de-sac. The lid and conjunctiva of the right eye revealed a pure culture of Gram-negative bacilli which were nonacid fast, nonspore forming, and slightly motile. With the aid of standard biologic tests, the organism was identified as Escherichia coli communior. Lid and

conjunctival cultures of the left eye showed a nonpathogenic Staphylococcus albus.

Direct smears made from the eviscerated contents revealed Gram-negative bacilli. Pure cultures of Escherichia coli communior identical to those obtained from the conjunctiva and lid margins at the time of admission to the hospital were grown from cultures taken at the time of evisceration.

Animal inoculation. An emulsified culture of the isolated bacillus was prepared and the following animal inoculations were carried out:

MOUSE. Adult white mice died within 18 to 24 hours following the intraperitoneal injection of 0.1 cc. of an 18-hour culture. Escherichia coli communior were recovered from cultures taken at autopsy of the mice.

GUINEA PIG. An intraperitoneal injection of 0.5 cc. was made, with no effect.

RABBIT. Adult white rabbits were used for intraocular studies. Injection of 0.01 cc. of an 18-hour culture of the organism into the cornea of a rabbit produced a fulminating panophthalmitis within 48 hours as did 0.05 cc. injected into the anterior chamber. The lesions in the rabbit presented changes in the globe similar to those found in the patient. When the cornea was inoculated by scarification with a needle which had been dipped into the culture or by instilla-tion of the culture into the conjunctival sac, infection did not result.

Sensitivity to antibiotics. By standard in vitro bacteriologic methods, the organism was found to be resistant to penicillin but was markedly sensitive to streptomycin.

Pathology. Fixed sections of the specimen obtained at operation showed an acute inflammatory reaction, a few Gram-negative bacilli, and early organization of a hemorrhage.

CONCLUSIONS

Although very rare, this case demonstrates the possibility of Escherichia coli communior as an etiologic agent in panophthalmitis. It also shows the importance of obtaining direct smears and cultures from the conjunctiva as an aid in determining the cause of intraocular infections. Judging from the behavior of the transference of the organism to rabbits, it seems probable that this infection was metastatic.

The organisms were not sensitive to penicillin but were found to be sensitive to streptomycin. Had the nature of the infection been determined early, and an adequate supply of streptomycin been available, the infection might have been successfully combatted.

10515 Carnegie Avenue (6).
635 West 168th Street (32).

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INTRAORBITAL MENINGIOMAS

A Clinicopathologic Study*

Winchell McK. Craig,[†] M.D., and Louis J. Gogela,[‡] M.D.
Rochester, Minnesota

Until recently, intraorbital meningiomas have been almost exclusively a problem of the ophthalmologist. With the demonstration of an intracranial route of approach for their removal, intraorbital meningiomas now have come to be fully as important to the neurosurgeon as are meningiomas elsewhere.

Primary intraorbital meningiomas are comparatively rare; they have been recognized and removed surgically in 17 cases at the Mayo Clinic. Secondary, or invading intraorbital meningiomas occur more frequently.

The first report with tangible evidence of what may well have been an intraorbital meningioma was that of Scarpa[1] in 1816. He described an intraorbital growth which seemingly had its origin within the sheath of the optic nerve. This tumor was removed successfully without injury to the eye. A few years later, Wishart[2] described a similar growth in some detail.

Byers,[3] in 1901, collected from the literature of the 19th century reports of 102 intradural tumors which occurred within the orbit. Although his work was comprehensive, an accurate appraisal of the nature and the frequency of these intradural tumors was precluded by the then-existent confusion in the histopathologic identity of the various neoplasms. Most, undoubtedly, were gliomas and sarcomas.

Hudson,[4] in 1912, placed the classification of primary tumors of the optic nerve on a sounder footing in that he grouped them into three categories: gliomas, endotheliomas, and fibromas. With increasing recognition of the meningioma or endothelioma as such, reports of cases of intraorbital meningioma subsequently appeared in the literature with greater frequency. Goar,[5] in 1926, and Mayer,[6] in 1928, fixed the total number of intraorbital meningiomas described in the literature at about 40. However, whether the intradural tumors had had a primary origin within the orbit or whether they had extended into the orbit from an intracranial source had not been determined in many instances.

The origin of these tumors still is somewhat indefinite. Since the classical article on meningeal tumors by Schmidt,[7] in 1902, these growths have been thought to arise from clusters of arachnoid cells. Cushing and associate[8] pointed out that "from a histopathological standpoint, there is no apparent reason why the arachnoid layer of the optic nerve sheath should be any more exempt from tumefactions than the intracranial arachnoids."

It was the opinion of most of the earlier workers that the endotheliomas and psammomas of the orbit took their origin from the optic sheath or the sheath of Schwalbe.[9-11] The intraorbital meningioma on which Heed[12] reported was intimately attached to the pial sheath of the nerve, and it seemed that the growth sprang from this tissue.

Some of these tumors apparently arise within the optic sheath and then break through into the orbital cavity as pointed out by de Lapersonne.[13] Van Duyse,[14] in 1923, felt that his particular example was a tumor of peridural origin with secondary invasion into the optic sheath. Dandy[15] des-

cribed bilateral, collarlike endotheliomas which extended both anteriorly and posteriorly from their sites of attachment at the point of reflection of the dural sheath at the optic foramina. Cushing and Eisenhardt[8] stated that the favored point of origin of these tumors was unknown, but considered the "vicinity of the foramen" the most likely site.

Some investigators have suggested other sites of origin than the sheath of the optic nerve, or sheath of Schwalbe. Wiegmann,[16] in 1929, reported that he had removed an intraorbital meningioma. He concluded that it was "impossible" for the growth to arise from the optic sheath in view of the fact that the tumor lay outside the bellies of the muscle. Benedict,[17] in 1923, also removed a meningioma which was situated "outside the muscle cone," and Levkoeva,[18] in 1931, reported a "free-lying" intraorbital meningioma.

Levkoeva[18] concluded that the meningioma in his case had probably arisen from the "dura mater of the orbit." "However," he stated, "its development from the periosteum is not to be excluded." Others also have suggested a relationship of the orbital periosteum to meningiomas. Schreck,[19] in 1939, after studying 15 intraorbital meningiomas removed at the University of Heidelberg, concluded that these tumors arise not alone from the sheath of the optic nerve, but can occur "completely separated and free with the orbital tissues."

As was clearly pointed out by Cushing and associate,[8] meningiomas possess a tendency to expand along the lines of least resistance and force their way into "all anatomical crannies and pockets." This fact precludes critical evaluation of many of the so-called intraorbital meningiomas which have been reported in the literature. For example, the meningioma that Byers[3] reported, which had supposedly originated within the orbit, was found later at necropsy to have (very probably) extended through the intervaginal space into the orbit from its primary site along the olfactory groove. Cushing's series of 29 meningiomas of the olfactory groove included one meningioma which encroached on the intraorbital contents through the optic foramen.

Meningiomas of the sphenoidal ridge may cause unilateral exophthalmos and must be differentiated from intraorbital tumors. Elsberg and associates[20] also warned that tumors producing unilateral exophthalmos may have extended into the orbit through an enlarged superior orbital fissure or may have destroyed bone and penetrated into the orbit. However, other meningiomas, such as the suprasellar growths, which seemingly would be more likely to invade the orbit through the intervaginal space, do not do so for some "unaccountable reason."

MATERIALS AND METHODS

Several fresh specimens obtained at necropsy were examined for possible sources of tissue which might give rise to meningiomas within the orbit. The contents of the posterior two thirds of the orbit, the optic foramen, and the orbital fissures were released en masse by a transverse vertical section just behind the globe. The blocks of tissue were fixed, imbedded, sectioned, and stained by routine methods with hematoxylin and eosin. A careful study of this material then was made with particular reference to the presence, within the orbit, of cells, tissues, and other structures characteristic of the intracranial meninges. Search was made for the typical clusters of arachnoid cells and psammoma bodies.

The major portion of the study was made on cases of meningioma. The number of cases studied will be mentioned with the results. At the outset, all intraorbital meningiomas were placed into one of two sharply and mutually exclusive categories as determined by findings at the time of operation or necropsy. The tumors designated as "primary" within the orbit were those which

formed within the orbit and did not extend to occupy a position within the orbital cavity from a primary source elsewhere. The group of secondary intraorbital meningiomas was composed of meningiomas which extend into the orbit from other sources. Selection of the cases in this latter group was determined by actual invasion of an orbital opening by the tumor, by actual presence of the ex-

ANATOMIC FINDINGS

As mentioned before, the retrobulbar intraorbital contents provided by several necropsies were examined for arachnoid cells or proliferations which could conceivably act as nidi in the formation of meningiomas. In every instance, clusters of arachnoid "cap" cells and small calcified psammomas were found within the meningeal sheath
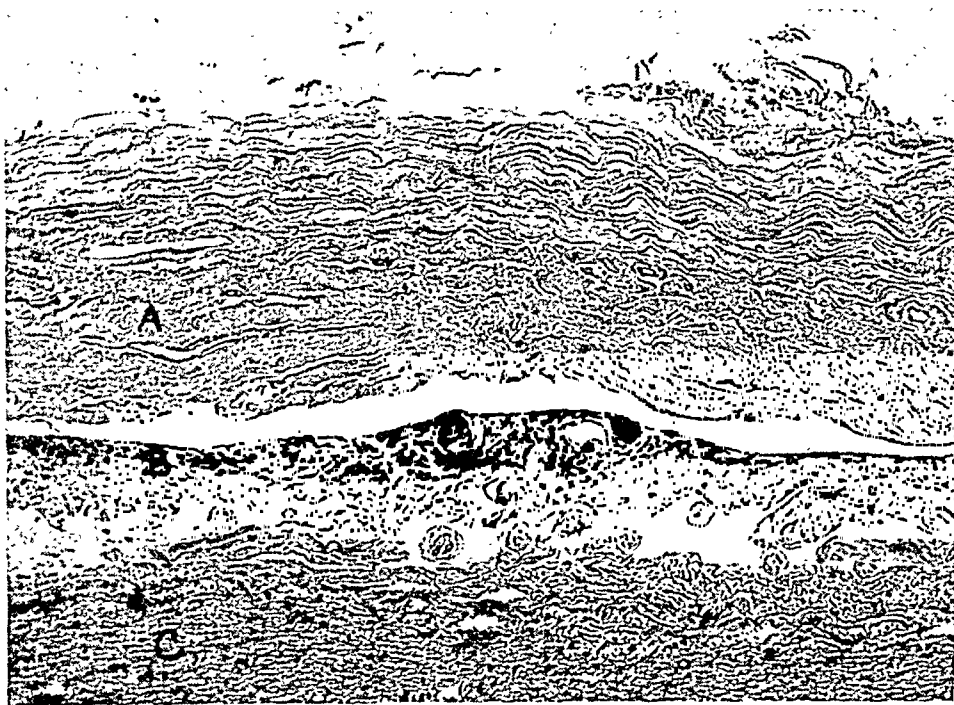
Fig. 1 (Craig and Gogela). Longitudinal section through a normal optic nerve and sheath illustrating clumping of arachnoid cells into a "cap"; (A) dura; (B) arachnoid cluster with psammomas; (C) optic nerve. The widened subdural space is an artefact (hematoxylin and eosin, ×90).

tended mass within the orbital cavity, or by the presence of a hyperostotic dorsal orbital plate and measurable exophthalmos.

In an attempt to correlate the presenting signs and symptoms of the primary tumor with its intraorbital location, special effort was made to note its relationship to the various intraorbital structures. The secondary tumors were studied specifically to determine the route of orbital invasion and findings which would be helpful in distinguishing this class of tumors from the primary group on clinical, or other grounds.

covering the optic nerve. However, similar formations were not observed along the course of other intraorbital nerves or vessels. Nor were clusters of arachnoid cells ever discovered free within the interstitial tissues peripheral to the sphenoidal fissure. The periorbita, or intraorbital periosteum, consisted of a heavy sheet of collagenous fibers and was devoid of lining cells of any sort.

Examination of a single longitudinal section through the optic nerve and its sheath often disclosed 15 to 20 fusiform clusters of 6 to 8 layers of typical, closely packed arachnoid cells. Small, deeply staining, cal-

cified psammomas were frequently observed nestling within these groups of cells (fig. 1).

CLINICAL FINDINGS

PRIMARY INTRAORBITAL MENINGIOMAS.

Primary intraorbital meningiomas have been recognized in 17 cases and treated surgically at the Mayo Clinic. The diagnosis was verified microscopically and a careful

the coverings of the optic nerve but which lay more or less freely either within or outside the muscle cone or were attached firmly to the periorbita.

The tumors were foraminal in location in three cases (fig. 2). In two of these they were bilateral. Nine growths enveloped the optic nerve or were firmly attached to its optic sheath, and the five remaining tumors appeared to arise from some source within
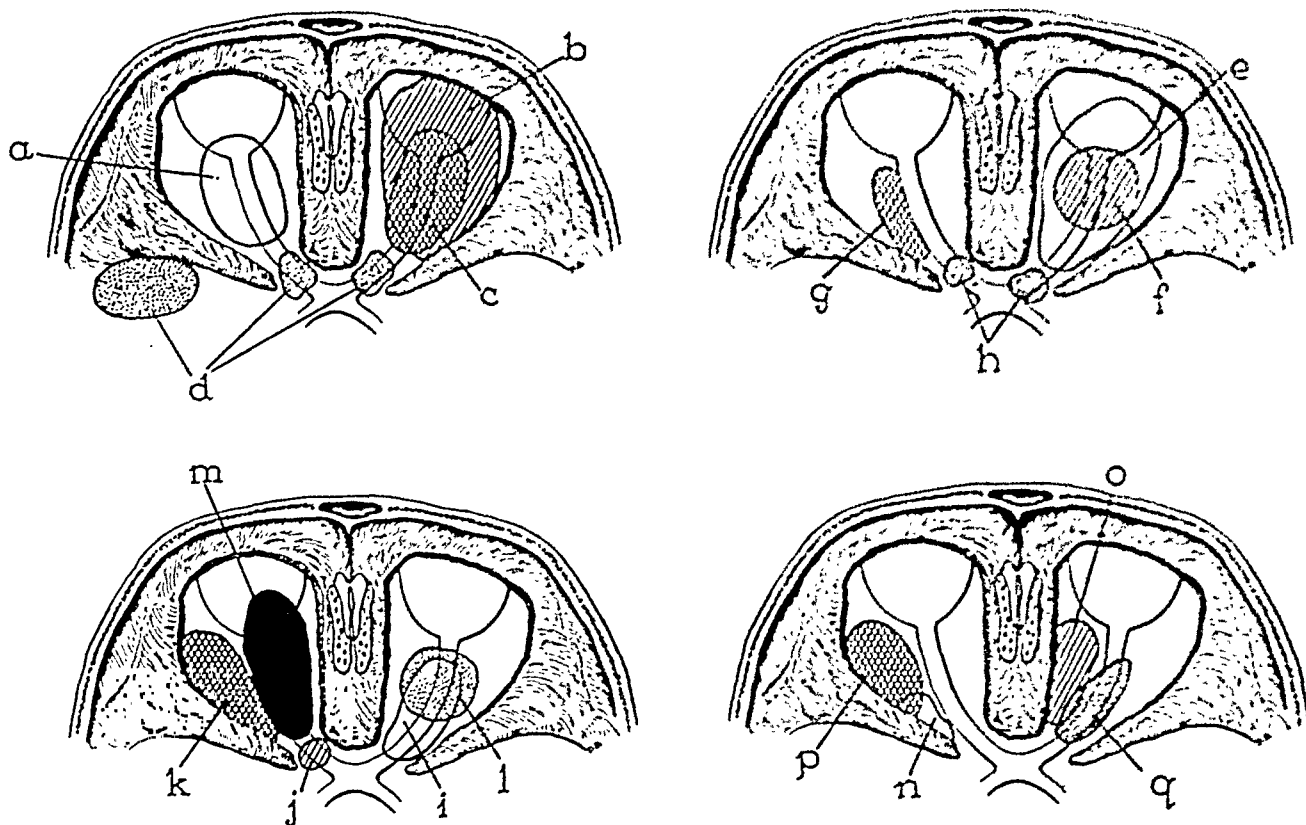
Fig. 2 (Craig and Gogela). (A to Q) Location and attachment of primary intraorbital meningioma in 17 cases.

study was made at the time of operation to establish that they were primary intraorbital growths. Included in this group are the meningiomas taking their origin within the confines of the optic foramen and subsequently extending both intraorbitally and intracranially.

The primary tumors were placed into 1 of 3 groups: (1) The foraminal meningiomas; (2) the growths which arise from within the sheath of the optic nerve; and (3) those which did not seem to stem from

the orbit other than the sheath of the optic nerve.

Thirteen (76 percent) of the patients were females and four (24 percent) were males. A similar sex ratio was found in the cases of the secondary meningiomas also. The ages of the patients who had primary intraorbital meningiomas extended from 14 to 55 years; and the majority of the patients were in the late middle years of life. The average age of the patients at the time of examination was 41 years. However, in-

itial symptoms and signs appeared at an average age of 35 years.

The presenting signs and symptoms consisted of visual impairment, measurable proptosis, and headache. Either visual failure or proptosis, or both, were present in every instance. Headache was recorded in only five cases and was generally described as being mild and occasional. The site of the pain was usually supraorbital or retrobulbar.

The presence or absence of proptosis or visual impairment and the time of onset of the two appeared to be related to the site of the lesion. In the three cases in which the tumors were confined to the optic foramen, progressive loss of vision was the only presenting symptom. Exophthalmometric readings failed to disclose proptosis in any of these cases. Case 1 is representative of this group.

Case reports.

Case 1. A housewife, aged 30 years, registered at the clinic on November 11, 1938. The family and personal history were irrelevant. At the age of 12 years, the patient noted that she was beginning to lose vision in the left eye. The loss of vision in that eye advanced gradually but continuously to complete blindness. The patient felt well otherwise.

About 18 months prior to registration, she noted that vision in the right eye was beginning to fail. Six months after the onset of symptoms referable to the second eye, the patient consulted a physician who performed encephalographic, spinal fluid, and serologic studies, all of which gave negative results. A diet designed to determine an allergenic basis for the optic atrophy failed to bring about a beneficial response. Since the onset of visual failure in the second eye, the patient had had a general feeling of ill health, had become nervous and had lost 10 pounds (4.5 kg.).

General physical examination at the clinic disclosed a small, slight, white woman who appeared younger than her stated age of 30 years. Objectively, physical findings were normal with the exception of those relating to the eyes. Neurologic examination gave essentially negative results except for changes in the ocular reflexes secondary to the amaurosis.

Proptosis was not present, and the eyes rotated normally. The patient was completely blind in the left eye and was able to distinguish moving objects only in the temporal field of vision of her right eye. Ophthalmoscopic examination disclosed pallor of the left disc, grade 4, on a grading basis of 1 to 4, with temporal loss of substance, grade 2. The

right optic disc similarly was extremely pallid and there was residual edema of two diopters.

Flocculation tests for syphilis and tests for possible lead or arsenic poisoning revealed nothing of significance. The blood sedimentation rate was 8 mm. in one hour (Westergren) and the concentration of protein in the cerebrospinal fluid was 30 mg. per 100 cc. Roentgenograms of the head, the optic foramina, the sinuses, and thorax showed nothing abnormal.

A diagnosis of an inflammatory or neoplastic chiasmal lesion was made and right transfrontal craniotomy was performed on December 8, 1938. On elevation of the right frontal lobe, dual, cufflike neoplasms were observed which encircled and compressed the optic nerves at the optic foramina. The tumors were dissected free and, because of some remaining vision in the right eye, the dorsum of the optic canal on that side was decompressed in the hope that there would be some restoration of function in that nerve.

The patient convalesced without incident and was dismissed from the hospital on the 13th postoperative day. Neurologic examination gave negative results at that time and findings on ophthalmoscopic examinations and examinations of the ocular fields remained unchanged. A few months after dismissal, the patient reported that she felt well and had noted some subjective improvement in vision in her right eye.

On microscopic examination the tumors proved to be meningiomas of a heavily calcified psammomatous character similar to that illustrated in Figure 3.

In this case, the tumors were slow growing and small and were situated so that any pressure they may have exerted was ineffective in producing exophthalmos.

In Case 2 the tumor originated within the sheath of the optic nerve. Visual failure and proptosis both were present.

Case 2. The patient, a nun, aged 35 years, registered at the clinic on March 21, 1947. Her chief complaint was progressively decreasing vision in the right eye during the five preceding years. The loss of vision had been almost total for a period of one year. Vision in the left eye was unaffected. Although her right eye had been feeling "heavy in the morning," she had failed to note any definite proptosis of the right eye. Except for a few sharp, right supraorbital headaches which were relieved with aspirin and rest during the preceding 18 months, the patient had felt well. The family and personal histories were noncontributory.

General physical examination revealed nothing abnormal and neurologic examination gave negative results except for depression of the light reflexes incidental to amaurosis. Vision was reduced to perception of light in the right eye and was normal in the left.

Exophthalmometric measurements disclosed prop-

tosis of 7 mm. on the right. Extraocular movements were normal. Extreme pallor and some loss of substance of the right optic disc were noted. The left eye was normal in all respects. Roentgenologic studies showed that the right optic foramen was smaller than the left and the bony collar was denser. Flocculation tests on the blood gave negative results.

The condition was diagnosed as right intraorbital tumor, possibly meningioma, and right transfrontal craniotomy was performed on April 9, 1947. The dura was stripped from the roof of the right orbit; both the dura and the roof of the orbit appeared normal. The meninges were slit along the

given a course of roentgen therapy. The exophthalmometer disclosed proptosis of only 2 mm. at that time. Vision in the right eye was nil.

On microscopic examination, the growth was found to be a meningioma of the meningotheliomatous type.

In some cases, proptosis is the chief presenting complaint. Case 3 is an example of this and of the type of intraorbital meningioma which bears no evident relationship to the sheath of the optic nerve.
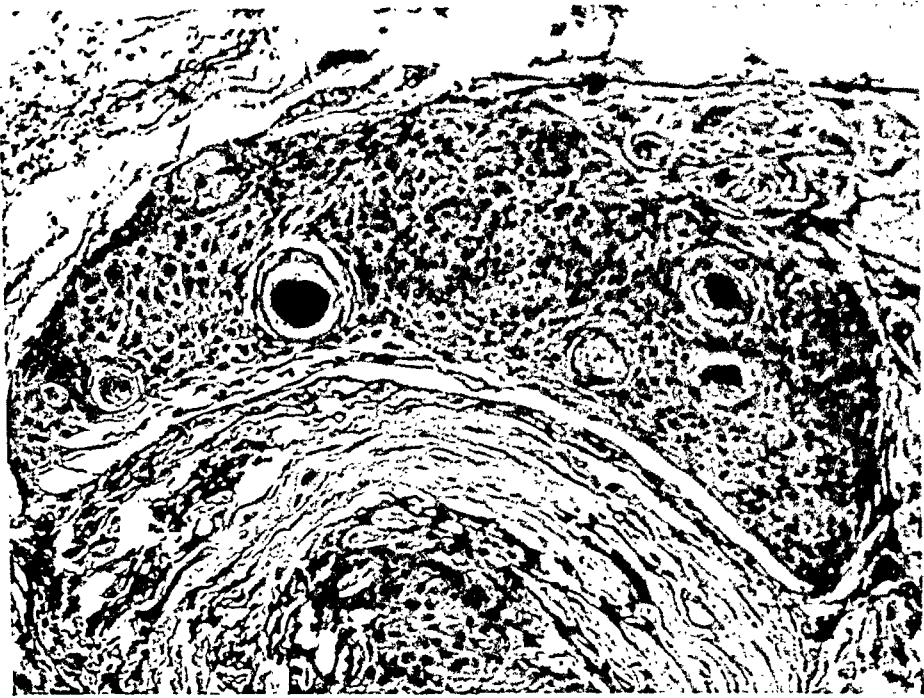
Fig. 3 (Craig and Gogela). Calcified psammomas within a lobule of evenly dispersed meningioma cells (hematoxylin and eosin, ×130).

sphenoid crest, as for exploration for an intracranial meningioma, and the right optic nerve was found to be atrophic and compressed at the optic foramen by a small bit of tissue extending intracranially from within the orbit. There was no evidence of an intracranial meningioma otherwise. Consequently, the optic canal was unroofed and the orbit was decompressed; there appeared to be some osteomatous thickening of the lesser wing of the sphenoid. The sheath of the optic nerve was opened widely and a mass of tumor was recognized to the right of the nerve. With a view toward preserving the optic nerve and the muscle cone, removal was necessarily incomplete. Postoperative convalescence was uneventful and the patient was dismissed from the hospital on the ninth postoperative day.

Four months later, the patient noted a "sensation of pressure" behind the right eye and was

Case 3. A white business man, aged 54 years, registered at the clinic on October 1, 1946. Four years previously, he first noted protrusion of the right eye and fullness of the upper lid. A short time thereafter, he consulted a physician who recommended roentgenographic studies of the sinuses and the orbit. No changes suggestive of a space-occupying lesion were found at that time, nor had such changes appeared one year later. In April, 1945, the orbit was explored elsewhere through an incision in the brow and a bit of tumor was removed for microscopic study. This was reported to be a meningioma.

The patient's only complaints at the time of examination at the clinic were prominence of the right eye and fullness of the right upper lid. He had no pain, no evident limitation of ocular movements, and no subjective visual impairment.

General physical examination gave negative re-

sults except for a moderate degree of obesity and mild hypertension. The systolic blood pressure was 150 mm. Hg and the diastolic was 96. Neurologic examination disclosed no abnormalities.

The right eyeball protruded forward and laterally and there was some slight ptosis of the right upper lid. A definite mass was palpable in the superior nasal quadrant of the orbit. When specifically tested for diplopia, the patient noted doubling of vision on looking upward and to the left. Vision was recorded as being 6/6 in the left eye and as 6/15 in the right. Flocculation tests on the blood gave negative results and roentgenologic studies of the head and orbit failed to suggest the presence of a lesion.

A right transfrontal craniotomy was performed under ether anesthesia on February 3, 1947. The roof of the right orbit was removed, and it was at once evident that the intraorbital contents were under increased pressure. When the capsule was divided and the intraorbital fat retracted, a flat tumor was found along the medial wall of the orbit. Because the mass was firmly adherent to the wall, total removal was not possible. Microscopic study of frozen sections made at the time of operation disclosed the growth to be a meningioma. On examination of the fixed specimen, the tumor was classified as meningioma of the fibroblastic type.

The patient was ambulatory on the third postoperative day and was dismissed from the hospital on the 11th postoperative day. At the time of dismissal, there was still considerable edema of the soft tissues of the right eye; however, the globe was in good condition and vision in that eye had not changed.

On reëxamination seven months later, the patient felt well but exophthalmos of 8 mm. and some ptosis of the right upper lid still persisted. Vision was recorded at 6/6 in the left eye and 6/10 in the right.

Comment.

With the exception of the alteration of light reflexes incidental to the atrophic changes in the optic nerve in some cases, neurologic examination gave uniformly negative results in all but one case. In this one case, pathologic neurologic findings were ascribed to coincidental multiple lesions.

In addition to routine roentgenographic studies of the head, special poses designed to demonstrate the orbital and the optic foramina to the optimal advantage were employed. Roentgenographic findings suggestive of a lesion in the region of the orbit were recognized in 6 of the 17 cases. Bony proliferation of the roof of the orbit or

the wing of the sphenoid bone or in both sites was recognized in four cases. Two of these tumors arose from the sheath of the optic nerve and two from a source within the orbit but apparently not from the sheath.

SECONDARY INTRAORBITAL MENINGIOMAS.

The tendency of 148 meningiomas located in the region of the anterior fossa of the cranium to invade the orbit was studied. The tumors were classed into four groups according to the site of origin as reported at the time of operation (table 1). The largest

TABLE 1

TENDENCY TOWARD ORBITAL INVASION BY PRIMARY INTRACRANIAL MENINGIOMAS

Site of Origin	Total Tumors Examined	Invading Orbit	
		No.	Percent
Sphenoidal ridge	64	25	39
Olfactory groove	24		
Basofrontal region	16	5	31
Sellar region	44	5	11
Total	148	35	24

single group (64 tumors) consisted of tumors arising along the wings of the sphenoid bone. The site of origin of the remaining meningiomas was designated along the olfactory groove and in the basofrontal and the sellar regions.

The 44 sellar meningiomas include all those within and about the sella turcica. At operation, they were variously described as being "intrasellar," "suprasellar," "parasellar," or attached to the "crest of the sella."

Of the four groups, those tumors arising along the sphenoidal ridge displayed the greatest proclivity toward orbital invasion. Twenty-five (39 percent) of a total of 64 tumors presented clinical and surgical evidence of encroachment on the confines of the orbital cavity. Proptosis was present in every instance and was due to 1 of 5 various conditions: (1) Formation of an osteoma on the roof of the orbit; (2) destruction of bone and extension of the tumor through

the defect; (3) simultaneous formation of an osteoma on the roof of the orbit and extension of the tumor into the orbital cavity; (4) extension of the tumor through the orbital fissures; or (5) simultaneous extension through the optic foramen and the orbital fissures.

Sixteen (64 percent) of the 25 invading meningiomas which arose along the sphenoidal ridge compressed the contents of the orbit as a result of formation of an osteoma on the orbital roof and walls. Four tumors extended through an orbital fissure; two through defects produced by destruction of bone; two invaded the orbit through both an orbital fissure and the optic foramen, and one produced ocular symptoms by simultaneous formation of osteoma and invasion of an intraorbital tumor.

None of the meningiomas situated near the olfactory groove in this series evidenced any definite signs of orbital compression.

Of 16 basofrontal growths, five were encroaching on the orbit at time of surgical exploration. In three instances, the tumors invaded the orbital space through areas of destroyed bone. In the two remaining cases, the exact manner of extension of the growth was not determined.

Five of 44 tumors located in the region of the sella turcica were discovered to have extended to, and into, the optic foramen. In no case had extensive invasion of the orbital cavity proper occurred.

Of the 35 intracranial meningiomas secondarily invading the orbit 28 (80 percent) occurred in females. Fifteen (43 percent) of the patients were in the fifth decade of life.

All the invading sphenoidal ridge and basofrontal meningiomas produced proptosis, whereas the sellar tumors produced exophthalmos in only one case. Visual difficulties were complained of in approximately 80 percent of the cases of sphenoidal ridge and basofrontal meningiomas; whereas, in all five cases of sellar meningiomas, visual

symptoms were produced.

There was a striking paucity of other neurologic complaints which would presumably have assisted in distinguishing these tumors from primary intraorbital meningiomas. Nine patients complained of headache; three noted failing memory; two perceived decreasing olfactory sensation; and one had fainting spells.

Except for depression or absence of light and accommodation reflexes and extraocular palsies in some instances, neurologic findings were essentially absent in these groups. In no instance was there any notable disturbance of bodily functions.

Roentgenograms disclosed changes in bony or soft tissue in all but three cases. Most commonly, there was evidence of osteomatous thickening of the wings of the sphenoid in the cases in which meningiomas arose in the region of the sphenoidal ridge. The sellar tumors eroded the optic foramen or caused formation of new bone in the region of the tuberculum sellae turcicae. The basofrontal group produced an area of increased density within the orbital space or a paranasal sinus in three cases.

PATHOLOGIC FINDINGS IN PRIMARY INTRA-ORBITAL MENINGIOMAS

The primary intraorbital meningiomas were reddish, granular or nodular masses, varying in size from the small foraminal growths which measured a few millimeters in all diameters to a meningioma of the sheath which was twice the size of the eyeball. In this last case, proptosis of 17 mm. was present. Although the neoplasms often appeared encapsulated and usually presented well-defined boundaries, others had infiltrative tendencies. The extraocular muscles and the motor and sensory nerves within the orbit were engulfed by the expanding lesion in some cases (fig. 4). Total removal of such tumors results in loss of the function performed by the entrapped structures.

Four of the primary intraorbital meningiomas were of the meningotheliomatous type, 11 were psammomatous, and two were of the less common fibroblastic type. All of the foraminal growths were psammomatous. Three of the sheath tumors were meningotheliomatous and six were psammomatous. Of the five so-called extradural meningio-

the nuclei were irregular, pyknotic, and hyperchromic. These changes are probably indicative of intracellular degenerative changes.

The special Perdrau and Mallory phosphotungstic acid stains disclosed an absence of intercellular reticulin and collagen fibers. The presence of an occasional mitotic figure
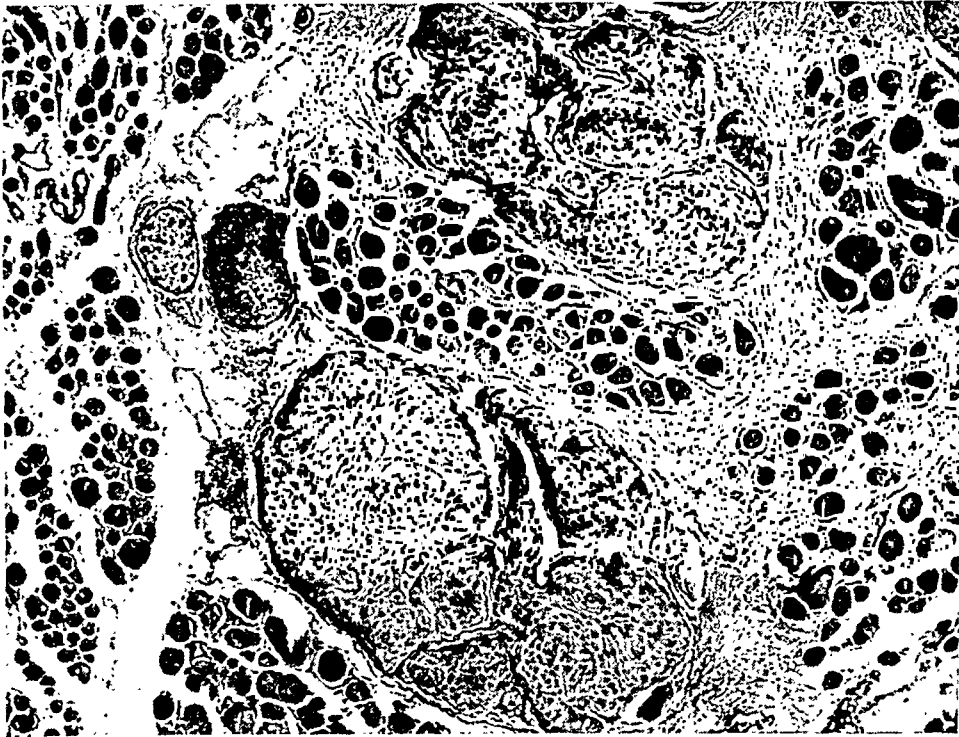
Fig. 4 (Craig and Gogela). Psammomatous meningioma. Small whorls of cells are clustered into lobules imbedded among striated muscles and nerves (hematoxylin and eosin, ×75).

mas, one was meningotheliomatous, two were psammomatous, and two were fibroblastic.

In tumors of the meningotheliomatous type, the cells were arranged in a solid pattern forming a cytoplasmic blanket in which the cellular boundaries were distinguished with difficulty (fig. 5). The substance of the tumor occurred in lobules limited by minimal strips of interstitial fibrous tissue. The nuclei were generally large, round or oval, vesicular, and were rather uniformly dispersed. Higher magnification of tissue in the same case as Figure 5, however, disclosed some departure from this strictly uniform, monotonous pattern in that some of

suggested a low degree of malignant activity.

The cells composing the meningotheliomatous type of tumor resembled the arachnoidal rest cells, or "cap" cells, which occurred in clusters within the optic nerve sheath (fig. 1).

The tendency toward "whorl" formation which distinguishes the psammomatous type is shown in Figure 4. The tumor cells were grouped into small circular lobules which were further subdivided into concentric whorls of meningotheliomatous cells. It is this characteristic whorling which serves as the important distinguishing criterion in identifying the two most common types of

meningiomas. The cell type is identical in the two. However, the cells forming the peripheral layer or two of the psammomas assume an attenuated appearance.

Figure 4 further serves to illustrate the invasive tendency of the meningioma, the two psammomatous lobules being firmly imbedded among bundles of striated muscle fibers and nerve fibers.

On examination under higher magnifica-

characteristics of the two preceding types of meningiomas, the fibroblastic growths introduce certain new features. A definite, basic tendency toward whorling, distinctive of the psammomatous meningioma, may be recognized in Figure 7, which is from 1 of the 2 fibroblastic meningiomas encountered within the orbit. Numerous irregular spaces lend a suggestion of looseness to the tissue.

Examination of the detailed structure of
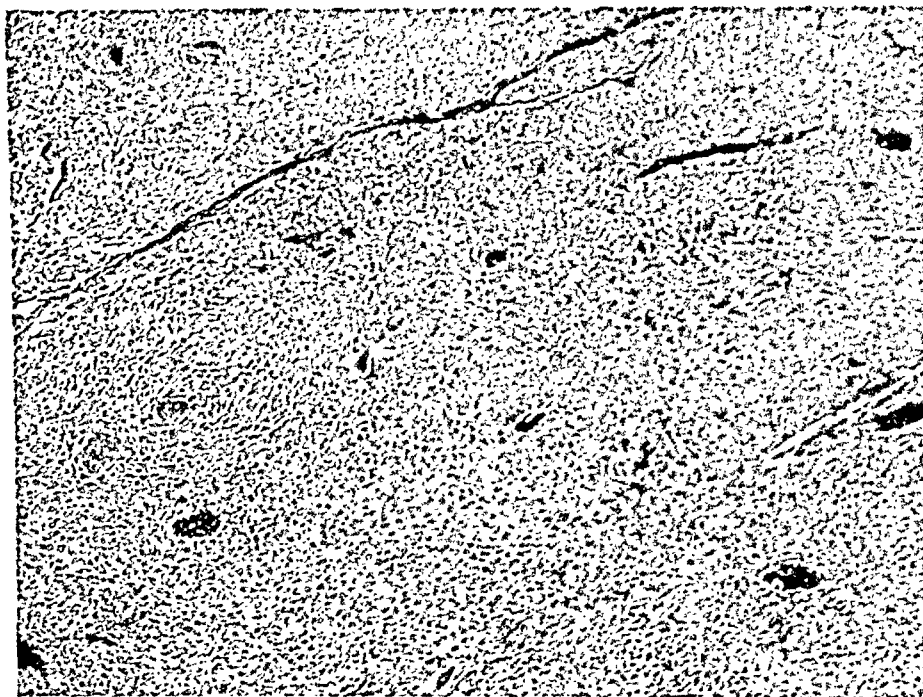
Fig. 5 (Craig and Gogela). Meningotheliomatous meningioma. Cells are more or less uniform and are evenly dispersed. Collagen and reticulin fibers accompany blood vessels only (hematoxylin and eosin, ×75).

tion some psammomas had been formed by the lamellar arrangement of cells about a small central capillary. More commonly, however, the cells were merely layered down on a cluster of central cells. The innermost cells often tended to degenerate and become granular (fig. 6). These bodies subsequently became hyalinized and infiltrated with calcium salts to form heavy, deeply staining, calcified masses (fig. 2).

The third histologic type of meningioma recognized in this series falls into the group designated by Bailey and Bucy[21] as "fibroblastic." While retaining some of the general

the tissue disclosed some marked departures from the more regular, compact arrangement of tumor cells seen in the preceding growths. The cells were irregular and lacking in definite boundaries and the cytoplasm appeared to trail off into light, eosinophilic, interstitial material of a homogeneous or finely fibrillar make-up. The nuclei tended to be vesicular and irregularly oval in shape. The numerous vascular spaces usually appeared well formed and were lined with endothelial cells. An occasional mitotic figure was recognized.

Special preparations of this specimen dis-

closed the presence of intercellular fibers. Silver stains brought to light delicate fibrils of reticulin interspersed among the cells and heavier strands of reticulin accompanying the larger vessels in their course. Moderate amounts of lightly staining, eosinophilic, intercellular wisps of collagenous material were demonstrable with Mallory's staining.

In this particular case, the tumor recurred and a subtotal exenteration of the

is generally considered as having introduced the less radical procedures. He made an opening through the conjunctiva and into Tenon's capsule between the rectus superior and the rectus internus. After he felt the tumor with his finger, he pried it out with a pair of scissors. Lagrange[23] modified the procedure by introducing external canthotomy.

In an effort to obtain more adequate ex-
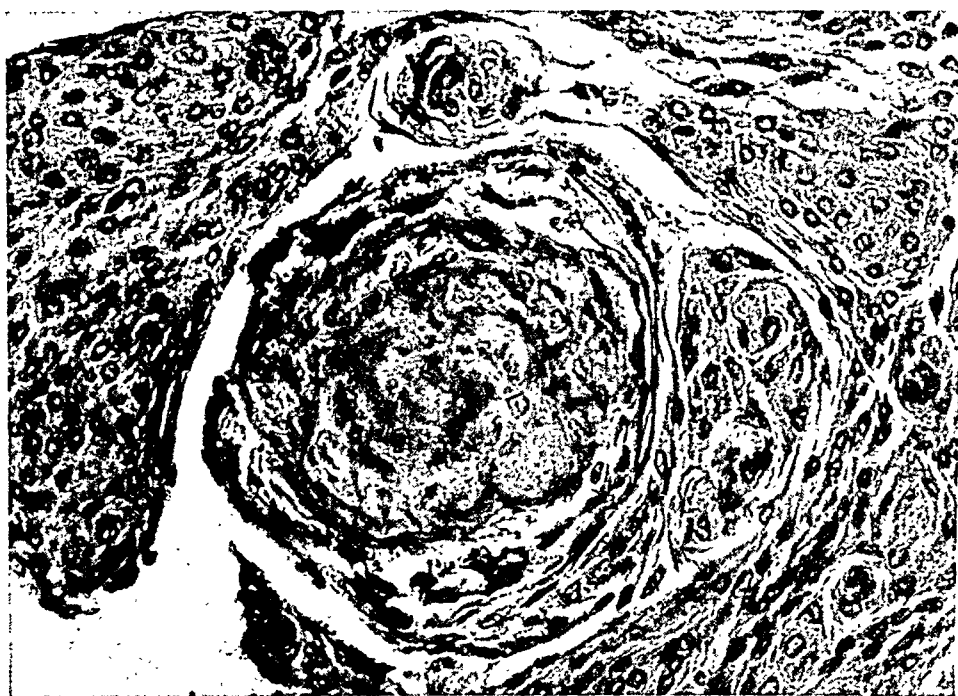
Fig. 6 (Craig and Gogela). Small, granular degenerating psammoma. Nuclear remnants are discernible (hematoxylin and eosin, ×350).

orbit was performed nine years after initial removal.

Surgical treatment

Although Scarpa removed an orbital growth which arose from the external sheath of the optic nerve without injury to the function of the eye as early as 1816, Byers's extensive list of more than 100 intraorbital tumors of various types disclosed that, in about 70 percent of the cases, extirpation of the eyeball and the tumor was performed.

Knapp,[22] in 1874, urged conservatism in the treatment of intraorbital neoplasms, and

posure in approaching deep-lying, lateral, intraorbital tumors, Krönlein,[24] in 1888, devised an osteoplastic resection of the outer orbital wall extending down to the inferior orbital fissure. This procedure was later recognized to have definite limitations.

On anatomic examination of the orbit and its contents, McCotter and Fralick,[25] in 1943, pointed out that there are four anterior anatomic approaches to the removal of orbital tumors: (1) Resection of the temporal wall; (2) the external ethmoid approach nasally; (3) the brow incision for tumors located above the globe; and (4) the incision through the conjunctival fornix.

They concluded that only relatively small masses can be removed when these approaches are used.

Clinically, it had been recognized that the inaccessibility of intraorbital tumors and the inadequate approaches for their removal had long hampered satisfactory treatment of these growths. Although the tumors of the anterior part of the orbit could be removed readily by one of the "ophthalmic" procedures, those in a "retrobulbar" location

also that of cerebrospinal fluid leak and consequent meningitis which served to deter the ophthalmic surgeon.

The inadequacy of the various available procedures was recognized at the time of Byers's survey in 1901 when, in commenting upon the prognosis of intraorbital tumors, he stated, "The danger is not from recurrence in the strict sense of the term, but from the continued development of the intracranial portion of the tumor which it is
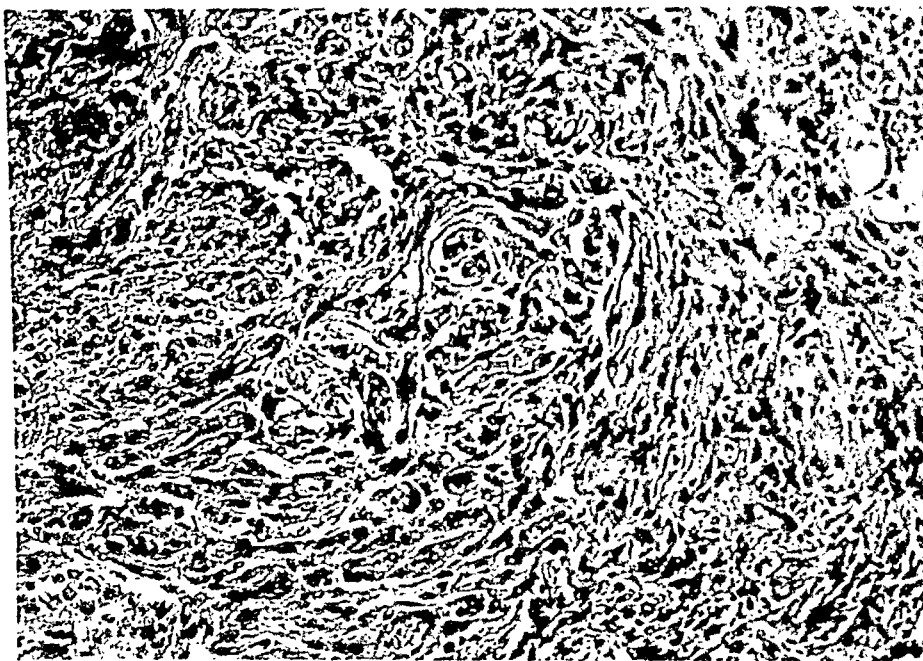
Fig. 7 (Craig and Gogela). Fibroblastic meningioma. A superficial tendency toward whorl formation is evident. Numerous small vascular spaces are present (hematoxylin and eosin, ×165).

had to be extirpated by touch which was an uncertain procedure.

Necessarily, many of the retrobulbar growths were removed incompletely and intracranial extensions were missed and allowed to expand within the cranium. Often, the exact nature and extent of the lesion were not recognized. Functioning eyeballs were sacrificed in an attempt at complete extirpation of tumors which could have been removed completely with preservation of sight if surgical exposure had been adequate. However, it was not only this risk of incomplete... and possible early recurrence, but

impossible to remove at the time of operation."

Accordingly, with the pioneer work of Cushing and associates and Dandy[15] in the use of the intracranial approach to the orbit, interest in the best methods of treatment of intraorbital growth received a stimulus. Simple modifications of standard surgical approaches afforded the neurosurgeon the advantages which would correct some of the ills which stopped the ophthalmic surgeon in his attack on these growths.

As Cushing and Eisenhardt so aptly put it, "The instincts and training of the neuro-

surgeon incline him at the outset to get to windward of the lesion with which he is to deal." On removal of a tumor via the intracranial route, Adson and Benedict[26] remarked that the procedure "suggests many possibilities for the transcranial approach

optic-nerve sheath by the transtemporal route.

This mode of attack first suggested itself to Dandy[15] in 1918 when he sought to correct an exophthalmos due to an osteoma in a woman, aged 28 years. He resected a bony
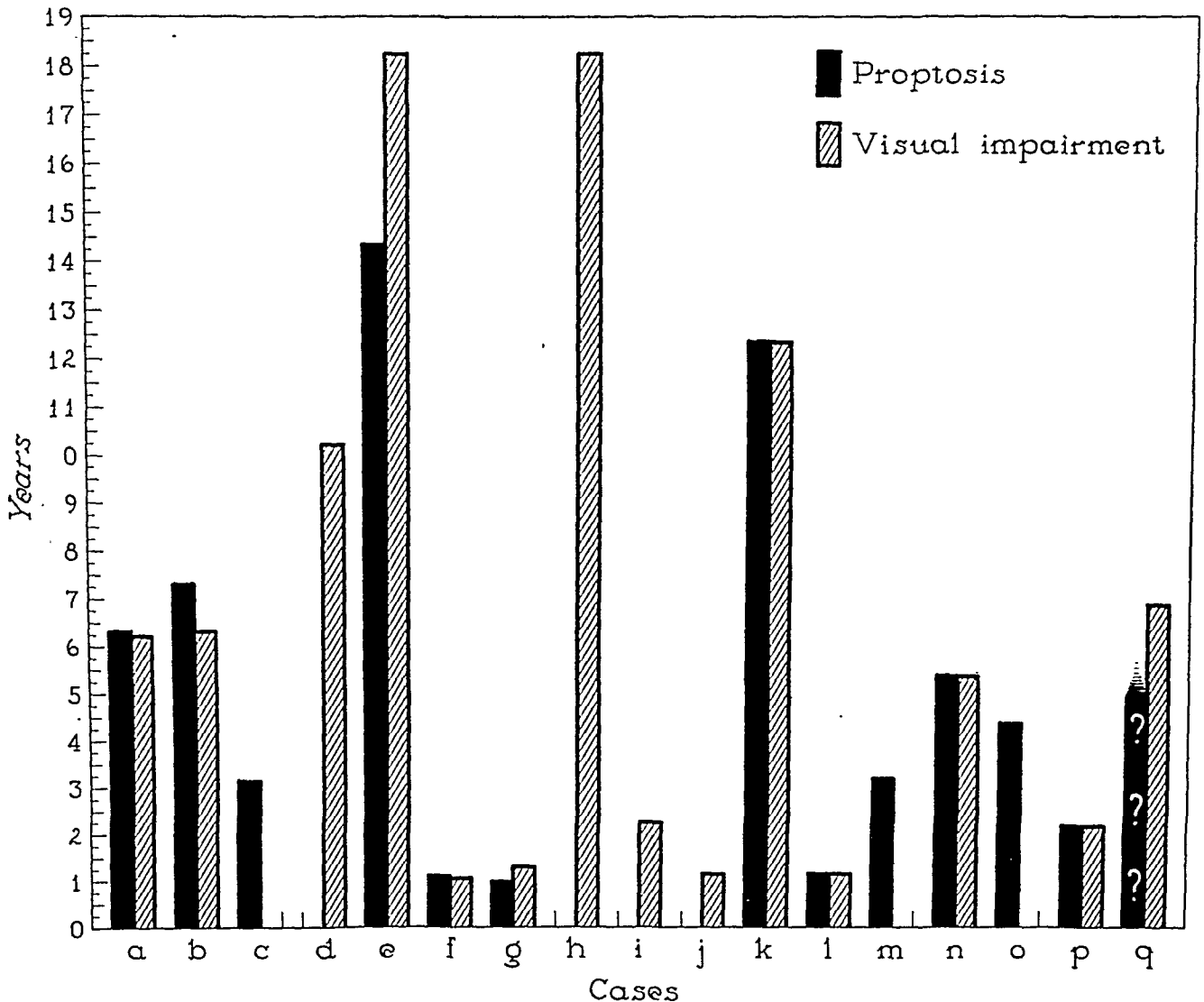
Fig. 8 (Craig and Gogela). Relative duration of proptosis and visual impairment in 17 cases of primary intraorbital meningioma. The case letters correspond with those in Figure 2.

to vascular and neoplastic lesions situated in the retrobulbar space of the orbit."

Dandy[27] employed the intracranial approach in removal of a combined intracranial and intraorbital growth for the first time in 1921; the particular case was one of bilateral meningioma of the optic sheaths. A short time later, Cushing and associate[8] exposed and removed a meningioma of the

growth extending around the optic foramen, and, since the roof of the orbit appeared normal, he did not consider seriously its removal because, among other reasons, "of the deformity which would result by the gravity of the unsupported brain."

The original operative case of Dandy's[15] was that of a girl, aged 13 years, who had had bilateral, progressive decrease of vision for

six years. At the time of operation, the patient was almost completely blind. Exploration disclosed firm, collarlike growths enveloping both optic nerves and extending into the foramina. The visible intracranial portion of the larger mass was resected and the operation was terminated. At a second stage operation a short time later, the posterior half of the orbital roof and the dorsum of the optic foramen were chiseled away and the tumor was traced to the globe and removed subtotally. Dandy[27] emphasized strongly the need for a simultaneous approach to the cranial and orbital cavities when such tumors were considered to be present.

The case in which Cushing and associate removed an intraorbital meningioma was that of a woman, aged 39 years, who had had progressive protrusion of the eyeball with blindness for eight years. Failing to find any evidence of intracranial tumor on lateral osteoplastic exploration, he next attacked the orbit, chipping away the orbital surface of the sphenoid. He resected and removed the optic nerve along with the tumor. Cushing and associate, in commenting on this approach, remarked that the amount of "space for maneuver" which is afforded is "greatly restricted." Hence, his operative approach must be branded as less than satisfactory.

Despite the fact that Durante,[28] as early as 1887, used the frontal intracranial approach in a case of unilateral exophthalmos probably of meningeal origin, and despite the recommendations of Dandy[27] and Cushing and associate,[8] as to the type of surgical procedure best suited to these tumors, surgeons appeared to have been influenced only a little during the years which immediately followed.

Naffziger's[29] extensive experience with transfrontal decompression of the orbit for progressive exophthalmos has further served to illustrate and confirm the satisfactory nature of the intracranial route of approach to retrobulbar tumors.

Most surgeons,[6, 16, 19, 27, 32] however, continued to employ the anterior approach into the orbit or the Krönlein osteoplastic flap. Elschnig[33] in 1927, even recommended resection of the frontal lobe of the brain through the anterior orbital approach if the new growth encroached on the brain. Thompson,[34] in 1935, in presenting an intraorbital meningioma which he removed along with the globe through a Krönlein flap, felt that this approach was indicated for "intraorbital tumors" and the "Dandy operation" was indicated for the "prechiasmal type of tumor." He apparently drew a sharp distinction between the two.

Stallard,[35] in 1935, remarked that the operation of choice for the removal of the intraorbital "endothelioma" seems to be "partial or total exenteration of the orbit," depending on the size and extent of the neoplasm.

Shortly after Adson and Benedict, in 1934, reported the removal of a hemangio-endothelioma of the orbit through a transcranial approach, Love,[36] in 1935, published an account of the same procedure for the removal of an intraorbital meningioma.

The technique employed in the transcranial approach to tumors situated within the posterior portion of the orbit is essentially similar to that used most generally by neurosurgeons in the removal of tumors involving the pituitary gland. The procedure was described in detail by Love and Benedict[37] in 1945.

The scalp is dissected free from the underlying temporal muscles through a curved incision extending upward and forward from the ear. On elevation of the bone flap, the dura is stripped from the orbital roof (or the floor of the anterior fossa). The dorsum of the orbit is then perforated and contents carefully explored. If the tumor mass should be found to expand intracranially, the meninges may be incised along their attachment

at the sphenoidal ridge and the optic foramen may be approached from the intracranial side.

General anesthesia with open drop ether over the end of a Magill intratracheal tube is generally employed.

The transcranial approach to primary intraorbital meningiomas was used in 11 of our 17 cases. The tumors were removed through a brow or anterior incision three times and through the approach afforded by the Krönlein technique once. In two cases, subtotal exenteration was considered advisable. Since its introduction, the transcranial operation was used to the exclusion of the others in all but two cases.

No deaths resulted from any of the operative procedures, nor were there any serious postoperative complications to contraindicate the intracranial operation in favor of the less extensive procedures. The results of operation measured in terms of improved visual function were dependent largely on the location of the lesion and the preoperative duration of symptoms. Little return of vision was expected and obtained in those cases in which atrophy of the optic nerve was present to any degree.

Proptosis was definitely reduced in four cases treated by the transcranial operation and in the one case in which the Krönlein procedure was employed.

The tumor recurred in two cases, in one of which the tumor was of the rapidly growing fibroblastic type.

COMMENT

In order that reports of free-lying, unattached, primary intraorbital meningiomas may not be discredited, some source for these tumors must be postulated. In some instances, the tumor mass may lie between an orbital roof which is apparently intact and the extraocular muscles. It may be suggested that these growths arise from free strands of meningeal tissue invading the orbital cavity through the orbital fissures or that the intraorbital periosteum possibly serves to give rise to these meningiomas of unexplained origin.

Another explanation is that these "extradural" meningiomas may have had an arachnoidal attachment which subsequently disappeared during the process of growth.

Within the cranial cavity, the optic nerve is first enveloped only by the pia mater, but soon gains a covering of arachnoid. On reaching the optic foramen, the nerve acquires the third or dural layer and continues with its triple meningeal sheathing as it traverses the orbital chamber to penetrate the globe.

The closely adherent periosteal and meningeal layers of the intracranial dura mater separate into the periosteum of the orbit (or the periorbita) and the outer meningeal layer of the optic sheath. This periosteum is continuous with that of adjacent bones through every orbital opening.[25, 38] At the superior orbital fissure, it continues as the external layer of the dura. The potential subdural and the subarachnoid spaces formed by the meningeal coverings of the optic nerve are continuous with the corresponding intracranial spaces.

Anatomic descriptions fail to state whether any of the coverings of the nerves to the extraocular muscles are still present after these nerves have entered the orbital cavity. The ophthalmic artery and the ophthalmic veins are apparently devoid of meningeal vestments.

Examination of serial sections of these anatomic structures in this study disclosed that meningeal tissue does not accompany these nerves and vessels into the orbit. Nor were any arachnoidal cell clusters found to lie imbedded within the normal retrobulbar intraorbital tissues. Yet, 3 of the 5 extradural tumors were of the meningotheliomatous or psammomatous type, tumors composed of a definite cell type arising only

from a similar preëxisting cell type.

Since no pathologic changes were encountered in the intracranial dura over the orbit at the time of operation, some other source must be postulated. The periorbita is composed of fibrous tissue and, therefore, cannot give rise to the meningotheliomatous or psammomatous tumors. It is suggested, therefore, that these extradural tumors may possibly have originated as arachnoid tufts which had grown into and through the dural layer of the optic sheath and had come to lie completely outside the dura.

Elsberg,[39] in 1933, and Kernohan,[40] in 1941, among others, have observed the presence of such extradural tumors in the region of the spinal cord, and the latter has offered just such an explanation for the presence of these growths in this region.

The presence of the foraminal meningiomas and of the meningiomas attached to the optic-nerve sheath may be explained adequately by the clusters or "caps" of arachnoidal cells occurring so abundantly along the intraorbital course of the optic nerve as suggested by previous investigators. In all probability, the cufflike growths arising within the optic foramen are but "sheath" meningiomas situated within a specific location. However, why this special predilection should exist and why these growths should demonstrate a tendency toward bilaterality is difficult to explain.

Microscopic examination of normal optic nerves and their sheaths did not disclose the clumping of arachnoid cells to be any more frequent or more exaggerated within the optic foramina than anywhere else along the intraorbital course of the optic nerve. Yet, 2 of the 3 foraminal tumors included in this series were bilateral, one of the growths appearing fully 16 years after its mate. Similarly, in Dandy's[15] single case of "cufflike" meningiomas the tumors were bilateral.

Reports of the occurrence of primary intraorbital meningiomas in children[6, 9, 30, 41] suggest that when these tumors occur, they do so in young persons. Hudson[17] stated that 50 percent of intraorbital meningiomas occur during the first two decades of life. Study of the 17 cases in our series, however, disclosed that the lesions appeared at much the same age as do meningiomas elsewhere within the cranium. The patients who had primary intraorbital growths came to operation at an average age of 41 years and those who had primary intracranial lesions which invaded the orbit secondarily were an average age of 43.5 years at the time of operation.

Analysis of the presenting findings (proptosis and loss of vision) failed to support the contention that the relative duration of the two diagnostic criteria may serve as a guide in differentiating these tumors from other intraorbital growths preoperatively. Investigators[32, 43] have offered precedence of exophthalmos over visual failure as a point of diagnosis in distinguishing intraorbital meningiomas from gliomas of the optic nerve. However, study of Figure 8 obliges us to conclude that such observations are unreliable criteria. Whether proptosis is to be the initial complaint, or whether the onset of visual failure will be noted first, appears to depend on the intraorbital location of the meningioma.

Although roentgen studies of the head and orbit are valuable adjuncts in the differential diagnosis of intraorbital lesions, they are probably more of negative rather than positive value in identifying primary intraorbital meningiomas. The fact that roentgenologic findings were negative in 65 percent of the primary tumors in this series is contrary to the contention that positive roentgenologic findings are suggestive of the presence of a primary intraorbital tumor. Moreover, when changes were present, they were not of a uniform nature specifically indicative of a particular lesion.

The secondary tumors, on the other hand, produced roentgenologic changes in more than 90 percent of this group. These figures

compel us to conclude that the presence of evidence of pathologic change about the orbit in the roentgenogram favors the presence of a secondary, or invading, intraorbital meningioma.

SUMMARY AND CONCLUSIONS

Seventeen cases of primary intraorbital meningioma and 35 cases of secondary intraorbital meningioma were studied in this series. The primary intraorbital meningiomas were subdivided into three groups: foraminal, sheath, and extradural.

The foraminal and the sheath meningiomas probably arose from clusters of arachnoid cells within the sheath of the optic nerve. No similar source was found to account for the extradural growths. It is suggested that they may develop from enlarging cell clusters protruding through the sheath of the optic nerve.

Intraorbital meningiomas are four times more common in women than in men and tend to occur during the middle years of life as do meningiomas located elsewhere.

The order in which proptosis and visual impairment appear does not serve as a reliable aid in distinguishing intraorbital meningiomas from other intraorbital lesions. Roentgenologic changes about the orbit are usually suggestive of an invading or secondary type of intraorbital meningioma.

The transcranial route of approach best meets any contingencies which may arise in the attack on these tumors.

Mayo Clinic.

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TRUE PSYCHOSENSORY DILATION AND DELAYED PSYCHOSENSORY DILATION OF THE PUPIL*

A PRELIMINARY REPORT

NORMAN S. JAFFE, M.D.
Brooklyn, New York

It has long been known that the pupil will dilate in response to psychic and sensory stimuli. Fear, excitement, and rage all cause pupillodilation. Stimulation of sensory nerves similarly causes pupillodilation. The center and efferent pathway for these two different kinds of stimuli are considered identical and hence the phenomenon is known as the psychosensory reflex. This reflex has a relatively long latency period; between 0.292 and 0.46 seconds (Albrecht 0.292; Weiler, 0.36 to 0.44; Braunstein, 0.41 to 0.46).[1] The reflex consists of a quick dilation and contraction. The reaction is rapid and occurs bilaterally.

It is generally agreed that there is a cortical center for this reflex.[2] However, the efferent pathway has been the source of considerable controversy. It is more than of just theoretical importance since the reflex may be used in the practical differential diagnosis of anisocoria. The number of experiments performed in this connection has been legion, yet the conclusions drawn from them may be grouped into three main classes.

1. Dilation due to reflex inhibition of the oculomotor-nerve nucleus.

2. Dilation due to reflex peripheral sympathetic stimulation.

3. Dilation due to a combination of these two mechanisms.

Ury and Gellhorn[3] have concluded that reflex dilation occurs via inhibition of the third-nerve nucleus alone since third-nerve section abolished the reflex; whereas, it was still present after cervical sympathectomy.

They also considered that the function was purely central, since stimulation of the legs of cats with unilateral sympathectomy resulted in dilation of both pupils.

Working independently, Anderson,[4] Tschirkowski,[5] and Nishimura[6] showed that, with the cortex intact and the sympathetic intact, cutting the third nerve did not abolish psychosensory dilation. Most investigators today are of the opinion that both factors come into play and that one may be present without the other.

It is probable that this reflex does not depend on the liberation of adrenalin from the adrenal medulla since it is an extremely rapid reaction. It must, therefore, be the result of pure autonomic nervous activity.

Cannon[7] has shown quite decisively that the adrenal medulla liberates its secretion in significant amounts only under conditions of stress. Adrenalin is called forth to resist threatened dangers, to perform work, to maintain homeostasis. Thus, the sympathetic nervous system is reinforced by the medullary secretion. For maximum efficiency in coping with emergency states the body requires two mechanisms:

(1) Nervous—via immediate sympathetic stimulation; (2) hormonal—via a delayed reaction which depends on the mobilization of the hormone from the adrenal medulla.

The center for the hormonal mechanism was placed by Cannon and Rapport[8] in the upper part of the floor of the fourth ventricle. This may not be the highest center since stimulation of the hypothalamus will cause a discharge of adrenalin.

It will be shown in the following experiments that much of the confusion regarding the psychosensory pupillary reflex may be

attributed directly to the failure to recognize that there may be two phases to this reaction. The first, immediate, rapid reaction is purely nervous, due to sympathetic stimulation and probably coincidental third-nerve inhibition. The second, delayed, slow reaction is purely hormonal and depends on the liberation of adrenalin by the adrenal medulla. The second phase will only occur if the stimulus is great; that is, if an emergency state is set up. With mild stimuli only the first part of the reaction will occur.

EXPERIMENTAL STUDIES

EXPERIMENT 1

In this experiment only mild psycho-

to adrenalin. This is in accordance with Cannon's law of denervation.[9] For a more detailed explanation see a previous paper by me.[10] The present experiment was performed 2 to 3 months after the nerve sections. In no case was there any evidence of regeneration.

Each cat was placed in a cat box with the head protruding. Using Loewenstein's pupillographic technique,[11] 10 pictures per second were taken of both pupils under infrared illumination. After about three seconds, a gun was sounded. The reaction of both pupils to this psychosensory stimulus is shown in Figure 1. It is seen that the normal left pupil reacted well by dilating. The right
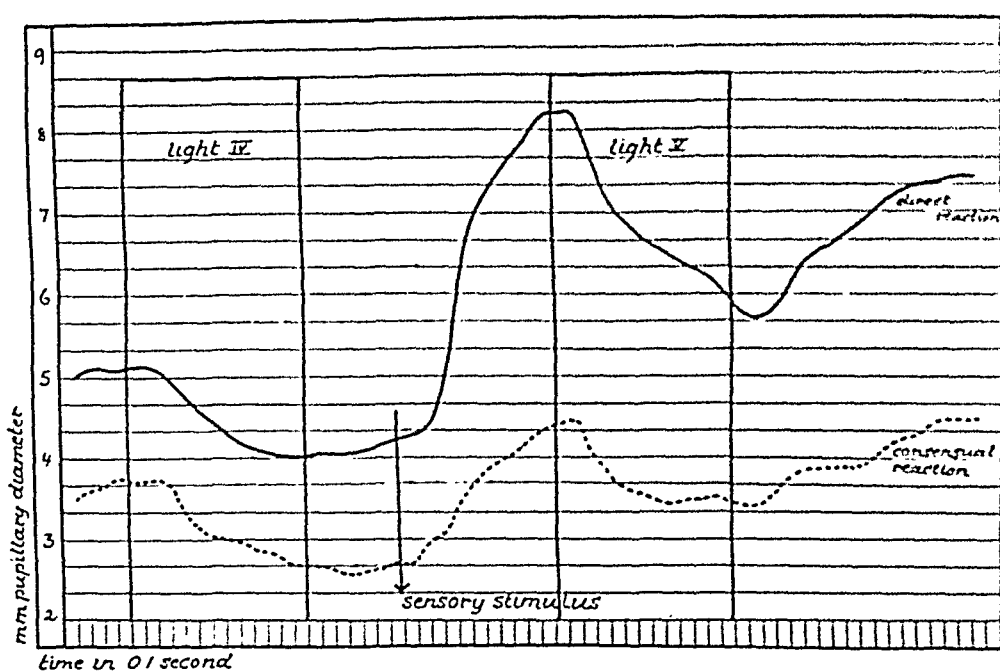
Fig. 1 (Jaffe). Dotted line represents the reaction of the sympathectomized right pupil. Continuous line represents the reaction of the normal left pupil. The pupils were stimulated by repeated light stimuli. Between the fourth and fifth stimuli a gun was sounded. The normal (left) pupil responded by dilating more than 4 mm. The sympathectomized (right) pupil dilated only about 1.5 mm. This demonstrates that peripheral sympathectomy largely, although not completely, abolishes psychosensory dilation.

sensory stimuli were used; for example the crack of a gun.

Postganglionic cervical sympathectomy was performed on the right side of each of eight normal cats. Horner's syndrome was apparent within 10 seconds after the nerve section. Within 10 days, in all cats, the denervated iris (right) became hypersensitive

pupil, however, showed a dilation which amounted to only one fifth the magnitude of the normal reaction.

The experiment was repeated using cats previously subjected to right preganglionic cervical sympathectomy. In all instances the results coincided with those above.

This is purely a nervous reaction and in-

volves a stimulation of the center in the cerebral cortex with subsequent peripheral sympathetic stimulation and third-nerve inhibition. In the normal eye, since the cortex, third nerve, and peripheral sympathetics are intact, the reaction is full. In the right eye we get a markedly diminished reaction because the peripheral sympathetic chain is not intact. There is no hormonal element in this reaction for, if adrenalin were liberated, the reaction in the denervated right iris would have far exceeded that in the normal iris because the effector cells of the denervated iris are hypersensitive to adrenalin (law of denervation). The small, residual reaction in the right pupil may be attributed to third-nerve inhibition.

Thus, it may be stated that mild psychosensory stimuli cause a dilation of the pupil and the integrity of this reaction is maintained by purely nervous factors—center in the cortex, peripheral sympathetic stimulation, and third-nerve inhibition; no discharge of adrenalin accompanies this reaction.

EXPERIMENT 2

In this experiment a strong emotional stimulus was used such as the excitement induced by ether anesthesia.

The eight postganglionic sympathectomized cats were used in this experiment. The cat was again placed in a cat box with the head protruding. Gauze moistened with ether was placed near the cat's nose. The animal immediately became excited. The normal left pupil dilated immediately. The right (denervated) pupil did not dilate until after 6 to 8 seconds of excitement. When it did dilate it dilated maximally and far exceeded the reaction on the normal side (figs. 2 and 3).

The same experiment was performed with the eight preganglionic sympathectomized cats. In all cases, there was an immediate dilation on the normal left side but a delayed and strong dilation on the operated right side. The reaction on the right side exceeded

that on the left side but it was slower and of smaller amplitude than that observed with the postganglionic sympathectomized cats.

It is clear that we are concerned here with both phases of the psychosensory reflex referred to previously.

The immediate reaction on the normal side was purely nervous and occurred as a re-
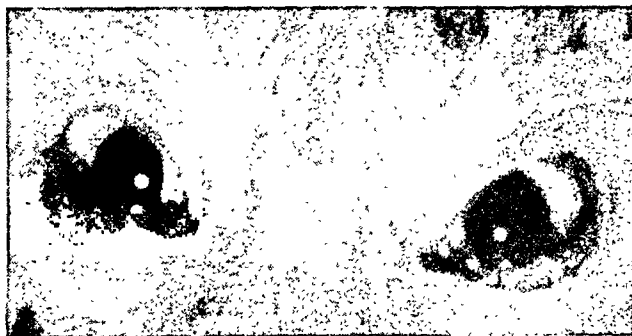
Fig. 2 (Jaffe). Cat with postganglionic cervical sympathectomy on the right side. Photograph shows cat under normal conditions. Note miotic right pupil (Horner's syndrome). Left pupil is normal in size.
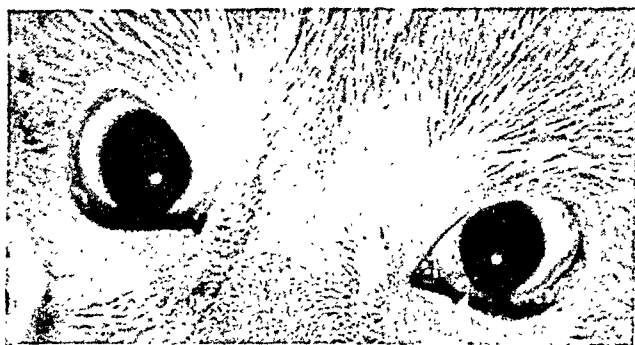
Fig. 3 (Jaffe). Same cat as in Figure 2 during ether excitement. Note that the sympathectomized right pupil responds by dilating more than the normal left pupil. This demonstrates the "law of denervation."

sult of simultaneous peripheral sympathetic stimulation and third-nerve inhibition. The delayed reaction seen on the operated side was due to stimulation of the centers for adrenal secretion with subsequent liberation of the hormone and its action on the denervated iris.

The delayed reaction is also seen with a preganglionic sympathectomized animal but it is not so marked since sensitization of denervated structures to circulating adrenalin

is twice as great in postganglionic sympathectomized animals.

That the reaction is due to sensitization is amply demonstrated by the fact that the normal pupil returns to its original size much sooner than the denervated pupil after the ether gauze is removed.[10] Thus, with a given increased adrenalin level, the denervated structure responds more markedly than the normal structure.

EXPERIMENT 3

This experiment eliminates the hormonal factor. In two of the postganglionic sympa-

Fig. 4 (Jaffe). Same cat after right postganglionic cervical sympathectomy and bilateral adrenalectomy. The cat is shown during the excitement stage of ether anesthesia. Note that the right pupil dilates less than the normal left pupil and the right palpebral fissure is narrow. The right pupil doesn't show the "law of denervation" since the adrenal glands have been removed.

thectomized cats, bilateral adrenalectomies were performed. One week after the operation, the ether experiment was again performed. The cats became excited and the normal pupil dilated immediately. The denervated pupil, after 6 to 8 seconds, dilated only slightly (about two fifths of the usual reaction). See Figure 4.

These animals could not, therefore, respond to the ether with both phases of the "fight or flight" reaction. The immediate nervous reaction was observed since the structures subserving this reflex were intact. The delayed, marked, hormonal reaction was practically absent since no adrenalin could be produced. The small, delayed dilation

was probably due to some hepatic liberation of adrenalin.

COMMENT

These experiments show that the psychosensory pupillary reflex is a complex phenomenon consisting of two separate and distinct mechanisms. The true psychosensory reflex is a nervous reaction which has its center in the cerebral cortex. It exerts its effect by simultaneous peripheral sympathetic stimulation and third-nerve inhibition. It is an immediate reaction which has a latency period of 0.3 to 0.4 seconds. It occurs whether the stimulus is weak or strong.

The hormonal mechanism is a distinct mechanism and occurs only in response to a strong emotional or sensory stimulus. The reaction is best termed "delayed psychosensory pupillary reaction." Its center is in the floor of the fourth ventricle (perhaps in the hypothalamus). It exerts its effect by reflex stimulation of the adrenal medulla with subsequent liberation of adrenalin. The adrenalin thus formed passes to the iris by way of the blood stream and acts on the pupillodilator apparatus (fig. 5).
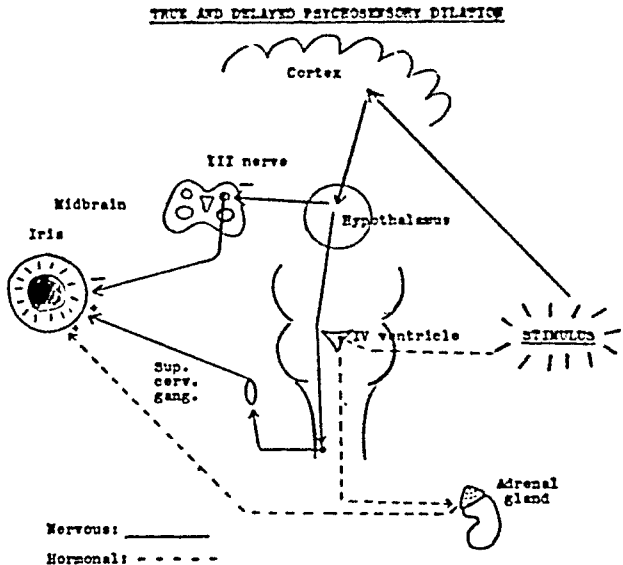
Fig. 5 (Jaffe). Diagrammatic representation of the pathways involved in true and delayed psychosensory dilation of the pupil. The continuous line represents the true or nervous reaction while the interrupted line represents the delayed or hormonal reaction.

Failure to recognize this delayed reaction in the past led to the erroneous interpretation of otherwise accurate observations.

As early as 1904, Anderson[4] noted that the normal pupil reacted to strong psychologic stimuli with an initial, rapid, and short dilation followed by a secondary dilation which developed and subsided more slowly and gradually. He attributed the initial reaction (the true psychosensory reflex) to stimulation of the sympathetic and the secondary dilation (delayed psychosensory reaction) to inhibition of the parasympathetic.

The latter view is untenable since reflex inhibition of the third nerve is a rapid reaction which proceeds from the cortex to the hypothalamus and then, by way of the inhibitory pathway, from the hypothalamus to the midbrain, and courses to the third-nerve nucleus which it inhibits. The distance traversed is shorter than that required for peripheral sympathetic stimulation. From the experiments herein reported it is evident that bilateral adrenalectomy would have eliminated the delayed, slow reaction. Consequently it could not have been due to third-nerve inhibition.

Ury and Gellhorn[3] more recently attributed reflex or emotional dilation of the pupil solely to inhibition of the third nerve since cutting the third nerve eliminates this. In Experiment 1, it was shown that when the cervical sympathetic chain is cut four fifths of the true psychosensory dilation is lost. Thus, the role of the sympathetic cannot be denied.

There is a further serious objection to this work. Cutting the third nerve gives a dilated pupil. Most workers believe this to be a maximally dilated pupil (problem unsettled). It cannot be expected that an emotional stimulus should further dilate such a pupil. They argue that instillation of pilocarpine contracts the pupil and still an emotional stimulus does not cause a dilation. However, it is well known that pilocarpine renders the pupil unresponsive to most stimuli (for example, reflex to light). Moreover, according to Walsh,[12] cutting the third nerve does not abolish psychosensory dilation.

Ury and Gellhorn further stated that the reaction must be a central one because stimulation of the legs of cats with unilateral cervical sympathectomy caused dilation of both pupils. However, it is probable that the dilation on the sympathectomized side was due to the delayed psychosensory reaction, since muscle contractions caused by stimulation give rise to adrenalin liberation with delayed stimulation of the sympathectomized iris. In this case, both pupils dilate but the pupil on the normal side dilates first.

Many more experiments have been performed and similar conclusions reached, but in all cases the same objections may be raised. Consequently no more instances need be cited. On the other hand, there has been much work done by others which firmly corroborates the results of the present experiments.

Byrne[13] showed that, after cervical cord transection, sciatic stimulation no longer evokes a primary reflex dilation but only a delayed form which usually occurs in 4 to 8 seconds after the onset of stimulation. The delayed dilation only occurred if the sciatic stimulation caused muscular contractions since the latter is associated with the liberation of adrenalin. If no muscle contractions occurred, no dilation occurred. Although Byrne used purely sensory stimuli his results have the same significance as those of this paper using psychosensory stimuli.

The work of Cannon[14] further shows that the reaction which depends on adrenalin liberation requires several seconds to begin. He used the denervated heart as an indicator of adrenalin liberation. Fright, rage, pain, asphyxia, and anesthesia caused, within 10 seconds, an increase in heart rate of 20 to 40 beats per minute.

SUMMARY

Much of the controversy over the psycho-sensory pupillary dilation is due to the failure to recognize that this reaction is complex and involves two separate and distinct mechanisms.

The first phase is purely nervous and involves stimulation of the cerebral cortex with subsequent peripheral sympathetic stimulation and third-nerve inhibition. It is a rapid reaction, with a latency period of 0.292 to 0.46 seconds according to three different observers. It subsides rapidly. It does not involve medullary secretion of adrenalin. It occurs with both weak and strong psy-chologic or sensory stimuli. This may be called the true psychosensory dilation.

The second phase is purely hormonal. It is a delayed reaction. It subsides gradually. It involves stimulation of the center in the floor of the fourth ventricle or in the hypothalamus with subsequent release of adrenalin by the adrenal medulla. It occurs only in response to strong psychologic or sensory stimuli. This may be termed the "delayed psychosensory dilation of the pupil."

86 Vernon Avenue (6).

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EXPERIMENTAL STUDIES ON SYMPATHETIC OPHTHALMIA*

RAYMOND C. COLLINS, M.D.

New York

I. INTRODUCTION

This whole study is based on the allergy theory of sympathetic ophthalmia. The supporters of this theory hold that sympathetic ophthalmia is caused by an allergy to uveal pigment, melanin. De Schweinitz[1] points out that Bail and Heim gave the suggestion of the allergy theory to Kümmel and Elschnig and that Elschnig[2] went on to develop it in 1910-1911. Woods[3] has been the great champion of this theory in the United States. Despite a vast amount of work, this theory has yet to be established as fact. However, there are many observations which make the hypothesis sound most plausible. They are:

1. The time interval between the injury and the onset of the disease falls within the sensitization period as found in other immunologic experiments.

2. The histopathologic picture of sympathetic ophthalmia points strongly to an allergic basis for the disease—an allergy to pigment, as has been stressed by Friedenwald.[4]

3. The antibody reactions favor this theory. Elschnig[2] has shown that uveal pigment is capable of acting as an antigen which would cause the production of complement-fixing antibodies.

4. The skin tests with uveal pigment as described by Woods[3] suggest an allergic etiology.

5. That allergy to pigment is a factor seems indicated by the not infrequent reports in cases of sympathetic ophthalmia of bleaching of the eyelashes, leukodermic patches of the eyelids, and deafness due to involvement of the pigment cells of the inner ear.

6. Friedenwald[4] has reported an interesting case in which the sympathetic affliction had burned itself out over a period of many years and the eye was examined histologically. The choroid was replaced by scar tissue within which not a granule of uveal pigment could be found.

7. If one can evaluate therapy of this disease, it has been reported that massive salicylate therapy gives favorable results. Salicylates have been shown to reduce antibody formation in experimental animals.

8. The presence of eosinophiles in large numbers in eyes suffering from sympathetic ophthalmia points to an allergic condition.

II. RECENT ADVANCES IN THE STUDY OF AUTOALLERGY

One drawback to the acceptance of the allergy theory of sympathetic ophthalmia has been the great reluctance with which many men will accept the idea that a person can become sensitized to his own normal bodily constituents. Many years ago, Ehrlich coined the term "horror autotoxicus" to cast disparaging light on the work being carried on with regard to autosensitivity. However, advances in recent years in this field have proven Ehrlich wrong and have shown that autoallergy is not only plausible but that it does actually occur. Just to mention a few of the recent startling experimental results to sensitivity to one's own tissues we have:

1. In 1945 Cavelti and Cavelti[5] produced the clinical and pathologic picture of glomerulonephritis in rats by sensitizing them to rat kidney with the aid of Group-A beta hemolytic streptococcus.

2. Burky,[6] in 1934, produced endophthalmitis phaco-anaphylactica in rabbits by sensitizing them by the use of beef-lens toxin.

3. Another outstanding advance in the field of autoallergy came in 1946 when Kabat, Wolf, and Bezer[7] produced acute dis-

seminated encephalomyelitis in monkeys by sensitizing them to monkey brain emulsion with the aid of adjuvants.

4. There seems to be some clinical evidence today that rheumatoid arthritis is the result of an individual's sensitivity to his own connective-tissue elements.

All of these observations indicate that autoallergy is an established fact and can no longer be held as a valid argument against the allergy theory of sympathetic ophthalmia.

Fig. 1 (Collins). Section of human eye. (a) Nodule of lymphocytic infiltration in the choroid. (b) Sclera.

III. ADJUVANTS

Many of the above-mentioned advances in the study of allergic conditions have come about as a result of the use of adjuvants. An adjuvant, as used in this sense, is defined as any material or materials which, when given in conjunction with an antigen, will intensify and prolong antibody production to this antigen. They will render a weak antigenic substance strongly so. Of all the numerous methods employed to increase antibody production the technique of Le Moignie and Pinoy,[8] (1916) with mineral oil emulsified in a lanolinlike substance, with or without the addition of killed tubercle bacilli, has been found to be the most effective.

The mechanism of action of adjuvants is a complex one which is not thoroughly understood. Most workers believe that adjuvants function by setting up a reactive tissue wall about the inoculum which localizes the antigenic material at the inoculation site and, through slow continuous absorption, produces hyperimmunization. They also feel that the large monocyte response called forth by the adjuvants increases the antibody formation (Rist,[9] Casals and Freund,[10] Freund, Casals and Genghof,[11] Friedenwald[12]).

IV. PATHOLOGY OF SYMPATHETIC OPHTHALMIA

The histopathologic picture of sympathetic ophthalmia has been adequately described numerous times by competent observers. Therefore, only a brief review will be given with examples for ready comparison and evaluation of experimental results to follow. Because many eyes suffering from sympathetic ophthalmia are removed late, a mistaken belief is that the histopathologic picture should always show the iris and choroid solid with lymphocytes, epithelioid cells, and some giant cells. However, the picture which one actually sees depends on the

Fig. 2 (Collins). Section of human eye. (a) Retina. (b) Pigment epithelium with intact choriocapillaris below. (c) Nodule of infiltration in choroid, showing epithelioid cells in center of nodule.

age of the condition, and it apparently develops in stages:

1. Stage one is characterized by a focal infiltration of lymphocytes especially in the choroid and often around large veins. Figure 1 is a photomicrograph of a nodule in the

giant cells. Figure 2 shows a nodule in the choroid of an eye removed because of sympathetic ophthalmia four months after a cataract extraction. The nodule consists of lymphocytes and epithelioid cells. The choriocapillaris is spared, and the choroid be-
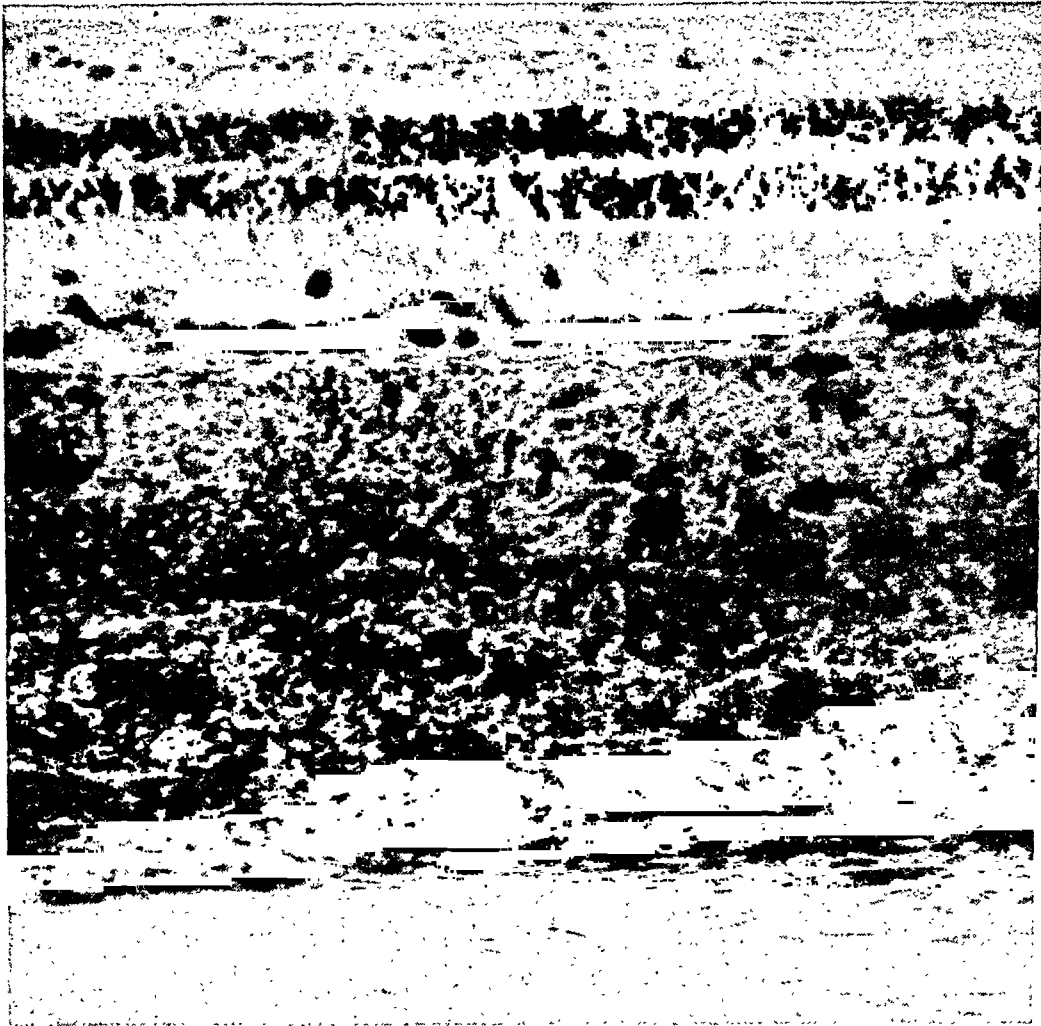
Fig. 3 (Collins). Section of human eye, showing tremendous thickening of choroid with lymphocytes and epithelioid cells.

choroid of an eye which was removed seven weeks after the original injury and immediately after the appearance of cells in the anterior chamber of the sympathizing eye. The nodule consists entirely of lymphocytes and there are only two such nodules in the whole choroid, as shown in the numerous sections prepared—the remainder being entirely normal.

2. Stage two is characterized by typical nodules in the choroid and iris of lymphocytes, epithelioid cells, and with or without

tween the nodules is normal. The time interval in this case is approximately the same as that during which the experimental animals were followed and is thus interesting for comparison.

3. Stage three shows the full-blown picture of the choroid uniformly infiltrated with lymphocytes and epithelioid cells and giant cells, especially the outer layers. Figure 3 illustrates this stage. This eye was removed because of sympathetic ophthalmia eight months after the original injury.

4. *Stage four* is the destructive phase in which the whole tissue is replaced by connective tissue.

No discussion of the pathology of sympa-

Fig. 4 (Collins). Dalén-Fuchs nodule in human eye.

thetic ophthalmia would be complete without mentioning the Dalén-Fuchs nodules. These are localized nodules of the pigment epithelium of the retina which were first described by Dalén[13] in 1904 and then by Fuchs[14] in 1905. They are formed by a localized proliferation of the pigment epithelium which has undergone autolysis and has been invaded by macrophages and epithelioid cells.

The Dalén-Fuchs nodules are considered by some to be pathognomonic of sympathetic ophthalmia. Others claim that they are found in inflammatory conditions, particularly tuberculosis. However, Friedenwald[4] stresses that the alterations of the pigment epithelium seen in other conditions never show the evidence of autolysis and phagocy-

tosis by epithelioid cells of the pigment granules as seen in sympathetic ophthalmia. Figure 4 shows a typical Dalén-Fuchs nodule from a human case of sympathetic ophthalmia.

V. EXPERIMENTAL WORK

1. *The goal* of this study was to produce in experimental animals a condition that simulated what is known as sympathetic ophthalmia in humans. This must be accomplished before the allergy theory can be established as fact.

2. *Choice of animal.* For this work we have chosen to use the guinea pig, because Zinsser[17] some years ago pointed out the similarity of the immune and anaphylactic reactions in guinea pigs and human beings. We learned from experience that white pigs with pigmented eyes or predominantly white pigs gave the best results in our work.

3. *Antigen.* In this work, macerated whole uvea was used as the antigen. It is true that the pigment of this tissue is believed to be the antigenic factor. Nonetheless, with our present meager knowledge regarding the chemistry and properties of melanin, it was felt that it would be impossible to obtain the pure product in its natural state.

Chemists working with this substance disagree about its solubility and properties. Despite the work of Elschnig,[2] von Szily,[15] and Woods,[3] who report on the use of pure pigment, it was felt that this was still impossible.

Mason,[16] after a review of the many works on the chemistry of melanin, states, "One is led to the conclusion that only the most gentle methods of separation of the pigment from its naturally occurring concomitants can be expected to yield an unchanged product. The weight of evidence indicates that, in the majority of cases in which isolation of melanin has been reported, the compositions found represent those of altered natural pigment. Since the recent study of Herrmann and Boss it has become evident

that the melanin granule is a highly complex aggregate not only of pigment, but also of at least three enzyme systems in a protein matrix. Should the pigment, which is apparently quinonoid, initially be bound to the granule by few or no primary valence bonds, it is likely on chemical grounds that destruction of the organization of the granule would result in rapid conjugation."

The pigment granule is intracellular, and it was felt that, with a limitless number of washings, one could never obtain pure pigment by mechanical means. Once chemical methods have been applied there is no way of knowing how the antigenicity of the melanin has been altered.

4. Procedures and results. In work on immunity it is known that young, healthy animals produce the highest titer of antibodies. Thus we used in all cases young, healthy guinea pigs.

SERIES ONE

Heterologous uveal tissue antigen. It is believed by many that uveal pigment is organ specific and not species specific, or only weakly so. Thus, in this series an attempt was made to sensitize guinea pigs to beef uvea (heterologous). Two animals were given intraperitoneal injections and four were given intramuscular injections of a mixture containing macerated whole beef uvea and adjuvants, which will be described later.

Three months after the last injection of this material the animals were killed and the eyes examined histologically. Of the six animals followed, one was positive (two eyes) and five were negative.

By positive is meant that the sections of the eyes showed good-sized areas of focal infiltration of lymphocytes and epithelioid cells in the choroid:

Figure 5 shows a nodule consisting of lymphocytes and epithelioid cells in the choroid of the left eye of the positive animal. Figure 6 shows a similar nodule in the

right eye of the same animal. The choroids of both eyes were filled with numerous such nodules. Bruch's membrane was intact and the retina was normal throughout.
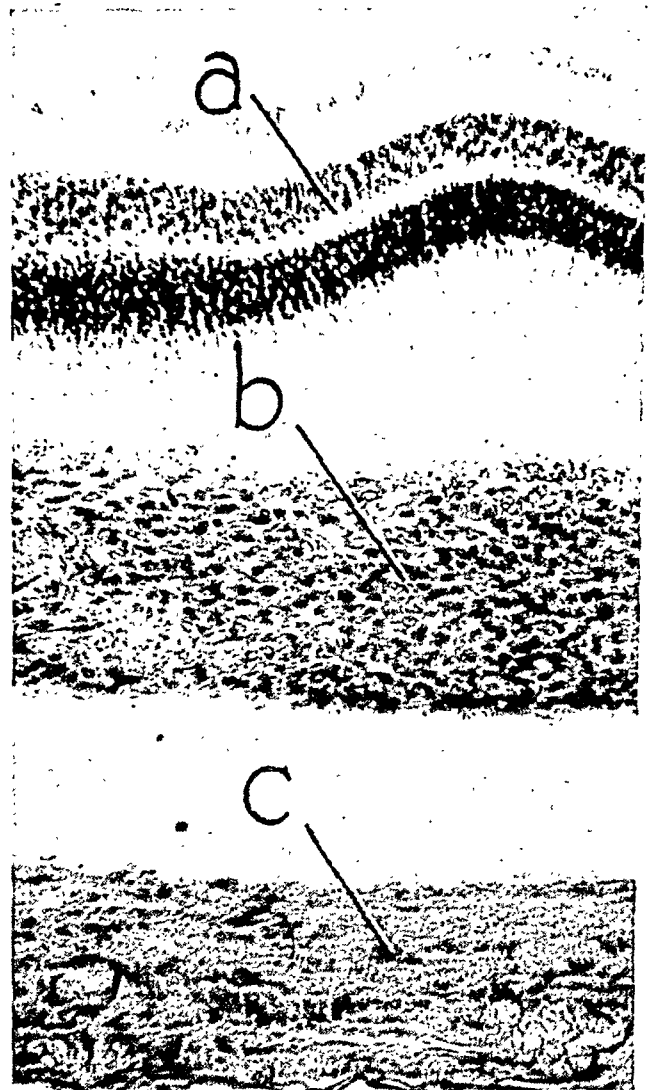
Fig. 5 (Collins). Section of left eye of guinea pig No. 292. (a) Retina. (b) Nodule of lymphocytic and epithelioid-cell infiltration in choroid. (c) Sclera.

SERIES TWO

Homologous uveal tissue antigen. In this series, an attempt was made to produce the picture of sympathetic ophthalmia in guinea pigs using guinea pig uvea as the antigen (homologous). The procedure was as follows:

A saline suspension of macerated guinea pig uveas was mixed with mineral oil, aquaphor, and heat-killed tubercle bacilli. Each
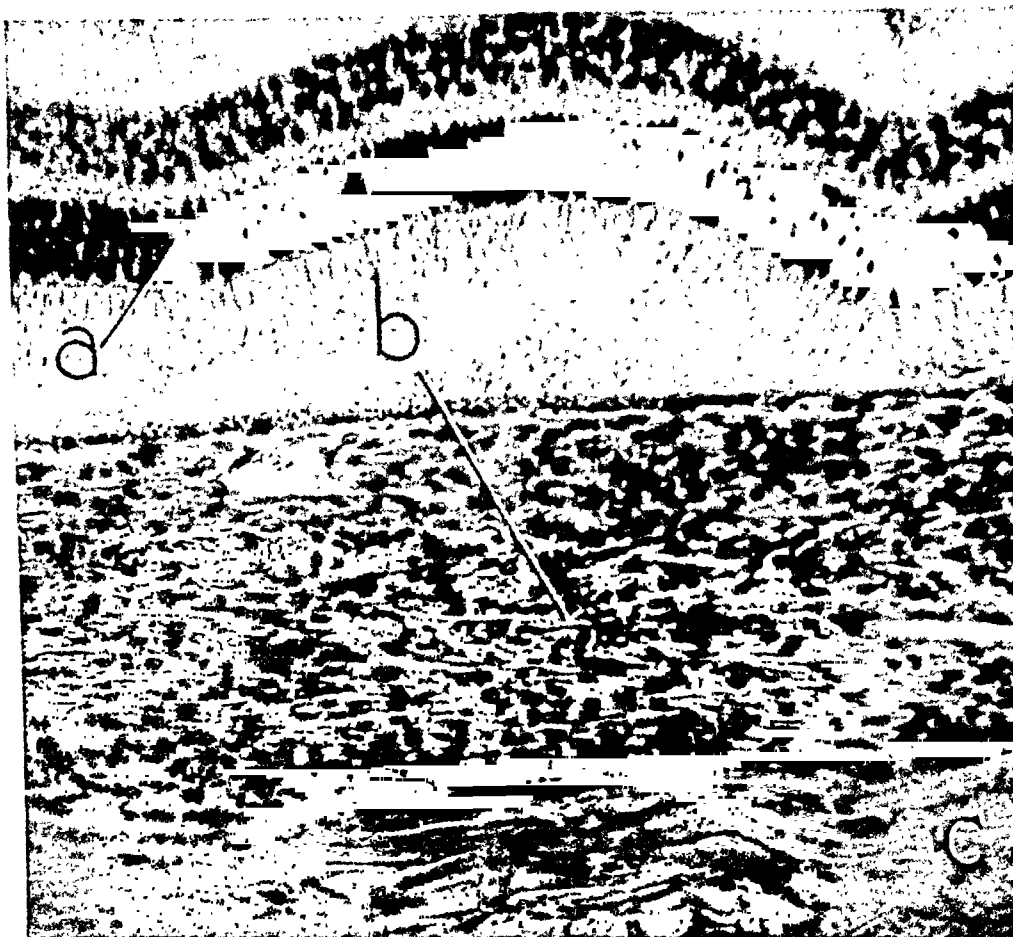
Fig. 6 (Collins). Section of right eye of guinea pig No. 292. (a) Retina. (b) Nodule of lymphocytic and epithelioid-cell infiltration in choroid. (c) Sclera.
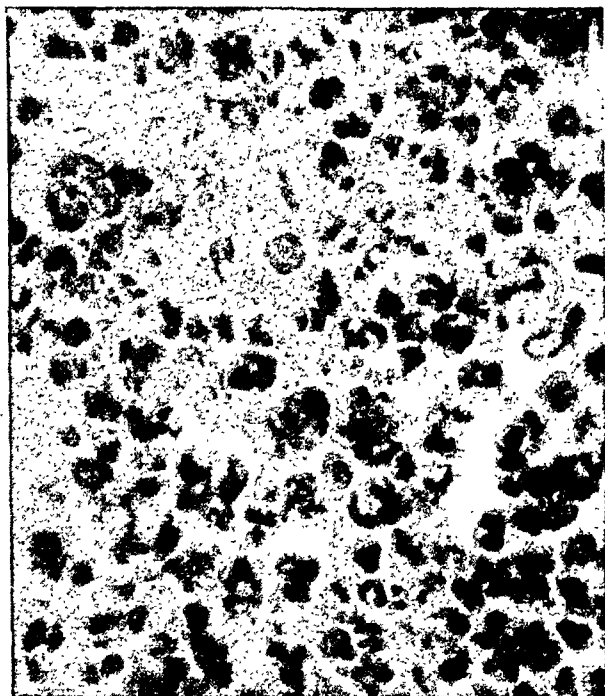
Fig. 7 (Collins). Biopsy of inoculation site.

injection was composed of 0.2 cc. paraffin oil, 0.1 cc. of aquaphor, heat-killed tubercle bacilli (0.5 mg. in the first, 0.85 mg. in the second, and 0.5 mg. in the third batch of antigen mixture), and 1.6 uveas per injection in the first mixture, 3.35 uveas in the second, and 0.7 uveas in the third.

This material was injected intramuscularly or intraperitoneally into 25 young, healthy guinea pigs. Each animal received 0.5 cc. of the above mixture in a leg muscle at weekly intervals for three doses. A fourth such injection was given at the end of five weeks. In a few, the fourth intramuscular injection was replaced by an intraperitoneal injection of the same amount. The animals were followed for from 3 to 6 months after their first injection.

Immediately before killing 12 of the animals, a sterile sample of blood was drawn

from the heart. Complement fixation tests run on these 12 sera showed no complement-fixing antibodies to guinea-pig uvea.

Because there is a virus theory of sympathetic ophthalmia, eight of these blood samples were studied for the presence of a virus. No virus was isolated by the routine methods of checking for these organisms. Likewise, because there is a bacterial theory of this condition, eight of the samples were cultured for the presence of bacteria and all of the specimens of blood were found to be sterile. An electrophoretic pattern was run on one serum and no increase of gamma globulin was demonstrated.

At the end of the chosen interval, that is, from 3 to 6 months, the 25 animals were weighed and killed. All 25 had gained much weight and appeared healthy. The eyes were removed immediately after death and fixed in Zenker's fixative and serial sections were made of all the eyes. Biopsies were taken of lung, liver, spleen, kidney, and inocula-iton site in all of the animals.

Figure 7 shows a biopsy of an inoculation site of one of the animals. It shows the
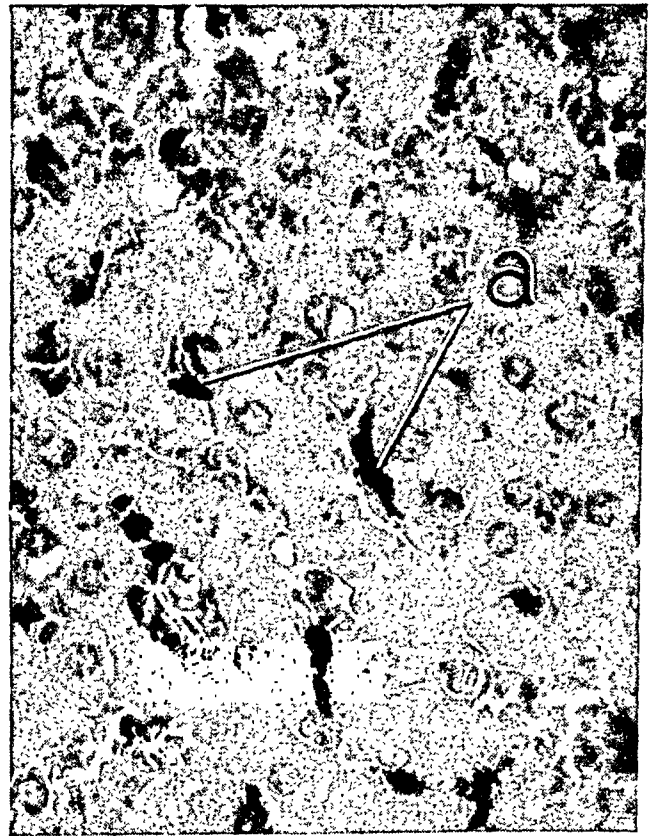
Fig. 8 (Collins). Biopsy of liver of treated guinea pig. (a) Kupffer cells filled with uveal pigment.

great mononuclear response called forth by the mixture, and the phagocytosis of pigment
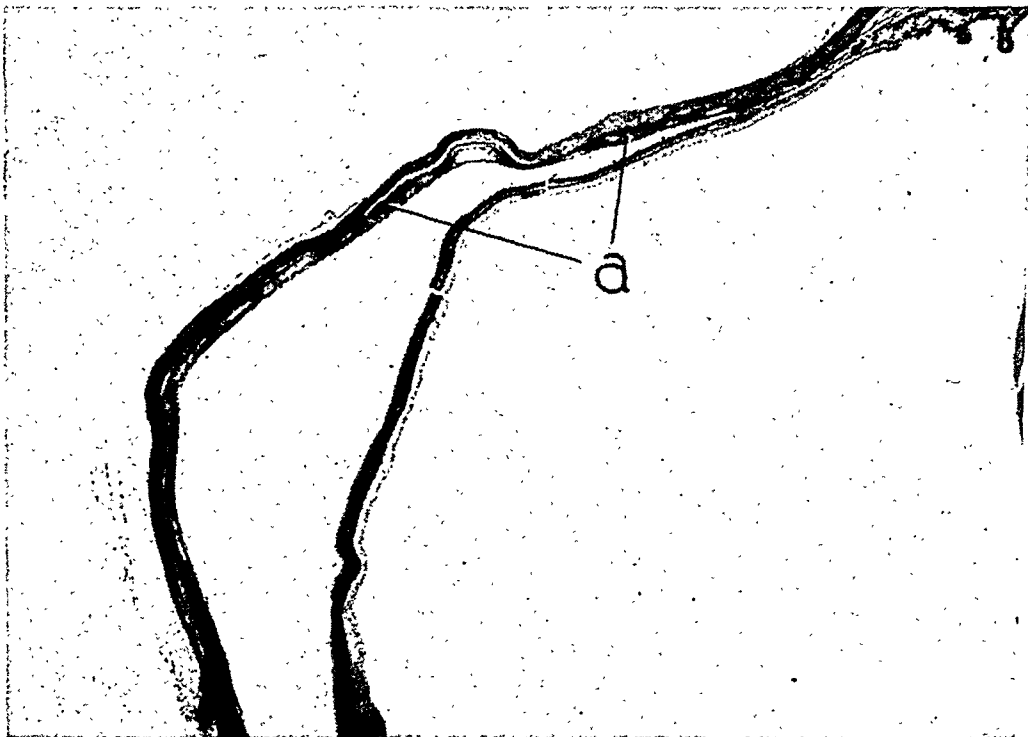
Fig. 9 (Collins). Low-power magnification of a section of left eye of guinea pig No. 253. (a) Nodules of infiltration in the choroid.
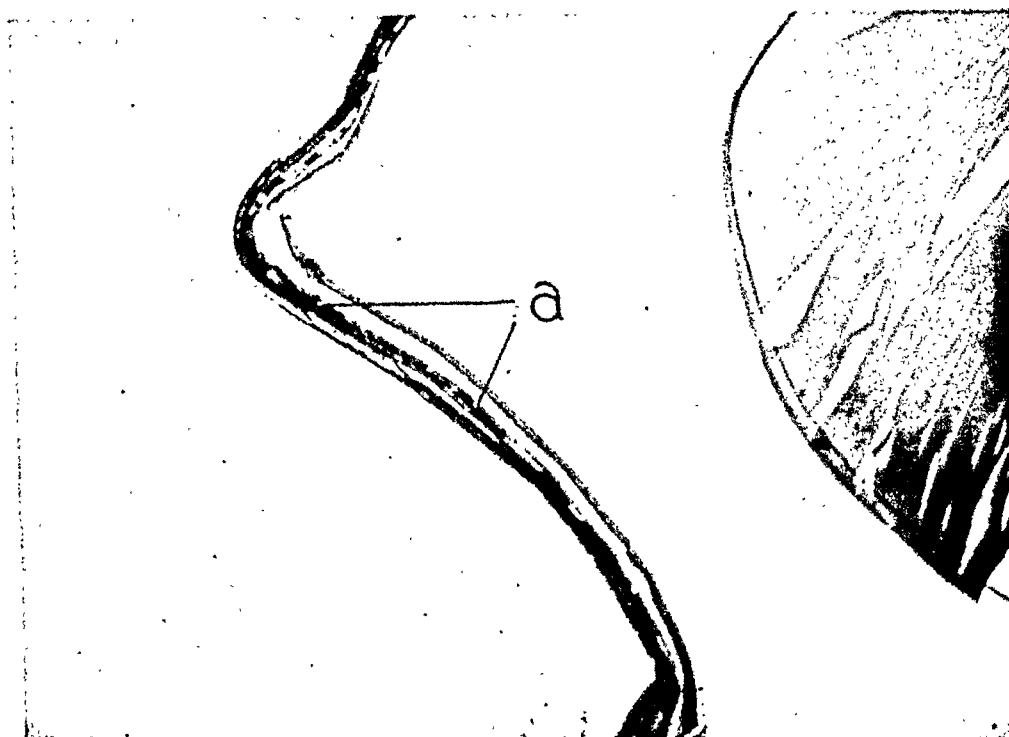
Fig. 10 (Collins). Low-power magnification of a section of the right eye of guinea pig No. 253. (a) Nodules of infiltration in the choroid.
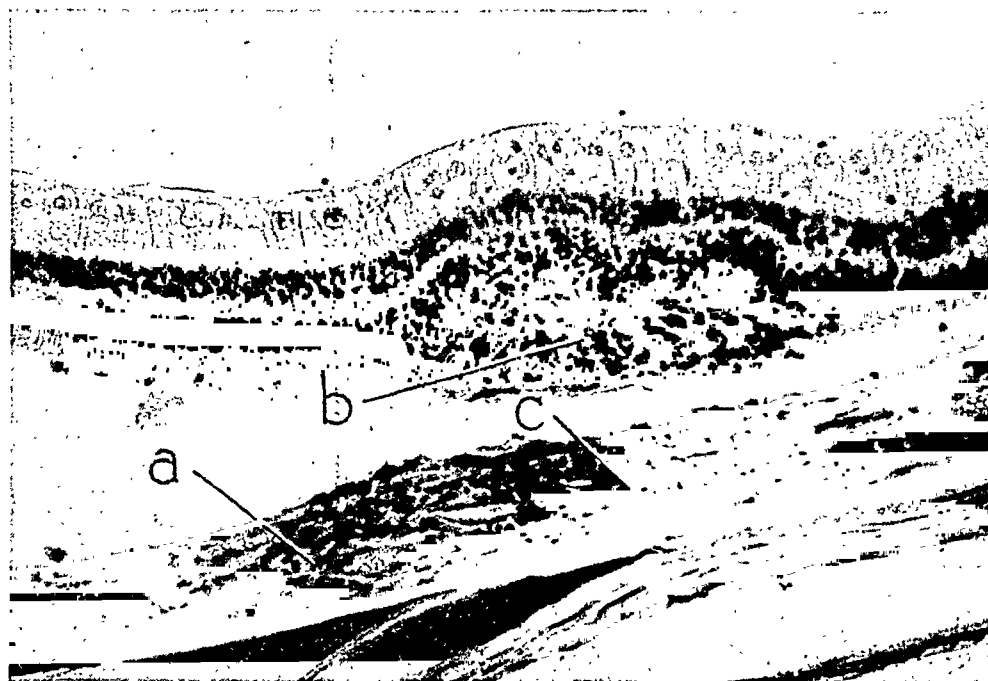
Fig. 11 (Collins). High-power magnification of a nodule in the choroid of the right eye of guinea pig No. 253. (a) Area of epithelioid cells in center of nodule in choroid. (b) Proliferation of pigment epithelium. (c) Area of lymphocytes in choroidal nodule.
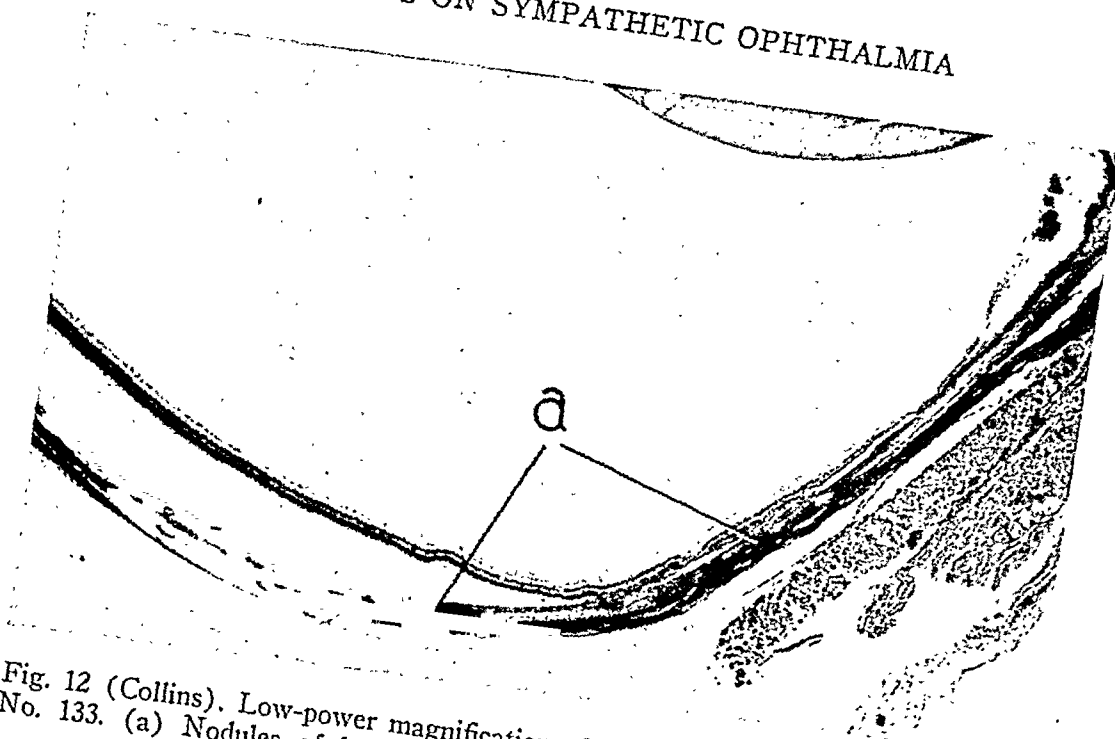
Fig. 12 (Collins). Low-power magnification of a section of left eye of guinea pig No. 133. (a) Nodules of lymphocytic and epithelioid-cell infiltration in choroid.
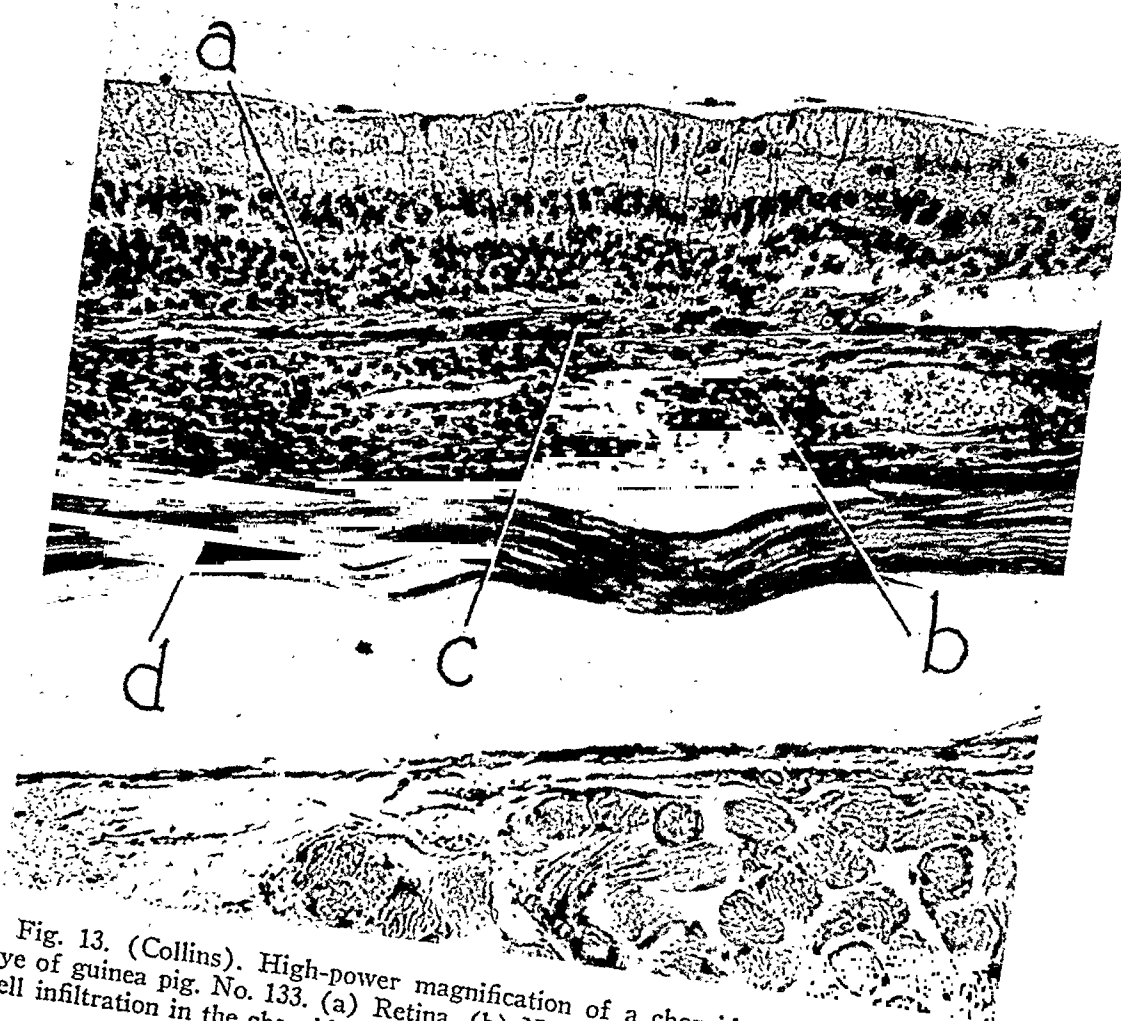
Fig. 13. (Collins). High-power magnification of a choroidal nodule in the left eye of guinea pig. No. 133. (a) Retina. (b) Nodule of lymphocytic and epithelioid-cell infiltration in the choroid. (c) Proliferation of pigment epithelium. (d) Sclera.

by these cells. As pointed out above, one theory of action of adjuvants is that they call forth a large response of mononuclear cells which, in turn, increase antibody production.

Figure 8 shows a biopsy of the liver of one of the animals. It shows how the re-

Figure 9 shows the nodules in the choroid of the left eye of guinea pig No. 253, and Figure 10 shows the same findings in the right eye of this same animal.

Figure 11 shows one of these choroidal nodules of experimental animal No. 253 under higher power. Bruch's membrane is in-
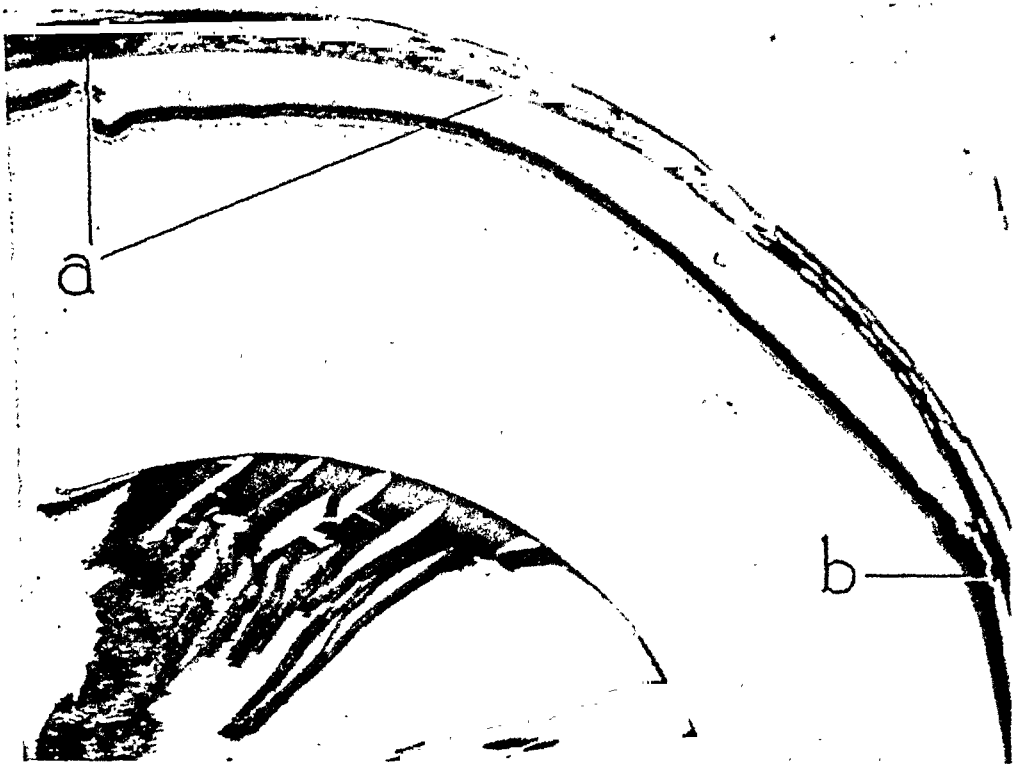
Fig. 14 (Collins). Low-power magnification of a section of right eye of guinea pig No. 133. (a) Nodules of lymphocytic and epithelioid-cell infiltration in the choroid. (b) Dalén-Fuchs nodule.

ticulo-endothelial system of the liver, the Kupffer cells, have phagocytosed the pigment. Biopsies of the lung and spleen also showed marked phagocytosis of pigment by this system. The reticulo-endothelial system is important in the formation of antibodies.

Of the 25 guinea pigs so treated, 12 (24 eyes) were positive, that is, showed large areas of focal infiltration of lymphocytes and epithelioid cells in the uvea and changes in the pigment epithelium resembling Dalén-Fuchs nodules. It is to be emphasized that the eyes of these experimental animals were never touched or traumatized in any fashion until they were removed for sectioning after the death of the animal.

tact and there has been a proliferation of the pigment epithelium of the retina and some loss of retinal substance over this nodule probably as a result of an autolytic process taking place in the nodule. Careful examination of these sections shows that there is no true invasion of the retina.

Figure 12 shows the nodules in the choroid of the left eye of another positive animal, No. 133, and Figure 13 shows a high power magnification of one of these nodules. The nodule is composed of lymphocytes and epithelioid cells, Bruch's membrane is intact, and the choriocapillaris is spared.

Since sympathetic ophthalmia is a bilateral condition, Figure 14 shows the nodules in

the choroid of the right eye of this same animal, No. 133.

Figure 15 shows a Dalén-Fuchs nodule from the right eye of animal No. 133. Here again one sees a proliferation of the pigment epithelium, epithelioid cells, and an evidence of an autolytic process as shown by a loss of the retinal substance over the nodule. Many of the eyes of the positive animals showed these nodules.

SERIES THREE

Controls. Nineteen guinea pigs were run as controls. Fourteen of these animals received four intramuscular injections at the same time intervals as was used in the treated animals, that is, 1, 2, 3, and 5 weeks.

Each injection, consisting of 0.5 cc., contained the same amount of adjuvant—aquaphor, mineral oil, and heat-killed tubercle bacilli (0.5 mg. per injection)—as was used in the test animals above.

In addition, each injection contained an amount of albino guinea-pig liver tissue equivalent in dry weight to the approximate dry weight of guinea pig uvea in each experimental animal injection. Albino guinea-pig liver was chosen as a neutral, noneye tissue which we could be certain contained no melanin.

Five of the 19 guinea pigs received the same series of intramuscular injections of adjuvant alone. Each injection contained the same amount of adjuvant—mineral oil, aquaphor, and heat-killed tubercle bacilli—as was used in the treated cases.

All of the control animals were followed for from 3½ to 5 months. At the end of the chosen time interval, the animals were killed and biopsies of the lung, liver, spleen, kidney, and site of injection were taken. The eyes were removed immediately after death and fixed in Zenker's fixative and serial sections were made of all the eyes.

Microscopic examination of every section showed all of the 19 control guinea pigs (38 eyes) to be negative, that is, there were no abnormal histologic findings in any of the eyes.

SUMMARY

1. Observations favoring the allergy theory of sympathetic ophthalmia were presented.

Fig. 15 (Collins). High-power magnification of Dalén-Fuchs nodule in right eye of guinea pig No. 133.

2. The histopathologic picture of sympathetic ophthalmia was briefly reviewed.

3. Experimental work showing an attempt to sensitize guinea pigs to uveal tissue with the aid of adjuvants, mineral oil, aquaphor, and heat-killed tubercle bacilli was presented. One (two eyes) of six guinea pigs, using heterologous uveal tissue, beef uveas, plus the above adjuvants, showed focal areas of lymphocytes and epithelioid-cell infiltration in the choroid of both eyes.

Twelve (24 eyes) of 25 guinea pigs using homologous uveal tissue, guinea pig uveas, plus adjuvants showed similar lesions. Many showed Dalén-Fuchs nodules.

Nineteen control guinea pigs given adju-

vants plus albino-liver tissue, or adjuvants alone, showed no abnormal findings in the eyes.

630 West 168th Street (32).

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DISCUSSION

DR. JONAS S. FRIEDENWALD (Baltimore): I think Dr. Collins' report is very impressive. I would like to have more detailed histologic pictures before I can make up my own mind as to whether the picture produced, and to what extent the picture produced, resembles that of sympathetic ophthalmia.

I should like to make one point in regard to whether or not melanin itself is the necessary antigen in an allergic theory of sympathetic ophthalmia. A number of years ago Dr. Robert Hare and I were studying the skin reactions of patients with sympathetic ophthalmia to various inocula, and comparing the reactions to those produced in the skin of these same patients by uveal pigment preparations.

We found that we could make an emulsion from the choroid of albino rabbits which, when injected intradermally into sensitive patients, elicited an epithelioid-cell and round-cell reaction quite analogous to that produced in the same patient by an emulsion of choroid from a pigmented rabbit, and consequently we concluded that the melanin itself was not the antigen, but perhaps the melanin granule contained a matrix which was the antigen.

DR. ROBERT DAY (Baltimore): Were there any changes in the anterior uvea or any clinical signs?

DR. DAVID G. COGAN (Boston): I would like to ask the essayist if he investigated other pigment-bearing structures; for example, in the choroidal plexus, and if there was any lymphocytic reaction anywhere else in the body. From the pictures, I would judge not.

DR. RAYMOND C. COLLINS (New York): The question as to whether or not there were any changes in the anterior uvea: The iris was entirely free. Many of them showed mild infiltration of lymphocytes in the ciliary body.

As to whether there was a lymphocytic reaction elsewhere in the body, biopsies taken as outlined, of the lung, liver, spleen and kidney, showed no lymphocytic infiltration, merely this phagocytosis of pigment that you saw on the slides.

DR. COGAN: Lymphocytic reaction in other pigmented-bearing structures? Did you investigate any other pigment-bearing areas?

DR. COLLINS: No, we did not.

DR. COGAN: That would be an interesting thing to do.

DETACHMENT OF THE ANTERIOR LAYERS OF THE IRIS (IRIDOSCHISIS)*

REPORT OF A CASE‡

JAY G. LINN,† M.D., AND JAY G. LINN, JR., M.D.

Pittsburgh, Pennsylvania

A separation or detachment of the anterior layers of the iris is a very rare condition, first described by Schmitt[1] in 1922 and named iridoschisis (iris splitting) by Loewenstein and Foster[2] in 1945. It is an acquired condition of a degenerative nature and is characterized by a separation of the iris into two distinct layers. The anterior layer appears as a thin transparent stratum of iris tissue attached to the posterior layer centrally in the region of the sphincter and peripherally near the iris root. The main body of this layer is composed of radial fibers which, in places, undergo fragmentation. The loose ends float singly or brush-like in the aqueous. The posterior deeply pigmented layer of the iris is easily seen through this anterior layer even where no fragmentation has occurred.

Ten cases have previously been reported in the literature to which we are adding an eleventh. They are as shown in Table 1.

CASE REPORT

Clinical history. B. C. L., a 58-year-old white man, was first seen by one of us (J. G. L.) in May of 1938, at which time he complained of blurred vision of the right eye. The corrected vision at that time was: R.E., 20/100; L.E., 20/200. He had always had poor vision in the left eye and an opera- tion was performed in 1912 to correct a left esotropia.

A diagnosis of chronic simple glaucoma of the right eye was made on the initial examination and a corneoscleral trephining operation was performed a few weeks later. Good filtration was obtained and the post- operative corrected vision was 20/50+3. The tension has remained normal or sub- normal since the operation.

In October, 1946, a reduction of the vision of the right eye caused by a nuclear cataract was noted. Ophthalmoscopy at this time revealed a pallor of the disc and pig- ment deposits in the retina.

In February, 1948, an atrophy of the iris with detachment of the anterior layers was first noted. The lenticular opacity had progressed and the fundus could not be seen.

Past medical history. Our patient had an appendectomy performed in 1928 which was followed in four weeks by a right nephrec- tomy for a kidney stone. Postoperative cul- ture from the kidney was positive for Myco- bacterium tuberculosis. He has enjoyed good health since that time.

Present ocular findings. In October, 1948, visual acuity of the right eye was 4/200 and of the left eye, 20/200. The right eye was divergent about 10 degrees. Both pupils re- acted normally to light.

Slitlamp examination. Right eye. There was beginning endothelial dystrophy of the cornea (cornea guttata). No keratic pre- cipitates were present and the aqueous was clear.

The iris had a surgical coloboma at the 12-o'clock position from the corneoscleral trephination. The entire iris was atrophic. This atrophy was more advanced in the ciliary zone. In this area, between the

TABLE 1

CASES OF IRIDOSCHISIS IN THE LITERATURE

Author and Year	Age and Sex	Associated Ocular Findings	Systemic and Other Factors
Schmitt[1] 1922	74 F.	Mature cataract	Neurodermatitis circumscripta chronica, asthma
Drapkin[3] 1923	74 F.	Cortical cataract	
Sander[4] 1925	78 M.	Immature cataract	
Vogt[5] 1926	70 F.	Chronic iridocyclitis	
Schoenberg[6] 1927	51 M	Chronic simple glaucoma	Traumatic history as a high diver
Imre[7] 1927	92 94		
Dollfus[8] 1927	F.	Cataract	Diabetes mellitus
Loewenstein and Foster[2] 1945	76 F.	Iritis, glaucoma, and nuclear cataract	Osteoarthritis
Loewenstein, Foster, and Sledge[9] 1948	46 M.	Secondary glaucoma	Blunt blow to globe
Linn and Linn	58 M.	Chronic simple glaucoma, nuclear cataract	Tuberculosis of kidney with stone formation

sphincter muscle and the base of the iris, there was a separation into two layers. This was more evident in the nasal half of the iris. The main body of the anterior layer consisted of radial fibers. Some of these fibers contained granules of uveal pigment. In the area between the 3- and the 6-o'clock positions there had been a rupture of these radial fibers. The free ends were floating in a brushlike manner in the aqueous. A depigmentation of the anterior layer had resulted in a translucency which enabled the slitbeam to pass through so that the deeply pigmented posterior layer could be easily observed. This translucency was reduced in the region of the sphincter which apparently was uninvolved because the pupil reacted promptly to light. Examination of the lens revealed a diffuse nuclear opacity.

Left eye. The cornea had a nebulous opacity involving the stroma of that portion just below the pupil. An endothelial dystrophy in the same stage as that of the

right eye was present.

There was beginning atrophy of the iris with some absorption of pigment of the anterior layers. Only in some areas had this depigmentation progressed so that the posterior layers could be seen through the anterior. No separation of the layers was evident. No cataract formation was evident in the lens.

Gonioscopy. Examination of the angle of the anterior chamber with the Allen prism revealed complete occlusion of the angle of the right eye by peripheral anterior synechia.

The angle of the left eye was open only in a small area of the nasal portion. No pigment could be seen in this area.

COMMENT

Histologic studies of the iris have been reported by Loewenstein, Foster, and Sledge[2, 9] which confirm the biomicroscopic findings. They found general atrophy of the iris
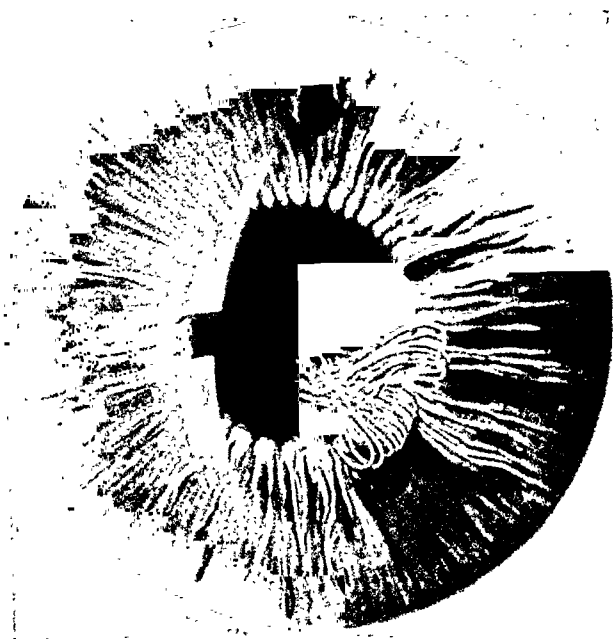
Fig. 1 (Linn and Linn). Appearance of the detachment of the anterior layers of the iris in the case herein reported.

tissue. The anterior layer consisted in some places of "thin floating membranes" and in others of "fragile grayish tissue like the finest lace." The free floating radial fibers were found to contain a blood vessel with a thickened endothelium. The blood vessel was filled with erythrocytes. The sphincter muscle was normal and the dilator fibers were hypertrophied. In their second case there was some evidence of phagocytosis of pigment.

An analysis of the reported cases reveals no specific cause for this peculiar form of iris atrophy. Senility, glaucoma, trauma, iritis, and diabetes have been suggested by individual authors. Apparently, any of these may be a factor which acts on the more delicate spongy tissue of the iris. The atrophy of the more dense and better differentiated tissues of the iris may follow at a later stage.

In no case has any synechia of the freely floating fibers to the cornea been recorded. No hyphema has resulted from rupture of these fibers.

Dollfus[8] performed an iridectomy on his patient which he followed in one month with a lens extraction. There was no complication of either procedure. We plan to extract the lens of our patient at a later date.

Our case is significant only in that the ruptured radial fibers of the anterior iris layer are possibly more prominent and the artist has been able to demonstrate them (fig. 1) better than in the previously reported cases.

SUMMARY

A case of detachment of the anterior layers of the iris (iridoschisis) is reported. The previously reported cases are listed. No specific cause can be assigned to this unusual degenerative condition.

7075 Jenkins Arcade (22).

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CORRELATION OF MICROSCOPIC AND SLITLAMP EXAMINATIONS OF DEVELOPING HEREDITARY CATARACTS IN MICE*

GEORGE K. SMELSER, PH.D., AND LUDWIG VON SALLMANN, M.D.

New York

A strain of Swiss albino mice which invariably develops hereditary cataract at an early age was placed at our disposal by Professor Landauer of the University of Connecticut. This stock appeared to be of normal, vigorous animals with the exception of the lens pathology to be discussed, and a deformity of all four feet which is inherited as a recessive character, called brachypody by Landauer. There is no reason to believe that this latter condition has any relation to the cataract formation.

It was planned to follow the progress of developing cataracts in these mice both by clinical study with the slitlamp and histologic examination, and to attempt correlation of the data obtained by the two methods. In addition, some preliminary studies were made which might suggest other approaches to the problem of the mechanism of the cataractous process. For these purposes a colony of animals was established, maintained on our stock diet supplemented with one based on growing chick mash with added vegetable and cod-liver oil and brewers' yeast. A control group of mice, also of the Swiss albino strain, but which is regularly free of the lenticular abnormalities, was maintained under the same conditions to provide normal material for comparison.

One hundred and five mice were examined, 70 of them on several occasions with the slitlamp and corneal microscope by one of us (L. v S.). Twenty-five of these were killed at various stages for microscopic study. The lenses of eight normal mice of various ages were also studied microscopically. Most of the sections were prepared by the celloidin method, 8 and 10 microns in thickness, and stained by standard procedures. Frozen preparations were made of 14 eyes and the sections examined for fat, cholesterol (Schultz reaction), and birefringent material.

OBSERVATIONS

The lenses appeared to be normal during the first 35 to 40 days of life. Occasionally fine remnants of the hyaloid vascular system were seen at the posterior surface of the lens but not in greater frequency or size than in normal mice of the same age. In two mice, both 39 days old, an irregularity of the specular reflex and a fine stippling were noted at the posterior pole with slitlamp examination. This appearance may be normal.

One of these lenses appeared to be quite normal when studied histologically, but the other three showed some deviation from the appearance of normal control lenses. This was evidenced by (1) the presence of small basophilic patches in the cortex near the posterior pole, (2) slight disorganization of the lens fibers at the posterior pole of the lens nucleus, (3) lack of preciseness in the posterior boundary of the nucleus (fig. 2).

It will be noted (fig. 2) that the lens abnormality involves the posterior border of the lens nucleus, very deeply stained, and all of the posterior cortex at this point. The posterior cortex (neutrophilic in staining reaction) appears to be slightly narrower than normal so that the nucleus lies nearer to the posterior pole than normally.

By 55 days of age cataracts were generally quite definite. The typical appearance seen clinically in this age group began with a circle of tiny gray dots around the posterior pole in the cortex of the lens, which was the earliest stage indentifiable as abnormal. A section of this lens is shown in Figure 3. The
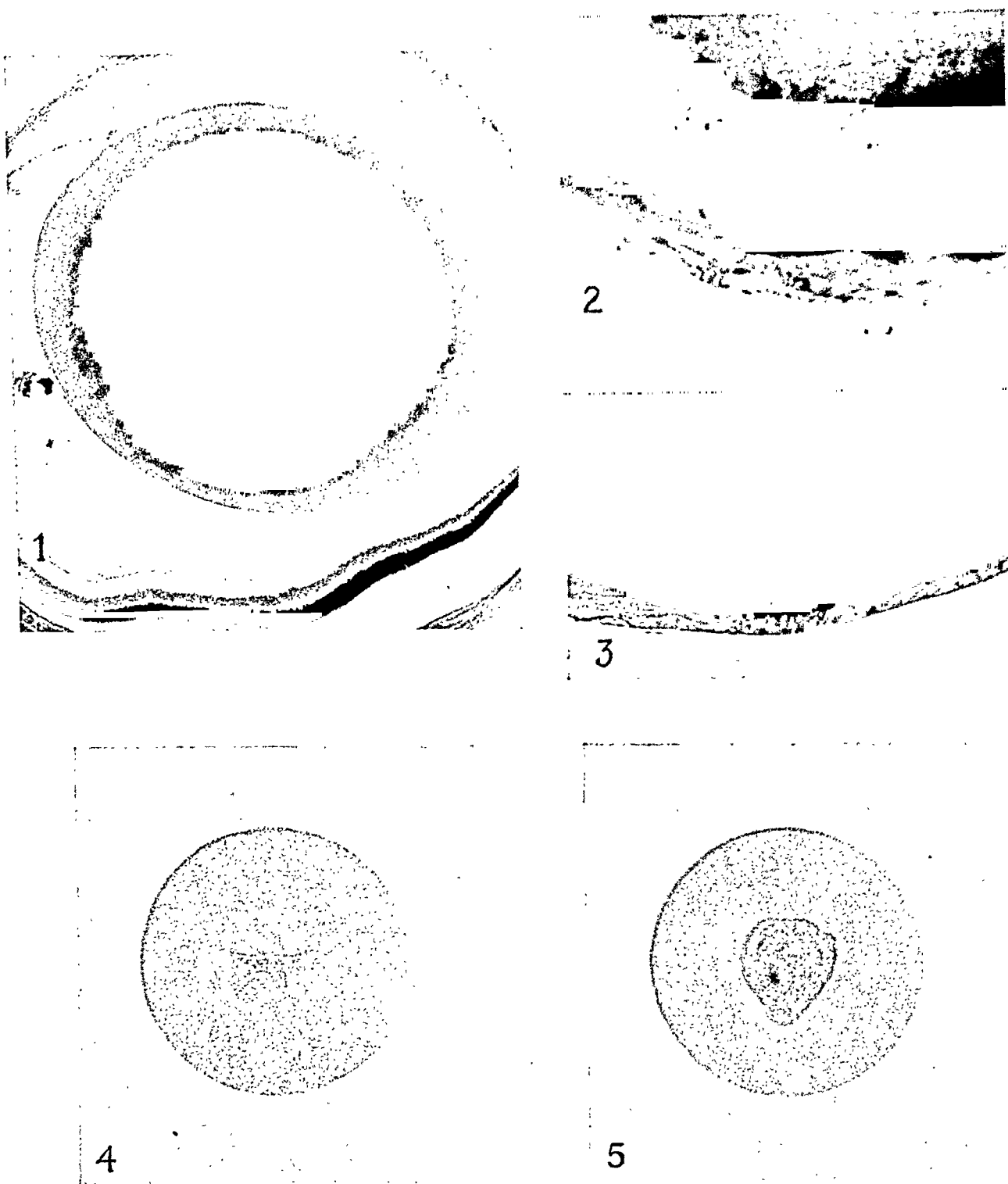
Figs. 1 to 5 (Smelser and von Sallmann). 1. Section of normal mouse lens.

2. Section of lens showing definite deformation at the posterior pole. Slight stippling, regarded as probably normal, was seen in this region with the slitlamp. Note the presence of some remnants of the hyaloid vascular pattern. Age of mouse 39 days.

3. Section through posterior pole of a lens which showed the earliest stage identifiable as abnormal by slitlamp examination. Note the very narrow cortical zone and the disruption of the more central fibers. Age of mouse 55 days.

4. Clinical appearance of an early stage in the cataract development. The opacity lies at the posterior pole of the lens. Age of mouse 66 days.

5. A slightly more advanced stage in the cataract formation. Age of mouse 66 days.

fibers of the posterior portion of the nucleus appear to be swollen and separated.

In addition, marked, though small, opacities were found clinically in the posterior polar region of other animals of this age group. They ranged from triradiate localized opaque masses to irregularly shaped opacities sometimes containing minute vacuoles. The clinical appearances of two such types are shown in Figures 4 and 5.

The histologic appearance of such an opacity, although represented by an older case, is shown in Figure 6. These opacities increase in size and density and often extend into the adjoining layers as a gray veil with fine striations. This veil could not be identified in histologic preparations.

In the further development of the cataract, irregular opacities appeared in the perinuclear area, as seen with the slitlamp, and, in some cases, minute vacuoles which seemed to lie in the subcapsular zone. Microscopic study of these lenses revealed a pyramidal homogeneous mass at the posterior pole very like that seen in earlier stages (fig. 6). The basophilic lens nucleus appeared to be displaced posteriorly and surrounded by cortex with a neutrophilic staining reaction. Around this zone was a markedly crescentic basophilic area, wide anteriorly and tapering rapidly toward the posterior pole.

On the anterior surface of this crescent were a row of small vacuoles (fig. 7). The lens cortex appeared to be normal. When the opacity involved the perinuclear zone it often formed a rather homogeneous layer around the nucleus which appeared clear. In other instances, a second more peripheral opaque zone became visible, separated by a clear interval from the more central layer. The histologic appearance of the anterior portion of such a lens is shown in Figure 7.

Finally, in a third group of animals the nucleus became cataractous before the layers of peripheral opacity developed. Sometimes a thin, dense sheath surrounded the nuclear opacity as shown in Figure 9. The further

progress of the cataract was apparently not influenced by the character of the intermediate state.

Vacuoles occurred frequently, but only in animals three months of age or older. In most cases these vacuoles appeared to be empty, but in a few they contained a stainable coagulum. Such a vacuole is shown in Figure 8. This vacuole was not noted in the slitlamp examination, but small subcapsular vacuoles were. These, on the other hand, were not found microscopically.

A water cleft was also noted in this eye in the slitlamp examination, and a cleft occurred at the anterior pole of the basophilic perinuclear zone. This cleft contained a homogenous material which stains very like the perinuclear material, although no structure is apparent. Many of the larger vacuoles, seen with the slitlamp, were arranged equatorially, as shown in Figure 9, although in some they appeared to fill the entire anterior part of the lens (fig. 10).

In practically all cases the lens was found to have ruptured at the posterior pole and the nucleus extruded into the vitreous. This occurred first at 70 to 80 days of age, although all animals were not so affected at this time. In older mice this phenomenon was almost invariable.

The extrusion of the lens nucleus was not obvious in the slitlamp examination, possibly because more anteriorly placed opacities obscured the view. The extrusion of the lens is not a technical artefact occurring during the histologic procedures, for it could be demonstrated by dissection of the globe prior to fixation. Such a lens is shown in Figure 11. Cataractous but intact lenses dissected out of the eye and placed in fixatives did not rupture.

Figure 8 shows what may be a very early stage in lens extrusion. The capsule is broken at the posterior pole and the lens nucleus appears to be slightly protruding. The typical appearance of these later stages is shown in Figure 12. The capsule has ruptured, and its
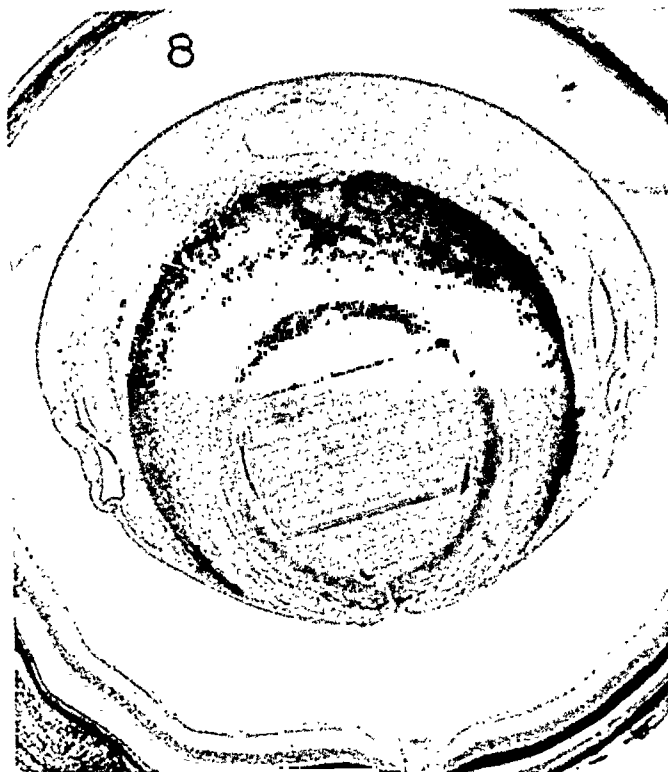
Figs. 6 to 8 (Smelser and von Sallmann). 6. Section through the posterior part of a cataractous lens showing the histologic appearance of an opacity similar to those shown in Figures 4 and 5, although it is from an older mouse, aged 125 days.

7. Anterior portion of a cataractous lens showing a row of small vacuoles lying deep in the cortex on the surface of a basophilic crescent-shaped band of material anterior to, and separated from, the lens nucleus. Age of mouse 125 days.

8. Section of a cataractous mouse lens, age of mouse 146 days, showing a coagulum filled vacuole in the anterior cortex, not noted in slitlamp examination. The nucleus appears to have been displaced posteriorly. The posterior lens capsule may have ruptured. This appears to be a very early stage of nuclear extrusion.

broken ends coil like a watch spring on either side of the opening. A dense basophilic mass, the remnant of the crescent of perinuclear material shown in Figure 7 was retained within the capsule and probably interpreted clinically as opaque nucleus.

After it was known that the lens frequently ruptured, evidence of that fact could be obtained on slitlamp examination by noting a flattening in the anterior surface of the lens and an increase in the depth of the anterior chamber.
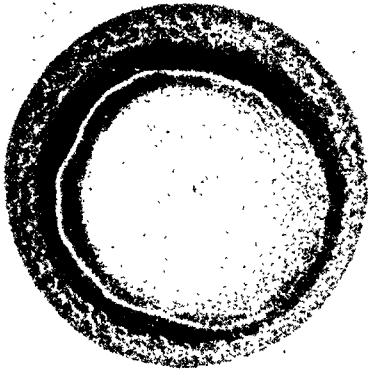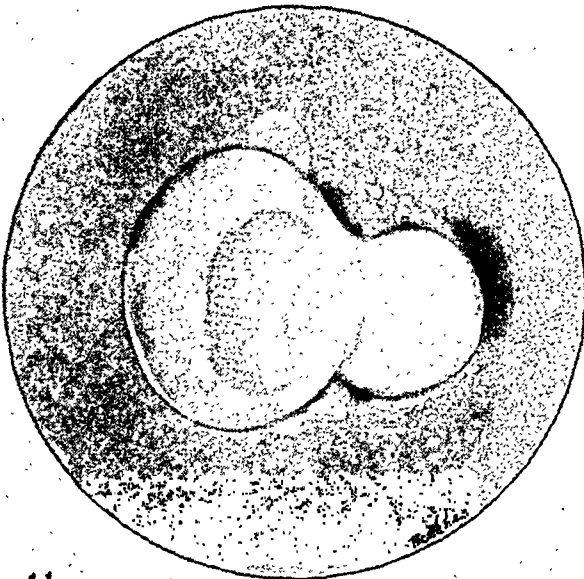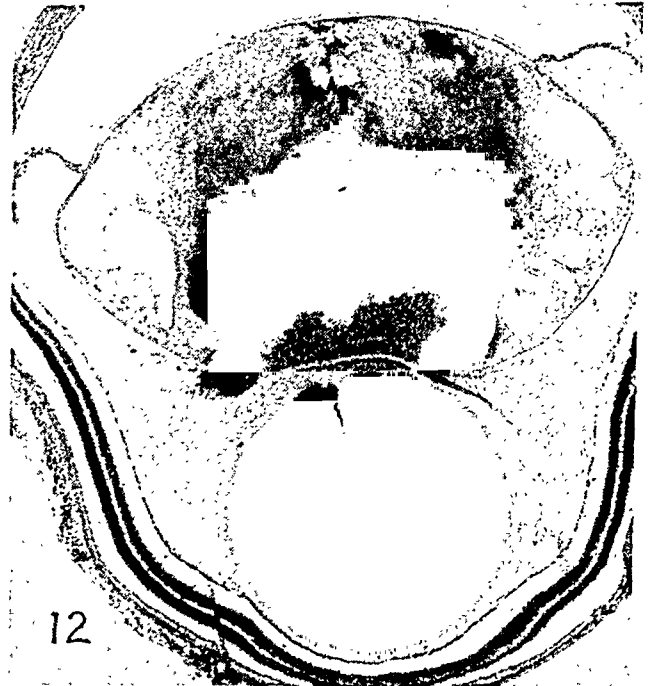
Figs. 9 to 12 (Smelser and von Sallmann). 9. Clinical appearance of a more advanced cataract showing many equatorial vacuoles. Age of mouse 95 days.

10. An extreme case of vacuolation of the cataract. Age of mouse 219 days.

11. Drawing of a ruptured lens dissected from the eye showing the extruded nucleus. Vacuoles can be seen in the equatorial region. Age of mouse 146 days.

12. Section of a lens after rupture of the capsule and extrusion of the lens. The retained deeply staining material was opaque and obscured the extruded nucleus in the slitlamp examination. The vacuoles are similar to those shown in Figures 9 and 11. Age of mouse 125 days.

Due to the relatively small volume of vitreous and large lens in mice eyes, the extruded lens nucleus and lenticular material often came into contact with the retina. Various degrees of retinal reactions were observed. Aggregations of small cells with deeply staining nuclei, possibly lymphocytes, were frequently found. The ganglion cells were sometimes misshapen or unrecognizable. In one case, elongated spindle-shaped cells,

similar to fibroblasts were found. Of the 12 eyes examined all but three showed some retinal abnormalities. In the three which did not, the lens material was not in direct contact with the retina. These may have been cases in which the lens was very recently ruptured.

lenses in which no crystals had been noted. In one case there was an agreement, in that neither cholesterol nor crystals were found.

The histochemical test for cholesterol and the slitlamp examination report on the crystals were in agreement in 50 percent of the cases. It should not be concluded from this

TABLE 1

CORRELATION OF IRIDESCENT CRYSTALS WITH THE HISTOLOGIC DEMONSTRATION OF FAT AND CHOLESTEROL IN THE LENS

Animal and Eye	Age (months)	Slitlamp	Microscopic Section	
		Iridescent Crystals	Cholesterol (Schultz Reaction)	Fat (Sudan Positive)
122 O.S.	4½	−	+	+
20 O.S.	6	−	+?	+
21 O.D.	6	−	+	+
82 O.S.	8½	++	++	+
82 O.D.	8½	+	+?	+
113 O.D.	9	−	+	++
83 O.S.	9	−	−	−
83 O.D.	9	+	+	+
1 O.S.	11	−	+?	+
3 O.S.	11	+	++	++
62 O.S.	12	++	+	+
62 O.D.	12	++	+	++
4 O.S.	old	++	−	−
4 O.D.	old	+	−	−

Fat stains (Oil red 0) applied to sections of the 14 eyes fixed in 3-percent formalin revealed considerable fat in droplets of variable size. These fat droplets would appear as vacuoles in the celloidin preparation, but it is certain that most, if not all, of the larger vacuoles, such as shown in Figure 12, did not contain fat.

In many instances cataracts of mice eight months or older were seen with the slitlamp to contain iridescent crystals which are usually considered to be cholesterol. These crystals had been noted in eight of the 14 eyes at the time of autopsy. No crystals were noted in the other six eyes. A histochemical test (Schultz reaction) for cholesterol was carried out on all sections and the results are given in Table 1.

Cholesterol was identified in six of the eight lenses in which the crystals were seen, however, cholesterol was also found in five

that the crystals do not necessarily represent cholesterol, for they may occasionally have been obscured in the slitlamp examination by overlying opaque masses.

In those cases where they have been found in vivo and no cholesterol was identified histologically, the crystals may have been so fine and dispersed that they were not visible in the sections. However, in these cases all of the sections cut from the eye were subjected to the Schultz reaction in order to discover isolated minute deposits of cholesterol, which was usually associated with fat and located in microscopically visible droplets.

It may be noted that cholesterol and fat were always found in the same lenses and as early as four and one-half months, whereas the iridescent crystals were not observed in animals younger than 8½ to 9 months of age.

The rupture of the lens capsule in this

type of cataract suggested that the thickness of the capsule should be investigated in lenses prior to its break at the posterior pole. Accordingly anterior and posterior capsule thicknesses were determined in a series of lenses of normal and cataractous mice. The measurements, made with an ocular micrometer, of the anterior capsule are much more precise than those of the posterior capsule. Each value given in Table 2 is the average of measurements of several sections and shows

gested to us that the lens epithelium might also show abnormalities. Qualitative examination of the epithelium of early cataractous, unruptured lenses revealed no obvious peculiarities. The central portion of the lens epithelium occasionally stained poorly and the nuclei seemed to be rather far apart. Accordingly nuclear counts were made in representative sections of a number of lenses from normal and cataractous mice. These sections were then projected at ×100 magni-

TABLE 2

THICKNESS OF THE LENS CAPSULE OF NORMAL AND CATARACTOUS LENSES

Normal				Cataractous			
Mouse and Eye	Age (days)	Thickness of Capsule		Mouse and Eye	Age (days)	Thickness of Capsule	
		Anterior (microns)	Posterior (microns)			Anterior (microns)	Posterior (microns)
106 O.D.	39	5.0	1.82	101 O.D.	39	4.2	1.8
106 O.S.		5.0	1.6	101 O.S.		4.6	1.8
107 O.D.	39	5.0	2.16	103 O.D.	39	4.2	1.6
107 O.S.		4.5	2.5	103 O.S.		4.0	1.4
				97 O.D.	55	5.16	1.72
				97 O.S.		6.0	1.6
				98 O.D.	55	5.6	1.0
108 O.D.	71	5.6	2.0	98 O.S.		6.0	1.0
108 O.S.		6.0	2.16	18 O.S.	70	8.0	1.0
109 O.D.	71	8.0	1.8	172 O.D.	86	6.12	0.92
109 O.S.		7.0	2.0	172 O.S.		5.6	—
313 O.D.	125	8.2	2.0	150 O.S.	113	6.9	3.2
313 O.S.		7.8	2.2	44 O.D.	125	6.2	1.8
314 O.D.	125	8.7	2.2	44 O.S.		9.0	1.7
314 O.S.		8.0	2.04				
316 O.D.	145	9.2	2.6	45 O.S.	146	7.4	1.1
316 O.S.		8.9	2.74				

Mice No. 101 and No. 103 appear clinically normal or very nearly normal.

that the lens capsules of mice of the cataractous strain are thinner than normal before a change in the lens can be seen with the slit-lamp.

This difference in the anterior capsules continues when the opacity of the lens becomes marked, but the posterior capsule becomes even thinner, in most cases, until it breaks. Of course, if the lens is swelling prior to its rupture, the capsule may be passively thinned by stretching. However, this process presumably is not very far advanced in mice whose lenses are still clinically normal at 39 days of age.

The thinning of the lens capsules sug-

fication and the length of the epithelium measured in millimeters.

All of these sections were 10 microns in thickness. The number of nuclei counted was divided by the length of the section of epithelium in which they were located to give the relative density of the cellular population in a known area of lens epithelium. These data, (table 3), although somewhat variable, show that there were about 25 percent fewer cells in a unit area of the lens epithelium in the cataractous mice. The data are not sufficient to determine whether a deficiency in epithelial cells existed in the very earliest stages and, therefore, it cannot

be concluded that the sparseness of the epithelial population is a primary or a secondary phenomenon resulting from stretching of the epithelium, if indeed this does occur.

Whatever the nature of the earliest changes in this or other cataract development may be, there is general agreement that the proportion of soluble proteins in the lens decreases. It was thought that, by electrophoretic analysis of the soluble lens proteins of early and late cataracts, a suggestion could be had indicating which of the

minations[†] were made on aliquots of the solutions submitted for electrophoretic analysis. These experiments were carried out twice—a total of six analyses of pooled groups of lenses. The mice in Groups A and B were of the same age.

Three electrophoretic patterns are shown in Figure 13. The size of the pattern is proportional to the concentration of the protein solution submitted and is, therefore, of no significance here. The area occupied by each of the several components is also proportional to the concentration of that component,

TABLE 3

NUMBER OF NUCLEI IN THE LENS EPITHELIUM OF NORMAL AND CATARACTOUS MICE

Normal			Cataractous		
Mouse No.	Age (days)	*Number of Nuclei / Length of Epith. ×100	Number of Nuclei / Length of Epith. ×100	Age (days)	Mouse No.
106 O.U.	39	86	72	39	101 O.D.
107 O.U.	39	78 (peripheral sections)	77	39	103 O.S.
			46	55	97 O.S.
108 O.U.	71	89	58	71	18 O.S.
109 O.U.	71	73	66	71	18 O.D.
			75	86	172 O.S.
			68	86	172 O.D.
313 O.U.	125	70	37	113	150 O.S.
314 O.U.	125	71	52	125	44 O.D.

* Number of nuclei = the number counted in 3 to 4 sections. Length of epithelium = the length of the epithelium measured in a drawing made at ×100 magnification by projection. This figure was multiplied by 100 to delete the decimal fraction. All counts were made on 10 μ sections.

lens proteins are reduced. Accordingly pooled lots of (A) normal mouse lenses, (B) lenses from the cataractous strain showing incipient lens changes, and (C) advanced cataracts were used. Since the amount of soluble lens protein in these three groups was both small and unknown, a large number of mice were used, particularly of Group C.

The lenses were thoroughly ground in phosphate buffer pH 7.4 and the insoluble protein removed by centrifugation. The clear supernatant was used for analysis without dialysis or other treatment.* Nitrogen deter-

and the proportion each makes up of the whole is of importance.

Three major protein fractions were found in each sample of lens protein. The ratio of the quantity of these three in the normal, from the slowest to the fastest, is 2.6 : 1.0 : 1.3. When similar ratios were constructed for the early cartaracts a marked decrease in the amount of the slow component was immediately seen, 1.27 : 1.0 : 1.2. The pattern given by the proteins of the advanced cataracts also showed a marked reduction in the slow component, with no change in the other two, relative to each other.

Nitrogen determinations showed that there was 62.9 percent less soluble protein in the advanced cataracts than in the normal. The slow component forms 52.9 percent of the soluble lens proteins in the normal lens and is reduced to 34.7 percent in the advanced cataracts. It is evident, therefore, that, although this reduction accounts for a large measure of the protein loss, it cannot account for all of it. The middle and fast components are therefore affected about equally by some proteolytic process, but at a rate much

Some features of the cataract under discussion are reminiscent of posterior lenticonus.

Patry, quoted in Collin's article, commented on the apparent displacement of the lens nucleus to the posterior pole of the lens. A similar condition was noted in this strain of mice. However, the hyaloid vessels appear to play no rôle in the weakening and distortion of the posterior part of the lens as has been suggested that they may in man. The hyaloid system did not seem unusually
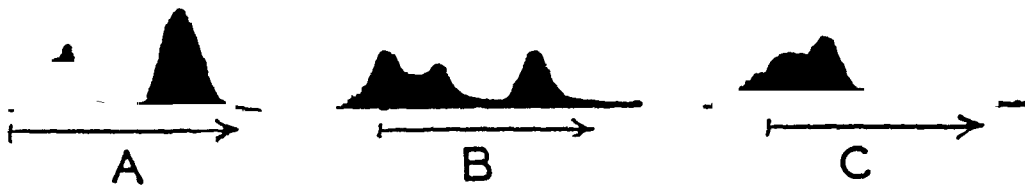
Fig. 13 (Smelser and von Sallmann). Electrophoretic patterns of the soluble proteins of (A) normal mouse lens, (B) early cataract, and (C) late cataract. The reduced size of the pattern in (B) is due to the amount of protein in the sample which was analyzed. The slow component is on the left.

slower than that attacking the slow component.

The reduction in quantity of the slow component in the advanced cataracts was 76 percent, of the middle 47 percent, and of the fast 48 percent. This effect on the proteins was marked even in the early stage investigated. The rates at which these three components moved in the electrophoretic field was not different in the several samples tested, indicating that the proteins present in the cataracts were the same as those found in normal lenses, although their proportion to each other and their quantity had been altered.

DISCUSSION

The cataract discussed here does not apparently have a counterpart which is common in man. E. Treacher Collins[1] described a few cases of posterior cortical cataract with rupture of the capsule at the posterior pole. Ziegler[2] described an hereditary posterior polar cataract which in the earliest stages seems somewhat similar to that studied here.

persistent in these mice and had disappeared entirely in all cases in which a rupture of the capsule had occurred.

The sequence of changes in these lenses was somewhat variable and marked differences sometimes occurred between the eyes of an individual. Completely normal lenses were found up to two months of age. Faint opacities were, however, detected as early as the 17th day of age and, in one case, as late as nine months. Dense opacities were usually present by 70 days of age. Vacuoles were not common until after the third month, by which time most of the lenses had ruptured and the nucleus had been extruded.

The occurrence of cholesterol in these cataracts is not surprising and has been reported in cases of hereditary cataract[3] The cholesterol appears late in the process and probably represents the end of a degenerative change rather than an early or an active phase.

The cause of swelling or even its occurrence has not been demonstrated in these studies, but the thinning of the capsule ap-

pears to be an early, definite morphologic change.

Electrophoretic analysis of normal beef, horse, and pig-lens proteins have been made by Viollier, Labhart, and Süllmann.[4] These analyses, carried out in veronal-acetate buffer, pH 7.9 with an ionic strength of 0.1 showed only two major components. Our analyses of normal mouse lenses clearly showing three major components of the soluble lens proteins were made in phosphate buffer at pH 7.4 with an ionic strength of 0.2. One additional analysis, however, was made with barbiturate buffer at pH 8.6 with an ionic strength of 0.1, which also revealed three components. The differences between the observation of Viollier and others and the present ones may be due to variation between the species or to the greater solubility of some proteins in salt solutions, since they used water in making the lens extract instead of buffer, as in our case.

It is impossible at the present time to identify the three components shown in the electrophoretic analysis of the mouse lens with the α and β crystalline or albumen found in other lenses by chemical methods. The relative vulnerability of one of the components (slowest) to the cataractous process recalls immediately, however, the studies of Krause,[5] who showed that β crystalline was rapidly attacked by proteolytic enzymes, in a slightly acid medium, whereas α crystalline was relatively stable.

SUMMARY

1. Morphologic changes, observed clinically and histologically, in a developing hereditary cataract have been described and compared.

2. The earliest observed changes involve slight disorganization in the posterior cortex and thinning of the lens capsule.

3. Decrease in the number of lens epithelial cells per unit area was noted in early cataracts.

4. Vacuolation of the lens and rupture of the capsule, thus discharging lens material into the vitreous cavity, were regularly observed.

5. The observation of iridescent crystals in the lens could not be well correlated with the demonstration of cholesterol histochemically.

6. Electrophoretic analysis of normal mouse-lens protein revealed three major components.

7. One lenticular component is reduced, in the formation of this cataract, at a rate nearly twice as great as that affecting the other components.

630 West 168 Street (32)

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DISCUSSION

DR. WILHELM BUSCHKE (New York): I should like to ask two questions in relation to this very interesting presentation.

The first question has to do with the problem of reduction of cell divisions in the epithelium. Was there any reduction in the thickness of the lens at any stages preceding the actual cataract, as compared with control animals at a comparable age?

The second question is in relation to your

finding that the lens capsule was thin. Were there any histochemical changes in the lens capsule, particularly in relation to the sulfate polysaccharide, for example, with metachromatic staining? If so, it would be interesting to speculate about the possible connection of these changes with the skeletal changes, on the basis of a common biochemical factor.

DR. GEORGE K. SMELSER (New York): If I understood Dr. Buschke correctly, his question was on mitotic activity. There were some mitoses found, but we made no count of mitotic figures in the lens capsules of either the normal or the cataractous.

The number of cells present in the very early stages was reduced in the cataractous strain, but not by 25 percent; it was reduced on the order of 10 or 12 percent in numbers. I did not give the figures because I don't think one should give them undue emphasis, because they were based on rather few cases. These observations were made in animals prior to the development of a clinically observable cataract or a clinically observable abnormality. The thickness of the capsule was definitely less before there was any clinically observable abnormality.

DR. BUSCHKE: I meant the thickness of the lens.

DR. SMELSER: The whole lens? I cannot answer that, except in this sense: In histologic sections there was no change. I would not have too much confidence in measurements made on them. I would prefer to have the volume differences here. There was no obvious change in the sections. We made no histochemical studies on lens capsule. We hope to get some stimulation and ideas on that later today.

CYCLODIALYSIS*

I. A DISCUSSION OF TECHNIQUES

OTIS S. LEE, M.D. AND JAMES H. ALLEN, M.D.
Iowa City, Iowa

The modus operandi of the cyclodialysis operation for glaucoma, according to Heine's original concept,[1] was the establishment and maintenance of a communication between the anterior chamber and the suprachoroidal space. Proof that this communication persisted was furnished by Elschnig[2] in 1932 and Barkan[3] in 1947 from microscopic examination of sections of eyes in which successful cyclodialysis operations had been made but were removed post mortem. Further evidence in favor of this idea was found clinically upon gonioscopic examination by Barkan, Boyle, and Maisler[4] in 1936 and Burr[5] in 1947. The latter observer found that a cleft, indicating a separation of the ciliary body from its scleral attachment, could be demonstrated[†] in the chamber angle in all successful cases of cyclodialysis. The size of the cleft apparently had little to do with the degree of reduction of the intraocular pressure. As long as one was visible, the intraocular pressure was within normal limits.

According to Heine's description of his operation, an incision 3-mm. long was made through the sclera approximately 6-mm. posterior to, and parallel with the limbus. A spatula was inserted between sclera and ciliary body through the incision and passed into the anterior chamber to a depth of approximately 3 mm. The spatula then was

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† Burr found that in some cases it was necessary to constrict the pupil with a strong miotic in order to view the cleft in the angle over the iris hump.
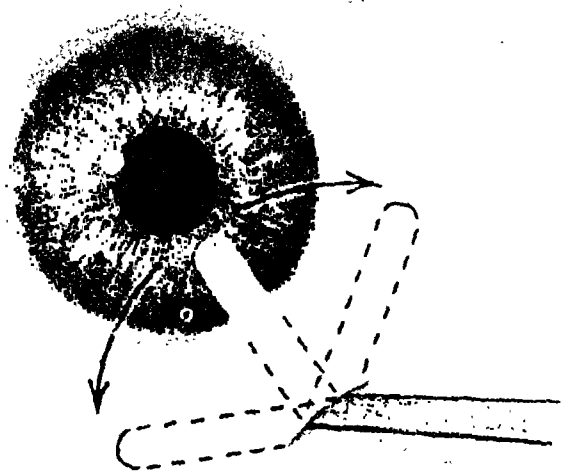
Fig. 1 (Lee and Allen). Heine's technique of cyclodialysis (after Blaskovics and Kreiker).

swept backward into the chamber angle (fig. 1). After breaking the attachment of the ciliary body to the scleral spur, it was then passed into the suprachoroidal space, first on one side and then on the other.

Blaskovics[6] pointed out that this method unduly traumatized the iris and ciliary body. It was possible for the spatula to tear through the base of the iris especially in cases with peripheral anterior synechias, or through the anterior portion of the ciliary body before breaking into the suprachoroidal space. This favored hemorrhage and post-operative iritis with stimulation of scar-tissue formation and subsequent obliteration of the newly created cleft thus sealing off the outlet for the aqueous humor from the anterior chamber into the suprachoroidal space. In order to minimize this, Blaskovics in 1935[6] introduced his modification which has become known as the inverse method of cyclodialysis (fig. 2). He reversed the Heine technique, separating the ciliary body from its attachment by sweeping the spatula from the suprachoroidal space into the anterior chamber. Thus, according to Shaffer,[7] the spatula followed a natural line of cleavage.

Since 1931, O'Brien[8] has been using and teaching a multiple thrust method of performing an inverse cyclodialysis. He made the scleral incision 5 mm. posterior to and parallel with the limbus. From this point he passed a spatula between sclera and ciliary body into the anterior chamber until the tip was just visible, then withdrew and re-inserted the tip into the chamber at progressively adjacent points, first to one side of the incision then to the other, until approximately half of the circumference of the ciliary body was detached from the scleral spur.

Although excellent results have been obtained by these last two techniques, annoying hemorrhages have still occurred occasionally and, when extensive, they have jeopardized the success of the operation. Therefore a slight modification of the O'Brien technique was made in an effort to reduce the incidence of hemorrhage even further (figs. 3a to 3c and 4).

ANATOMIC CONSIDERATIONS

The choroid and ciliary body are in loose apposition with the sclera except at three main points. The choroid is firmly attached to the sclera in the vicinity of the optic nerve
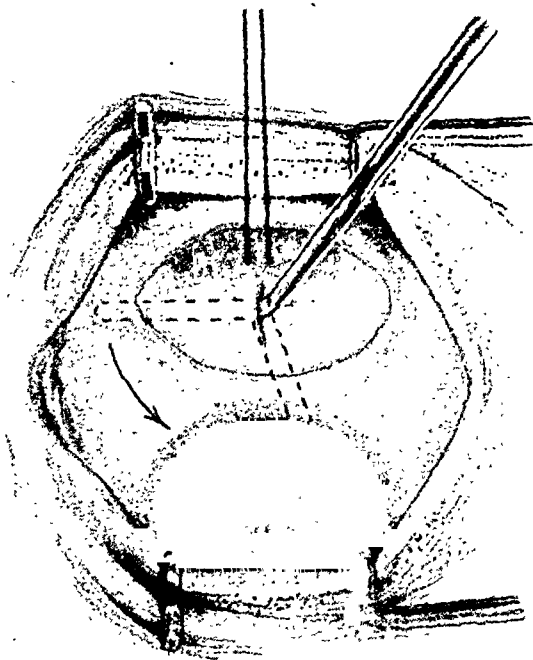
Fig. 2 (Lee and Allen). Blaskovics's technique of inverse cyclodialysis (after Blaskovics and Kreiker).
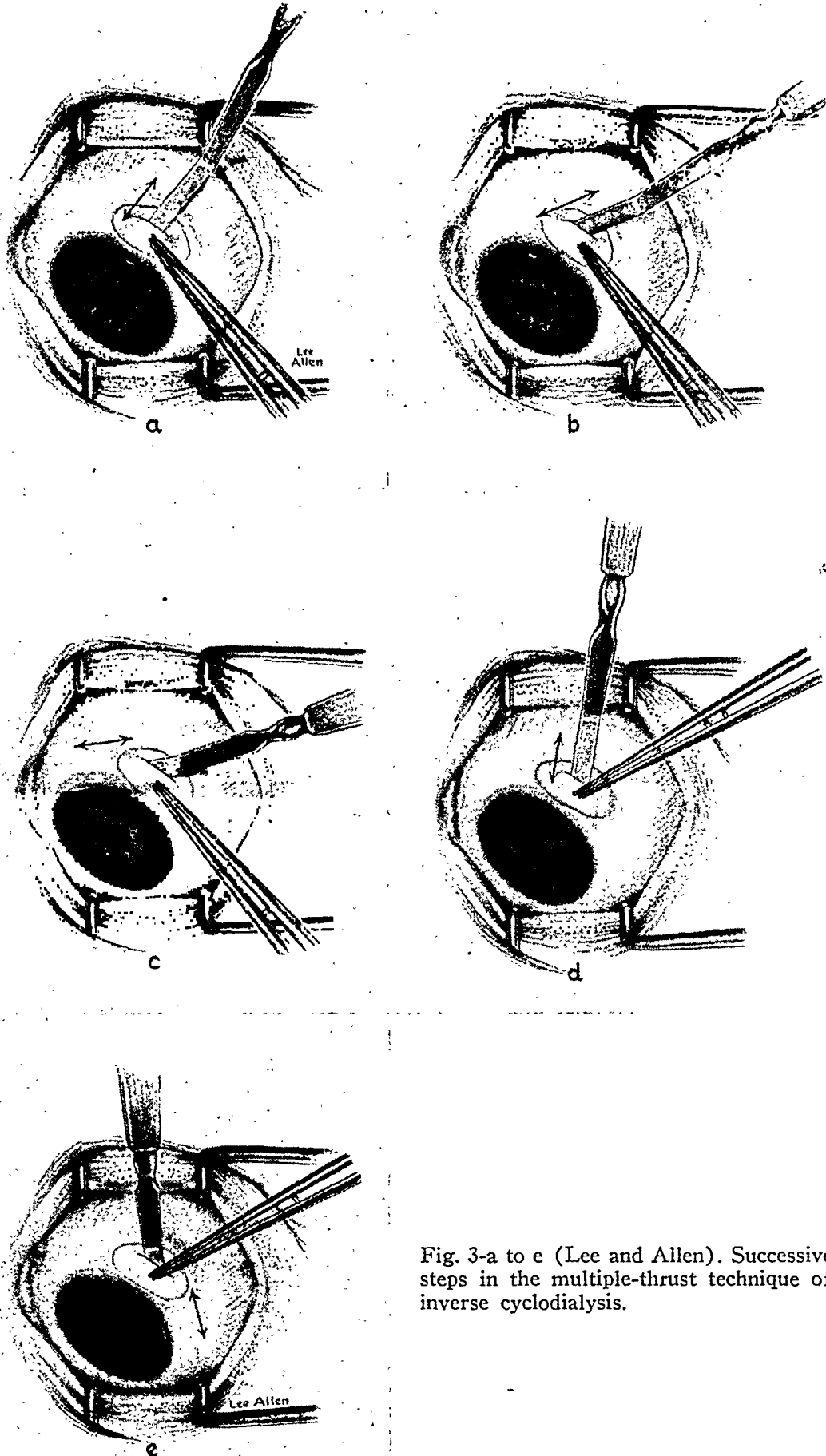
Fig. 3-a to e (Lee and Allen). Successive steps in the multiple-thrust technique of inverse cyclodialysis.

where the ciliary vessels pierce the sclera and also it is firmly attached to the sclera at the exits of the venæ vorticosæ posteriorly. The ciliary body is firmly attached only at the scleral spur anteriorly. Over the remainder of the choroid and ciliary body is the suprachoroidal space through which nonvascular lamellae of connective tissue run in all directions. The lamellae contain elastic fibers as well as pigment cells and are surrounded by endothelial cells, thus forming a maze of interconnecting endothelial-lined potential spaces called the suprachoridal lymphatic

Fig. 4 (Lee and Allen). Extent of excursion of cyclodialysis spatula indicated in solid black. Dotted line indicates line of attachment of ciliary body to scleral spur.

space of Schwalbe. The lamellae are fewer in the region of the ciliary body and steadily decrease from behind forward. The most anterior reaches of the suprachoroidal space immediately behind the scleral spur seem entirely empty.[9] The ease with which the choroid becomes separated from the sclera is illustrated by the large number of cases of choroidal detachment seen after cataract extraction.[10]

The blood supply of the uveal tract is derived from three sources: (1) The 10 to 20 branches of the short ciliary arteries

which enter the choroid around the optic nerve; (2) the two long posterior ciliary arteries, one traveling nasally and one temporally along the horizontal meridan between the choroid and retina to enter the ciliary body at its posterior border; and (3) the anterior ciliary arteries coming from the four recti muscles. There are two arteries from each except the lateral rectus from which there is only one. These vessels travel across the tendon insertions in the episcleral tissue to within 2 to 4 mm. of the cornea, then each sends a large perforating branch into the sclera passing through it perpendicularly to enter the ciliary body.

The venous drainage of the unveal tract occurs through the four venæ vorticosæ and the anterior ciliary veins which accompany the anterior ciliary arteries as they perforate the sclera.

TECHNIQUE OF CYCLODIALYSIS

1. CHOICE OF SITE OF OPERATION

This should be determined by gonioscopic examination of the chamber angle before operation, whenever possible. It is desirable to avoid dense anterior peripheral synechias and large blood vessels in the angle. In cases of glaucoma following cataract extraction the cyclodialysis should be made below to avoid the scar tissue.

2. PREPARATION OF OPERATIVE SITE

Usually either the superior or inferior temporal quadrant is chosen. Incision in the area immediately anterior to the superior rectus muscle as described by Blaskovics is not recommended because of the proximity of the anterior ciliary vessels. The sclera is bared by a short incision through the conjunctiva and Tenon's capsule. All visible episcleral vessels are cauterized with a thermal hot point. A scleral fixation suture is placed just anterior to the site of the scleral incision. It may be held either with a pair of forceps or a hemostat and the movement of the globe is thus controlled easily.

3. THE SCLERAL INCISION

In the Heine, Blaskovics, and O'Brien techniques the scleral incision is placed 5 to 6 mm. back of the limbus. Barkan and others[4] suggest that it be placed even further back in order to obtain a more extensive dialysis of the ciliary body. By placing the scleral incision 6 mm. or more back from the limbus, not only will it permit a sufficient length of spatula to be introduced into the suprachoroidal space to dialyze the ciliary body, but according to Salus[11] and Meller[12] it will also permit the spatula to section the nerves and vessels supplying the ciliary body as it sweeps through the suprachoroidal space, thus reducing formation of aqueous humor through atrophy of the ciliary body. Furthermore, should the ciliary body be injured while making the scleral section in this region, the less important nonvascular pars planum will be involved and not the more important pars ciliaris.

More recent studies, however, indicate that the disruption of nerve and blood supply to the ciliary body in the cyclodialysis operation contributes little if anything toward its success. In fact, rupturing the blood vessels should be avoided. Furthermore, one can dialyze half the circumference of the ciliary body without having to place the scleral incision farther back as recommended by Barkan and others, if one uses the multiple thrust technique of O'Brien instead of the sweeping techniques of Heine and Blaskovics.

Therefore, we prefer to place the incision approximately 3 mm. back from the limbus. By traction on the fixation suture, the scleral incision can be made safely, with danger of injury to the ciliary body reduced to a minimum. Traction on the suture actually lifts the sclera away from the ciliary body as the incision is being made.

4. THE CYCLODIALYSIS

By traction on the scleral fixation suture, the spatula can be introduced through the scleral incision into the suprachoroidal space with ease. After a very short distance, the spatula reaches the scleral spur. With firm but gentle pressure, keeping the spatula against the sclera, the dialysis is made and the tip of the spatula may be seen just within the inner margin of the limbus. It is slightly withdrawn and a series of short thrusts are made with the spatula always confined to the immediate region of the limbus and scleral spur. Approximately half the circumference of the ciliary body is separated from the scleral spur.

The cyclodialysis may involve the upper half, the lower half, or the temporal half of the ciliary body or, if the occasion demands it, the nasal half. The spatula is not permitted to enter the anterior chamber for more than 0.5 to 1 mm., nor is it swept backward into the suprachoroidal space. Its movements are limited to the immediate vicinity of the scleral spur. One need not fear performing a cyclodialysis past the horizontal meridan in order to avoid rupturing the long posterior ciliary arteries if one uses this technique. With the Heine or Blaskovics technique, one should avoid this region.

Even with the utmost care in technique and freedom from complications, there is a strong tendency for a narrow cyclodialysis to become reattached. The reason for performing a wide cyclodialysis is, then, not to obtain a large, filtering cleft but, by obtaining an extensive dialysis of the ciliary body, to reduce greatly the tendency for a complete reattachment, and to leave in a large percentage of cases, a small but adequate functional cleft in the chamber angle.

COMMENT

The purpose of the cyclodialysis operation is to permit internal drainage of the aqueous humor into the suprachoroidal space. This is accomplished when the attachment of the ciliary body to the scleral spur is severed. Further excursion of the spatula through the suprachoroidal space over the ciliary body

region is unnecessary since the ciliary body posterior to the scleral spur is in loose apposition with the sclera, and fluid can flow through this area without the help of instrumentation. This maneuver increases the amount of trauma to the ocular tissue.

Breaking of the perichoroidal lamellæ together with irritation of the ciliary body as the spatula sweeps over it might account for the severe iridocyclitis that sometimes follows a cyclodialysis operation. It certainly does result in a higher percentage of hemorrhages and more severe ones. Either of these conditions may be reasons for failure of the operation. Furthermore, in both the Heine technique and Blaskovics's modification, the spatula is carried into the anterior chamber for a considerable distance. This requires a skillful operator to avoid trauma to the iris and damage to the posterior surface of the cornea, especially when the chamber is shallow.

We are in full agreement with Barkan, Boyle, and Maisler that at least two fifths of the circumference of the ciliary body should be dialyzed to get the best results. O'Brien[13] recently has reëmphasized this and advocated approximately one half the circumference. However, one need not make the incision more than 3 mm. back from the limbus to accomplish this.

In cases with very shallow anterior chambers, we have performed a peripheral basal iridectomy together with the cyclodialysis. This additional procedure not only decreases the opportunity for formation of anterior peripheral synechias with resultant closure of the cyclodialysis cleft, but also frequently deepens the anterior chamber all around with its attendant advantages. Unlike the Wheeler[14] technique, a second incision is not necessary to perform the basal iridectomy. It can be made easily through the cyclodialysis incision since that is so near the limbus. In fact, to facilitate further the performance of the iridectomy, should this additional step be contemplated, the scleral incision should be made less than the usual 3 mm. back of the limbus.

SUMMARY

A method of inverse cyclodialysis is described in which the action of the cyclodialysis spatula is confined strictly to the region of the scleral spur. We believe this technique will reduce operative trauma with hemorrhages and postoperate irritation to a minimum and will increase the percentage of successes of the cyclodialysis operation.*

University Hospitals.

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* Case histories will be presented in later publications.

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ANISEIKONIA FOR DISTANT AND NEAR VISION

KENNETH N. OGLE,* PH.D.
Rochester, Minnesota

AND

WENDELL TRILLER, B.S.
Hanover, New Hampshire

Can the aniseikonia for near vision be essentially different from that for distant vision? Although different measurements at the two distances are often found,[1] the questions to be answered are: to what extent are those differences significant and are they due to a basic difference in the aniseikonia or are they a peculiarity of the method of measurement? The answers are important, on the one hand, to the design of the eikonometer and, on the other, to the clinician who must reduce to a minimum the time needed for the aniseikonic examination. From the physiologic point of view significant differences would be important for their possible relation to changes in astigmatism, motility, and unequal accommodation from distant to near vision. Unless unequal changes in the optical systems or in the neurologic processes of the two eyes occur, it is difficult to account for other than small differences in the aniseikonia.

The partial unreliability of the measurements for near vision on the regular (direct-comparison) eikonometer, especially in the horizontal meridian,[2] has prevented a thoroughgoing study of the problem. With the development of the space-eikonometer technique, however, a means for a cross check with the regular eikonometer is now available. A definite clarification of the problem requires the study of a large number of cases, together with a study of the reliability of the space-eikonometer. At the moment, the data available on both of these studies leave much to be desired. However, the data on 115 subjects whose aniseikonic measurements had been taken on both eikonometers for distant and near vision are to be found in the files of the more recent cases of the Dartmouth Eye Institute. Since these data constitute evidence toward the solution of the problem, they are presented in this paper.

The descriptions of both the regular (direct-comparison) eikonometer and the space-eikonometer can be found in the literature and will not be given here. It is pertinent to review only the essential differences in the two instruments.

The earlier instrument depends on the patient's making a more or less direct visual comparison of the relative dimensions of the images of a suitable target as seen by two eyes.[3-6] The target (fig. 1), which makes use of plates of polaroid for separating the images seen by each of the two eyes, consists of light details, either projected on a metallic screen or presented in a transparency.

A configuration of a vertical and a horizontal line intersecting at a central circular disc is seen binocularly (unpolarized), while two systems of opposing lines (arrows) are so polarized that one is seen by the right eye, the other by the left eye. Thus, the right eye would see the lines associated with the odd numbers only, while the left eye would see those with the even numbers only.

Each pair of opposing arrows constitutes a vernierlike device and, if there is a difference in the sizes of the images between the two eyes, any two arrows will not be aligned but rather displaced with respect to each other. By suitable optical systems the relative magnifications of the images of the two eyes can be adjusted until the patient reports that the arrows on opposite sides of the central fusion disc are aligned or are equally dis-

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* Now in the Division of Physics and Biophysical Research of the Mayo Foundation and Mayo Clinic, Rochester, Minnesota.

placed (in case a marked fixation disparity exists).

The test constitutes, therefore, a direct comparison of the images seen by the two eyes. The sensitivity depends on the accuracy with which the fusion of the central patterns of the target is maintained, and on the visual acuity of each of the eyes. A fixation disparity, which is usually present if a phoria exists, may cause an equal displacement of the images of the arrows and may reduce somewhat the sensitivity.

The space-eikonometer[7-10] depends on

cords supported in front of and behind the cross and parallel to it. A central cord is usually suspended through the center of the cross. The two front cords subtend a visual angle to the subject of about 12°. Carefully adjusted apertures restrict the field of binocular vision to the test elements, which are evenly illuminated and viewed against a black cloth background. All empirical clues to depth perception are thus reduced to a minimum.

For near vision (40 cm.), the cords are replaced by strands of silk thread, accurate-
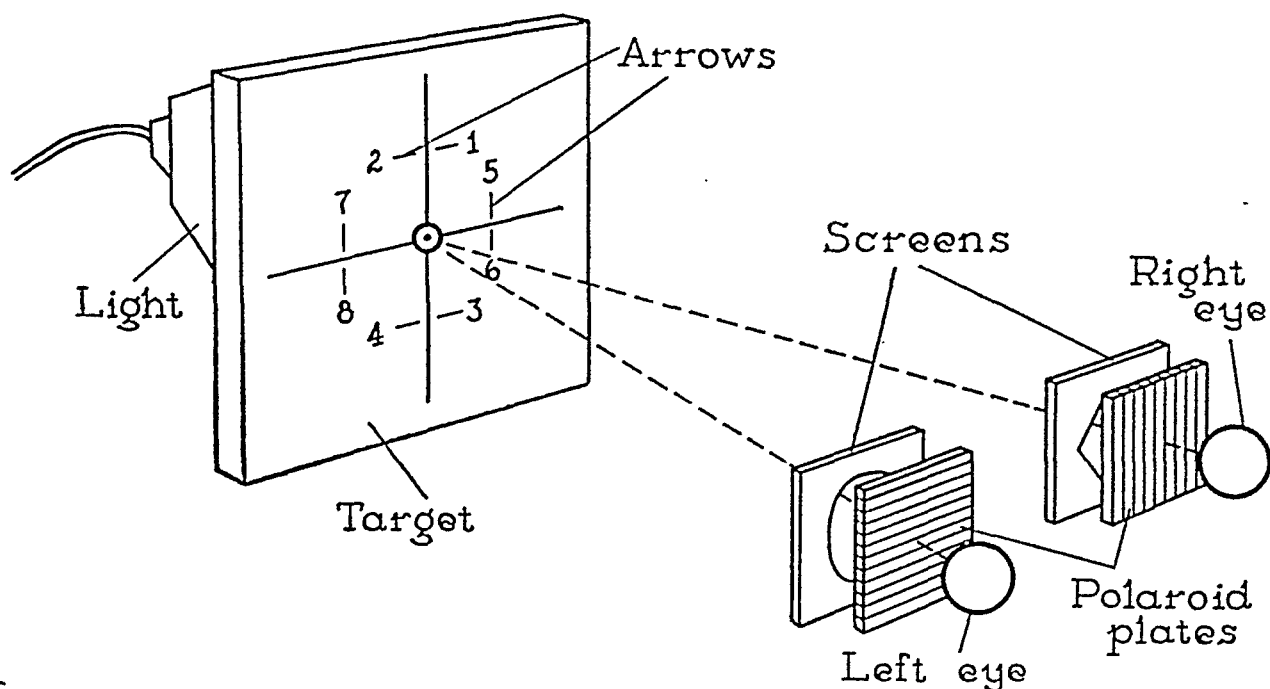
Fig. 1 (Ogle and Triller). The type of target regularly used in the direct-comparison or vernier eikonometer.

binocular stereoscopic spatial localization and on the fact that an aniseikonic error changes the usual disparity relationships between the retinal images of objects in space, with the resultant incorrect spatial orientation.[11,12] As schematically shown in Figure 2, the test detail is a space configuration, consisting, first, of an oblique cross made by a pair of intersecting cords stretched at right angles to each other and mounted in the frontoparallel plane; and, second, of two pairs of smooth vertical (to the visual plane)

ly mounted in a small box frame and attached to the eikonometer chassis. Experience has shown, however, that it is much more difficult to eliminate empirical clues to depth perception by this method at near vision, and the sensitivity of the test is found to be somewhat less than that for distant vision. However, if the test configuration is replaced by a "vectograph"[13] transparency of the same dimensions, those empirical clues are nearly eliminated and the sensitivity is only slightly less than that of

the test for distant vision. Most of the space-eikonometer data for near vision were therefore taken with the "vectograph" target.

Suitable optical systems permit the relative magnifications of the images of the two eyes to be adjusted, so that the several parts of the test configuration are perceived stereoscopically correctly oriented in space.

at one visual distance have not been an influencing factor in the measurements obtained at the other visual distance.

The 115 subjects included in this report were routine patients of the Dartmouth Eye Institute who had been referred for examination of aniseikonia. In many cases an additional spherical correction was needed for the near-vision tests. These additions were
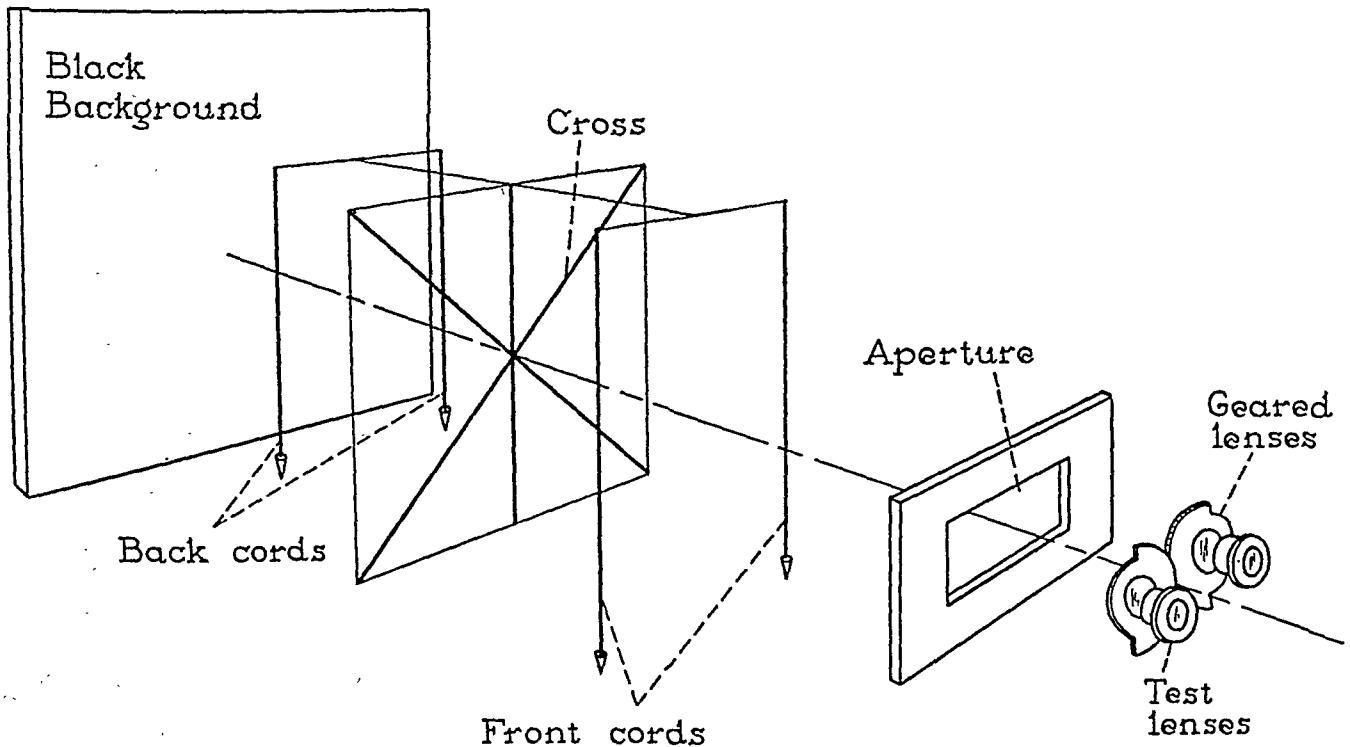
Fig. 2 (Ogle and Triller). Schematic drawing of the space-eikonometer.

The method of limits is used to determine the aniseikonic errors.

The data presented here are from the case record files for patients who have been examined on both the direct-comparison eikonometer and the space-eikonometer for both distant and near vision. Measurements to be compared are those of the aniseikonic corrections for the horizontal and vertical meridians, and the declination error.[14-16] The data were obtained by three clinicians, one of whom obtained all of the data on the space-eikonometer. Obviously, it would have been better if the measurements for near vision could have been made by a different operator. It is hoped that the data

always equal spheres, carefully adjusted for equal distances from the eyes, and should not, therefore, of themselves introduce any changes in the relative magnifications of the dioptric images in the two eyes.

It is not feasible to present in this paper a table of all data obtained.* However, typical results are shown in Table 1. In this are given the refractive corrections used during the examinations, and the phoria for near vision is indicated because of its possible influence on the data of the direct-comparison eikonometer for near vision. Under the eiko-

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* To those interested in studying the complete set of data, photostatic copies will be gladly sent by the authors.

nometer headings are shown the percentage magnifications that had to be introduced before the eye indicated, in order to equalize the relative magnifications of the images of the two eyes. These data are for the horizontal (H) (axis 90°) and the vertical (V) (axis 180°) meridians. For the space-urements for distant and near vision, though less so in the horizontal meridian of the direct-comparison eikonometer, as might have been expected. For a more specific evaluation, it is necessary to study the variability between the measurements for distant and near vision of each instrument in

TABLE 1

TYPICAL COMPARATIVE EIKONOMETER MEASUREMENTS OBTAINED AT DISTANT AND NEAR VISION

No.	Refractive Correction	Phoria* Near	Direct-Comparison Eikonometer				Stereoscopic Space-Eikonometer				
				Distant	Near			Distant	Near	δ
1	R+0.62−0.62×170 L−0.25−1.12×135	5 X	H V	L 2.25 L 1.75	L 2.0 L 1.75		H V	L 2.5 L 2.0	L 2.0 L 2.0	D+0.3 N+0.8
2	R−0.25−1.50× 40 L+0.50−0.50×180	12 X	H V	R 2.0 R 1.0	R 2.0 R 2.0		H V	R 1.5 R 1.0	R 1.8 R 1.2	D+0.5 N+1.0
3	R+1.75−1.75×175 L+2.00−0.75×130 With prisms B.I. at near	18 X	H V	R 3.00 R 2.50	R 6.0 R 2.75		H V	R 3.0 R 3.0	R 2.5 R 2.4	D+0.2 N+0.7
4	R+1.00−0.25× 85 L−0.25−0.50×120	15 X	H V	L 4.0 L 2.5	L 2.0 L 2.0		H V	L 1.75 L 1.75	L 2.0 L 1.8	D+0.3 N+0.2
5	R+0.75−1.25× 10 L−0.25−0.50× 80	3 X	H V	L 1.25 R 1.0	L 1.0 R 0.75		H V	L 0.75 R 0.25	L 1.0 R 0.5	D+0.2 N+0.3
6	R+2.25−1.25×175 L+6.50−5.00× 5 Add +2.50	4 X	H V	R 6.0 R 0.5	R 10.0 R 0.5		H V	R 7.0 L 1.0	R 7.5 L 3.0	D−1.0 N−1.0
7	R+1.00 S L+1.00 S Add +1.75	2 X	H V	L 0.5 L 0.25	L 0.75 L 1.0		H V	L 1.0 L 0.5	L 0.5 L 0.5	D 0.0 N 0.0
8	R+2.00−1.25×135 L−2.00−1.50×160 Add +1.25	orth.	H V	L 3.5 L 3.25	L 2.25 L 2.5		H V	L 2.0 L 3.0	L 2.5 L 3.0	D+0.5 N+0.5
9	R−2.25−0.75×160 L Plano−1.50×180 Add +1.50	6 X	H V	R 1.25 R 1.0	R 2.0 R 0.5		H V	R 1.5 L 0.5	R 1.75 0.0	D−0.2 N 0.0

* Prism diopters.
X—exophoria.

eikonometer the correction of the declination error, δ, is also given for distant and near vision. Unfortunately, it is not possible to indicate the precision of the data for each measurement, since this was not recorded on the data forms available. However, on the average, this was of the usual order of 0.25 percent to 0.5 percent magnification differences.

A cursory study of the data shows a reasonably close agreement between the meas-comparison to the variability or reliability of data obtained on the same instrument for both visual distances.

The quantitative relation between the distant and near findings for each instrument and each meridian is the slope of the line which best describes the data in a scatterplot diagram. Such a plot is shown in Figure 3, for data of the space-eikonometer for the horizontal meridian. In this figure, the measurements found for distant vision are plotted

along the abscissa, those for near vision along the ordinate. The slope of the line (which here will be called the mean regression line) best describing the location of the points is found by the method of least squares. For these data the sum of the squares of the distance of each point from the regression line has been minimized. The values of the slopes computed for the five sets of data are given in Table 2.

Other things being equal, one might expect on the average a 1 : 1 relationship between the two findings; that is, a measurement of one percent at distant vision would correspond to a measurement of one percent at near vision. Except for the direct-comparison eikonometer in the horizontal meridian, this 1 : 1 ratio is essentially realized, as an inspection of the table will show. Perhaps there is a tendency for the data for near vision to be slightly lower than those for distant vision. For the horizontal meridian in the exception noted previously, the near-vision data are substantially greater by 37 percent.

Because of the nearly 1 : 1 ratio, the standard deviation (which is the measure of variability) of the differences between the measurements for distant and near vision is also

a measure of the degree to which the near-vision aniseikonic error can be predicted by the distant vision measurements. That is, the standard deviation is the standard error of estimate of the data. On a percentage cumulative basis, 70 percent of the subjects had differences between the distant and near-vision findings less than that difference
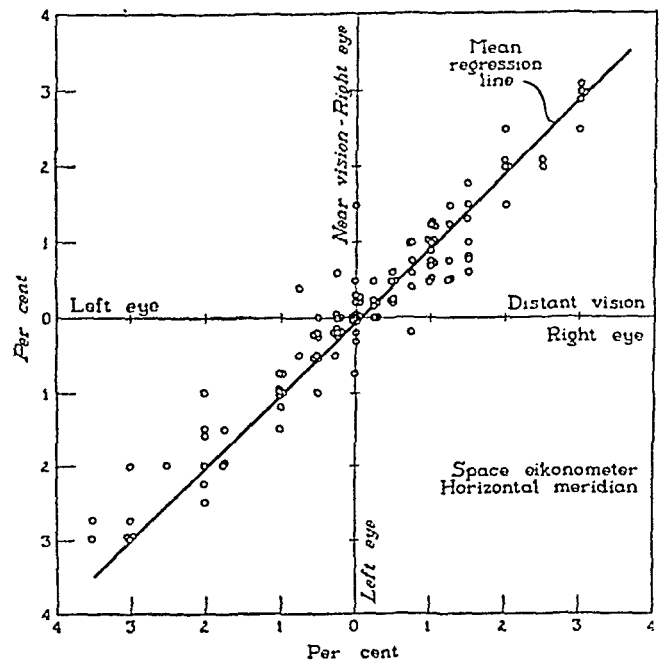
Fig. 3 (Ogle and Triller). Scatter plot of the comparative eikonometer measurements in the horizontal meridian for distant and near vision—space-eikonometer.

TABLE 2

THE SIGNIFICANT STATISTICAL QUANTITIES WHICH DESCRIBE THE RELATIONSHIP BETWEEN THE MEASUREMENTS OF ANISEIKONIC ERRORS AT DISTANT AND NEAR VISION IN THE HORIZONTAL AND VERTICAL MERIDIANS

| | | Direct-Comparison Eikonometer | | Stereoscopic Space-Eikonometer | | |
		Horizontal	Vertical	Horizontal	Vertical	Declination
Slope of mean regression line:	Near / Distant	1.37	0.99	0.96	0.92	0.97
Standard deviation (n −d)		0.69%	0.54%	0.40%	0.50%	0.19°
Standard deviation for reliability	Distant	0.42%	0.36%	(0.3%)*	(0.4%)*	(0.2°)*
	Near	1.10%	0.60%	(0.5%)*	(0.5%)*	(0.3°)*
Pearson correlation coefficient		0.84	0.94	0.97	0.95	0.91
Means of data	Distant	0.06%	0.00%	−0.26%	−0.37%	+0.02°
	Near	0.91%	0.09%	−0.28%	−0.45%	+0.05°

* Estimated values.

defined as the standard deviation. The standard deviations for the five categories are given in the second row of Table 2.

The extent to which the near-vision data are correlated with those for distant vision is indicated by a comparison of the standard deviations found previously with the standard deviations of the repeatability or reliability tests of each instrument determined through repeated tests. For the direct comparison eikonometer such data exist.[2] They can at the present only be estimated for the space-eikonometer. These values are given in the third and fourth rows of Table 2. The estimated values were ascertained by a study of the stereoscopic sensitivities of subjects in the space-eikonometer under controlled conditions,[9] and of the correlation between the space-eikonometer and the direct-comparison eikonometer,[8] together with the standard deviations from the repeatability of the latter instrument.

While the Pearson correlation coefficient is difficult to interpret for the data of the type presented, it is given, also in Table 2, for what it may be worth.

A study of the table shows that, on the basis of the data available, the aniseikonic error at a near visual distance is essentially the same as that measured for distant vision, within the precision with which the measurements can be made.

One could not expect a good agreement between the findings for distant and near vision with the direct-comparison eikonometer because of the known poorer repeatability of the instrument for near vision. The means of the measurements for the near-vision test also show a marked bias. Since this did not appear with the distant-vision data nor for near vision in the vertical meridian, it probably cannot be due to an instrumental error per se. The means of the several sets of data also suggest that an error of about 0.25 percent magnification existed in the optical systems or targets of the space-eikonometer used in this experiment.

Mayo Clinic.

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ENUCLEATION AND ALLIED PROCEDURES*

Part II. A Survey of Semiburied Implants†

JACK S. GUYTON, M.D.

Baltimore, Maryland

TRANSMISSION OF MOTION OF STUMP TO PROSTHESIS WITHOUT DIRECT ATTACHMENT

As early as 1917 Dimitry[194] designed a prothesis shaped like a Snellen reform eye but with a concavity in the posterior surface designed to clasp the stump by suction. He temporarily abandoned his idea because actual motility of the stump was not imparted to the prosthesis but, in 1942, he described deliberate creation of an elevated convex stump which would project forward far enough to fit into a prothesis with a posterior concavity of 11-mm. radius, and actually obtained a patent on this prothesis,[195] but he did not report any actual results.[196]

In 1940, Cutler[197] described the use of his "basket" type implant. This procedure afforded the first uniformly successful means of moving the prosthesis along with the stump. He implanted a cup-shaped acrylic framework, 15 mm. in diameter and 11 mm. deep, into Tenon's capsule, with its concave aspect anteriorly (fig. 1).

A double-armed suture was passed through holes in the bottom of the cuplike implant, out through the edges of Tenon's capsule and conjunctiva and through holes in a 5-mm. acrylic stud, rounded on the posterior end. Tenon's capsule and conjunctiva were next overlapped and firmly united by other sutures. The initial suture was then tied tightly enough to press the stud down into the basket, thus carrying Tenon's capsule and conjunctiva against the perforated acrylic framework so that, when healing was complete, a deep concavity with fairly rigid walls remained in the center of the freely movable stump. The prosthesis used after this operation had a smooth,

Fig. 1 (Guyton). Cutler's basket implant.

* From the Wilmer Ophthalmological Institute of The Johns Hopkins University and Hospital. Candidate's thesis for membership in the American Ophthalmological Society, accepted by the Committee on Theses.

† Part I of this paper appeared in the November, 1949, issue of the JOURNAL, pages 1517-1534.

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somewhat cone-shaped projection on its posterior surface which would fit into the concavity of the stump and thus acquire motility (fig. 2).

Cutler reported excellent results in 50 enucleations performed with his basket implant. This procedure was a tremendous advance over previous procedures, and it would undoubtedly have attained very wide-

Fig. 2 (Guyton). Prosthesis used after insertion of Cutler's implant.

spread use had not semiburied implants been introduced very shortly afterward.

SEMIBURIED IMPLANTS WITH DIRECTLY ATTACHED PROSTHESES

RUEDEMANN'S PLASTIC EYE IMPLANT

In 1941 Ruedemann[198] conceived the idea that a prothesis made of acrylic and shaped like a whole eyeball might serve as a permanent, nonremovable substitute for an enucleated eye if inserted into Tenon's capsule, the rectus muscles attached, and the anterior portion (shaped and colored to match the fellow eye) left exposed. The possibility of a nonviable structure with direct attachment to living, subepithelial tissue remaining permanently partially buried and partially exposed, with a consequent line of transition between epithelium and subepithelial tissue in the lining of the structure, is a natural occurrence in the case of teeth; nevertheless, Ruedemann's application of this principle to prostheses was completely original not only in the field of ophthalmology, but in surgery as a whole.

Ruedemann began implanting whole acrylic eyes into Tenon's capsule in 1941, and, in 1945, he first reported this procedure[1] before the American Ophthalmological Society. He had by that time performed over 100 such implantations. When he first began performing this operation, he used various sized and shaped eyes, "mostly wrong," and attached the eye in place with various suture materials and techniques, "also mostly wrong." However, by "trial and error plus much effort" he obtained more and more successful results, and implanted artificial eyes exhibiting normal motility and without retraction of the upper lid sulcus. He also had successes with delayed implantations into deformed sockets, using fibrous tissue for attachment if the recti could not be identified.

When Ruedemann first reported his operation, the technique he preferred was to attach the severed ends of the recti to perforated tantalum paddles by fine tantalum wire sutures, which were then attached to the plastic eye (figs. 3 and 4). The plastic eye matched the fellow eye in coloring and size. He listed the following complications: dyes fading, muscles coming loose, conjunctival discharge if conjunctiva retracted so as to expose tantalum suture or paddle, strabismus and ptosis if the eye was set too deeply in the orbit.

In May, 1945, Dr. Alan Woods visited Dr. Ruedemann in Cleveland and watched him implant two of his plastic eyes, and also examined a number of patients who had already undergone such an operation. Dr. Woods was so impressed he obtained Dr.

Ruedemann's permission to utilize this procedure, and he inserted the first of these implants at the Wilmer Institute in June, 1945. Between June, 1945, and December, 1945, 10 of the Reudemann implants were inserted. Nine were used at the time of

ing operation, the average period between operation and extrusion being 10 months. These extrusions apparently resulted from contracture of the fairly dense fibrous sheaths around the buried portions of the implants and from retraction of the con-
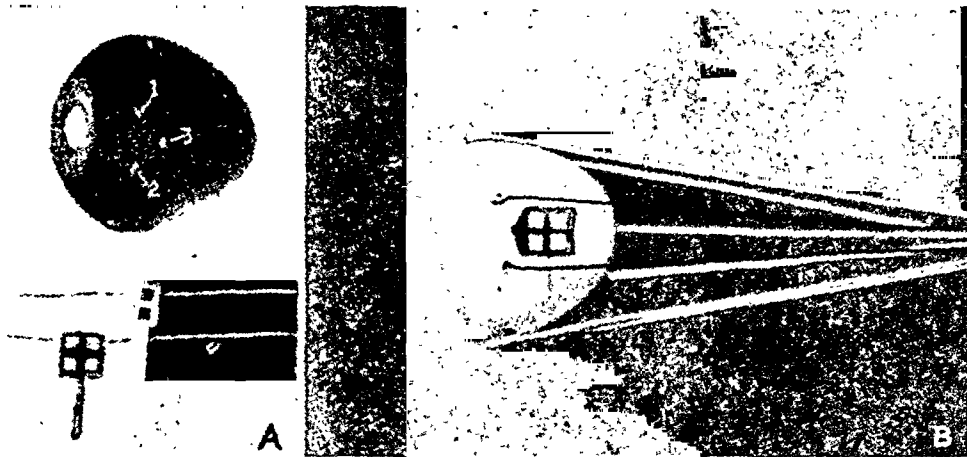
Fig. 3 (Guyton). Ruedemann's original plastic eye implant.

enucleation and one after removal of a displaced gold-ball implant. The initial results were excellent in four of these patients, there was appreciable tropia in five, with some persistent ptosis in three. In the remaining patient insertion of too large an implant resulted in immobility of the eye. One patient developed orbital cellulitis three months after an initially successful operation.

Nine of the implants were extruded at intervals of seven days to 22 months follow-

junctiva from the ends of the rectus muscles which eventually, despite repair, broke free from their attachments to the tantalum clips. One implant was still in place 29 months after operation, but there was some exposure of the paddles and attached muscle ends.

In a recent personal communication,[198] Ruedemann stated that every one of the
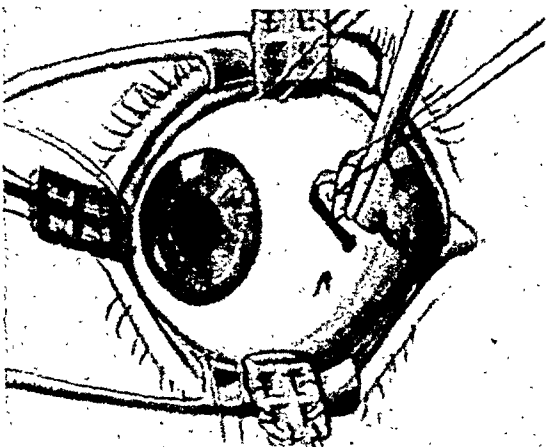
Fig. 4 (Guyton). Attachment of muscles to Ruedemann's whole acrylic eye via tantalum paddles.
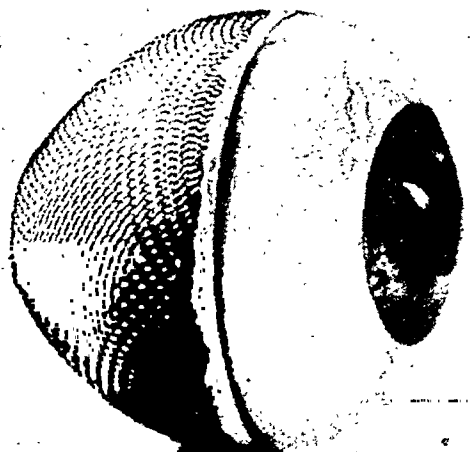
Fig. 5 (Guyton). Ruedemann's modified acrylic eye implant, with tantalum mesh for attachment of tissues.

plastic eyes he had implanted with muscles connected to tantalum clips was eventually extruded or had to be removed. Nevertheless, the eyes stayed in place long enough to suggest that improved techniques might result in permanently successful implantations.

As early as November, 1945, Ruedemann proposed utilizing a whole eye implant with tantalum mesh surrounding the buried portion,[199] and soon thereafter he began implanting such eyes (fig. 5).

The rectus muscles and the edge of Tenon's capsule were simply sutured to the anterior border of the mesh, with the sutures also passing through holes drilled through the plastic. Tenon's capsule and the muscles became firmly adherent to the tantalum mesh. When it was necessary to straighten the eye after it was implanted, Ruedemann found it difficult to separate muscles and Tenon's capsule from the mesh-work, but he has done so by means of a periosteal elevator. Since adopting this never type of implant, he has had only a few extrusions, which he thinks probably resulted from using too large a size.

scribed the first implant of this type (January, 1947) as "a positive contact ball and ring implant."[2] This ring implant consisted of an acrylic sphere with a short anterior cylindrical prolongation surrounded by a gold or vitallium ring attached to the plastic by four equidistant metal bars, and with a metal cup inset in its anterior surface (fig. 6). The ring implant was inserted following simple enucleation by folding the ends of the recti around the ring from within outward, folding Tenon's capsule and conjunctiva over the ring in the opposite direction, and suturing

Fig. 6 (Guyton). Cutler's ring implant.

these structures firmly in position with non-absorbable sutures (fig. 7).

After the socket was completely healed, a prosthesis was made to match the visible anterior segment of the other eye in size and color. This prosthesis was similar to acrylic prostheses worn after simple enucleation except that the scleral portion was smaller and more curved, so as not to extend into the fornices. A metal pin which fitted snugly into the cup of the implant was attached to the back of the prosthesis, the pin being positioned on the prosthesis so that the eyes were in perfect alignment. The pressure of the lids held the pin in its cup and produced firm attachment of the prosthesis to the implant so that full motility of the implant was conveyed to the prosthesis.

The use of this male-female coupling eliminated the necessity of inserting a whole

CUTLER'S RING IMPLANT WITH ATTACHABLE PROSTHESIS

In October, 1945, Cutler began inserting buried implants to which protheses could be coupled after the socket had healed. He de-

eye implant, which had to be individually made prior to operation and therefore could not be used for emergency enucleations. The coupling permitted construction and adjustment of the prosthesis after healing occurred, insured perfect alignment and position, and allowed for replacement of prostheses if they became faded, scratched, or otherwise imperfect. Cutler's introduction

by Cutler the follow-up was limited to only a few months. In a recent personal communication, Cutler[200] stated he was gathering follow-up statistics but that these were not yet complete. "The longest follow-up I have a record of is 2½ years; incidentally this patient has not had his prosthesis out during the past year and a half. None of my original implants put in since April, 1946,
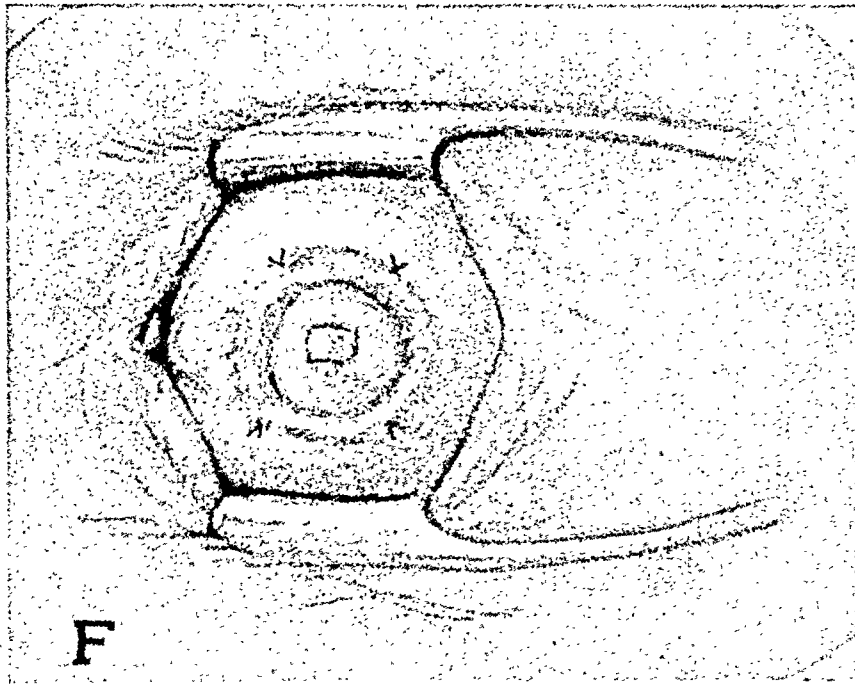
Fig. 7 (Guyton). Cutler's ring implant sutured in position.

of this two-piece principle was a notable step in the attainment of uniform final results.

Cutler reported the use of his ring implant in 22 patients. Five implants had to be removed. Three of these were the first he had used and were constructed of three pieces screwed together; in one case the patient developed orbital cellulitis and pneumonia six months after the implant was inserted; in the other two cases, the ring became exposed by erosion through its covering of Tenon's capsule and conjunctiva, and this led to a gradual increase in the exposure of the ring and the eventual detachment of the muscles. Cutler noted that attempts to repair the covering of a partially exposed ring were fruitless.

In the group of cases originally reported

have come out. I haven't done many secondary operations. However, I think one half have come out for various reasons and the other half are doing very well."

In June, 1946, O'Brien, Allen, and Allen[201] reported having inserted a few implants like those of Cutler into Tenon's capsule. They modified Cutler's original design slightly by substituting bridges across grooves for the ring. The recti were split after passing under the bridges and sutured together around the anterior peg rather than folded back on themselves. The few implants inserted during the six months preceding their report gave encouraging results. However, in a recent personal communication about semiburied implants, O'Brien[202] said, "I did make a preliminary report in San Francisco several years ago but I am not as enthusiastic

as I was at that time. It seems to me there remains a great deal to do before these things are satisfactory."

At the Wilmer Institute, 23 Cutler ring implants were inserted between March, 1946, and March, 1947. Two of these were reimplantations, one at the time a Ruedemann whole eye implant was extruded, and the other 15 days after extrusion of a previ-
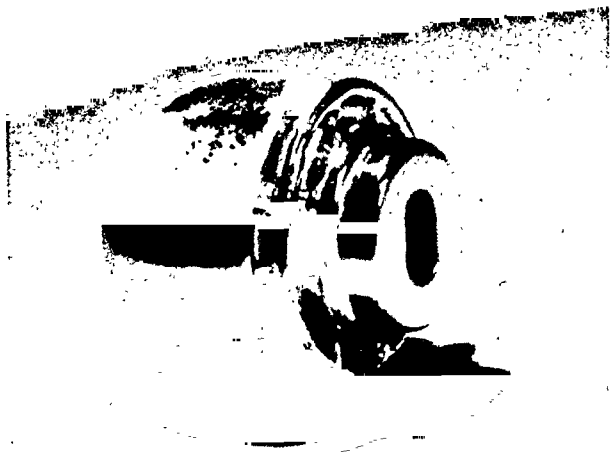
Fig. 8 (Guyton). Hughes's hollow vitallium ring implant.

ous ring implant. Both of these reimplantations were extruded within four months. Of the 21 ring implants inserted at the time of enucleation, seven were still in place and gave excellent cosmetic results after follow-up periods of 1 to 11 months (average five months). Fourteen were extruded at intervals of one day to 11 months (average five months) after insertion.

The events leading to extrusion were exactly the same as those originally noted by Cutler: exposure of a small segment of ring, usually in its upper portion, and gradual extension of this defect, with eventual detachment of the muscles. We likewise found, as had Cutler, that attempts to repair a defect over the ring were uniformly unsuccessful. However, in all fairness to the ring implant, it must be recorded that these

operations were performed by a number of different surgeons, who in some instances did not follow the exact technique of suturing advocated by Cutler, and that the implants we used had slightly less space between the ring and body of the implant than Cutler believed desirable. Also, the attachable prostheses used with the first implants were too flat and too large, so that attempted maximal rotation resulted in a strain on the attachments surrounding the ring.

Hughes[49] began inserting slightly modified ring implants into Tenon's capsule in October, 1946. His modification consisted of an implant made of hollow vitallium rather than of plastic, with the ring closer to the implant and attached by eight bars instead of four (fig. 8). The diameter of the buried portion was approximately 18 mm. if it was to be used immediately following enucleation, and 12 mm. if designed for the replacement of a buried implant.

His technique for initial implantation included preservation of strips of sclera in front of the insertions of each of the recti, 3 or 4 mm. in length and two thirds of the thickness of the sclera, thus extending the length of the rectus tendons so they would be sufficiently long to pass around the attachment ring without being under tension. For replacement of a buried implant, Hughes thought the ring implant feasible only if the buried implant was approximately in normal location with good motility and with enough connective tissue attached to the recti to fold over the ring and permit adequate attachment. Initial good results were obtained in the four cases described in his preliminary report, but all four operations had been performed within the preceding four months. In a recent personal communication, Hughes[203] cited some nice results with the late replacement implants, as well as with those inserted at the time of enucleation.

Cusick[204] has inserted 10 Cutler ring implants (nine primary and one secondary)

since October, 1946. The first one he inserted was extruded following gradual exposure of the upper portion of the ring after about two months. In his subsequent operations, he paid considerable attention to overlapping the upper structures more extensively than the lower ones, thus providing a relatively thicker covering for the upper portion of the ring, and he has had no more extrusions. He is probably correct in believing this manuever was responsible for his subsequent good results. Cooper[205] has had no extrusions of three ring implantations six months after the operations.

Rosen[206] has recently described as original an implant having the same slight modification which O'Brien, Allen, and Allen, first reported in June, 1946.

The present status of Cutler's ring implant may be summarized as follows: It is the first semiburied implant with a detachable prosthesis, and represents a distinct advance in enucleation procedures. Furthermore, if the ring implant is properly made and is inserted with careful technique and with wide overlapping of Tenon's capsule (especially above), the cosmetic results are not only initially excellent, but will probably be permanent in a majority of cases. This implant is seldom suitable for delayed implantations.

O'BRIEN'S SEMIBURIED EVISCERATION IMPLANT WITH ATTACHABLE PROSTHESIS

In the June, 1946, report of O'Brien, Allen, and Allen[201] already cited, the authors also described use of a few semiburied intrascleral implants, which they originated. The first of these gave excellent initial results but became gradually extruded. A change in the size of the implants and in the technique of insertion was made after the first few extrusions, and the implants they then inserted seemed less likely to extrude.

The implant in use at the time of their report consisted of an acrylic ellipsoid, 11.7 by 14 mm., with a short cylindrical peg 4

mm. in diameter extending forward from its anterior surface, and a plastic flange which could be fastened around this peg after the implant was inserted. The anterior surface of the peg was inset with a round cup for the reception of the pin of the attachable prosthesis. To insert this implant, a 4-mm. hole was trephined through the center of the cornea, a meridional incision 18 to 20 mm.
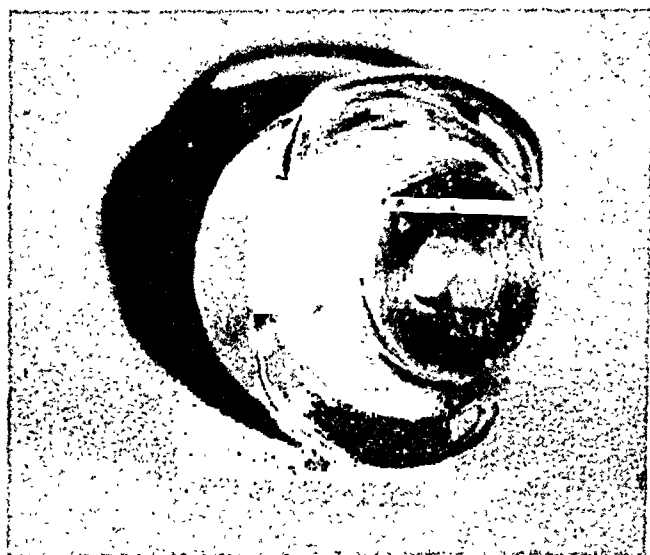
Fig. 9 (Guyton). Hughes's hollow vitallium evisceration implant.

long was made through the upper temporal sclera, the contents of the globe were eviscerated, the implant was inserted so that the peg protruded through the hole in the cornea, the scleral incision was closed and the flange around the peg fastened to prevent its slipping back through the cornea. No long-term results were available at the time of the preliminary report, and O'Brien[202] is not now as enthusiastic about these implants as he was in 1946.

Hughes[49] began using evisceration implants resembling those of O'Brien, Allen, and Allen as well as ring implants in October, 1946. His evisceration implants were made of hollow vitallium, and his later models had two small bridges through which strips of sclera could be passed for firmer attachment (fig. 9). His technique involved removal of the entire cornea. A preliminary report included four cases of evisceration with these semiburied implants. Two of the

implants were extruded within the short follow-up period, and a third case had to be reoperated. In a recent communication Hughes[203] said that he made some changes in the design of the implant, using two different sizes, and that he is now carrying out further investigations in this line.
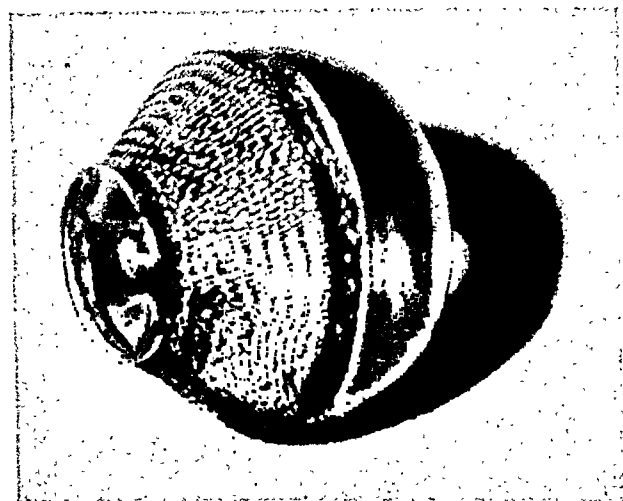
Fig. 10 (Guyton). Whitney and Olson's acrylic implant with tantalum mesh belt for attachment of recti and Tenon's capsule.

In summary, it may be fairly concluded that this type of evisceration implant has thus far proved disappointing.

SEMIBURIED ACRYLIC IMPLANTS PARTIALLY COVERED WITH TANTALUM MESH

In August, 1946, Whitney and Olson[3] first inserted a semiburied implant partially surrounded with tantalum mesh and adapted for an attachable prosthesis. This first implant was an acrylic ellipsoid, 18 by 20 mm., covered except over the slightly protruding anterior face by fine tantalum mesh (fig. 10).

After two of these implants had been inserted, Whitney and Olson decided that better motility would result if the posterior surface of the implant were left smooth and the sides of the implant covered with mesh.

This decision was based on the observation of two sockets in which buried doughnut-shaped implants of fine tantalum wire had been inserted the previous year: the stumps were initially freely movable, but after some months the motility gradually diminished, the position of the stumps apparently becoming "fixed" by extensive fibrosis.

One implant with a smooth posterior surface was inserted in October, 1946. Between September, 1947, and March, 1948, they inserted 10 additional implants which differed only in having a narrower rim of tantalum mesh, a groove around the anterior portion of the implant beneath the mesh, and a larger, shallower cup to serve as the female coupling (the small, deep cup first used had collected an odoriferous discharge). All of these implants were inserted at the time of enucleation. Thus far none have extruded, and the results have been excellent. The only complaints Whitney and Olson make are that some sockets have had more discharge than after simple enucleation, and that in some cases there is actual hypermotility of the prostheses.

In March, 1947, Stone[207] began insertion of implants (fig. 11) almost exactly like those of Whitney and Olson, and in October, 1947, he reviewed the results of 20 initial
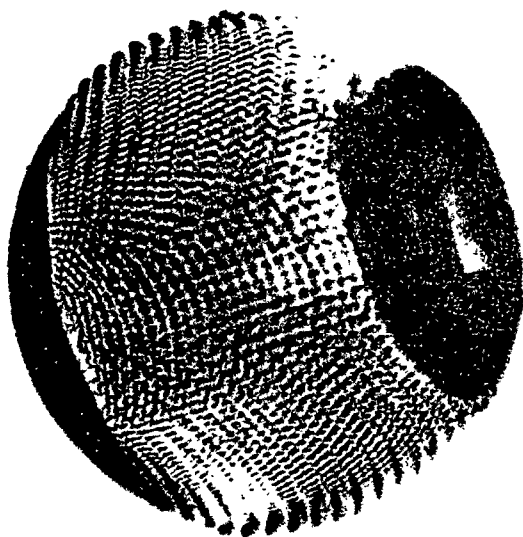
Fig. 11 (Guyton). Stone's acrylic and tantalum mesh implant.

implantations and four delayed implantations. There were no extrusions, and the motility of the implants varied from 50 to 100 percent of normal. The only complications were conjunctivitis in three cases.

In a recent communication, Stone[208] noted that there were as yet no extrusions. In two cases where reoperation was performed to obtain better motion from individual muscles he found "the fibroblastic proliferation of Tenon's capsule and the retrobulbar fat was so firm that it was impossible to separate it from the meshwork with a spatula. It was also so coarse that cutting with scissors was difficult. The conjunctival epithelium had firmly engaged itself at the anterior edge of the meshwork and it was also impossible to separate this junction with a spatula."

Since May, 1947, Cutler[200] has used an implant (fig. 12) similar to that of Whitney and Olson, in preference to his original ring implant. He terms this newer implant the "universal type," for use in enucleations, reimplantations, and his enucleo-evisceration operation (preservation of a scleral ring containing the attachments of the rectus muscles). He says "about 25 or 30 have been used since May, 1947, in Wilmington. One secondary came out after about five days in the hospital because I discontinued the pressure dressing in a patient who had a hemorrhage. I didn't think it *could* come out—but it did. The Gougelman Company up to 2 or 3 weeks ago, had sold, I believe, about 150 of these. No expulsions are known to them. ... The use of the mesh implant is short and simple. Catgut sutures only are used." (Whitney and Olson, and also Stone, prefer sutures of fine tantalum wire.) Cutler has found the range of movement with this type of implant is approximately the same as that with his original ring implant.

In summary, this Whitney-Olson type of semiburied implant appears to be better than any of those previously described. A considerable number have been implanted

during the past 12 months with consistently excellent results. However, it is well to remember that, with this as well as with other semiburied implants, "the theoretical disadvantage of the procedure is great. It controverts basic surgical dictum that a wound must be completely epithelized in order not to break down. Not only is the wound seemingly not epithelized, but there has also been introduced a foreign body which is not epithelized. When an analogous pro-
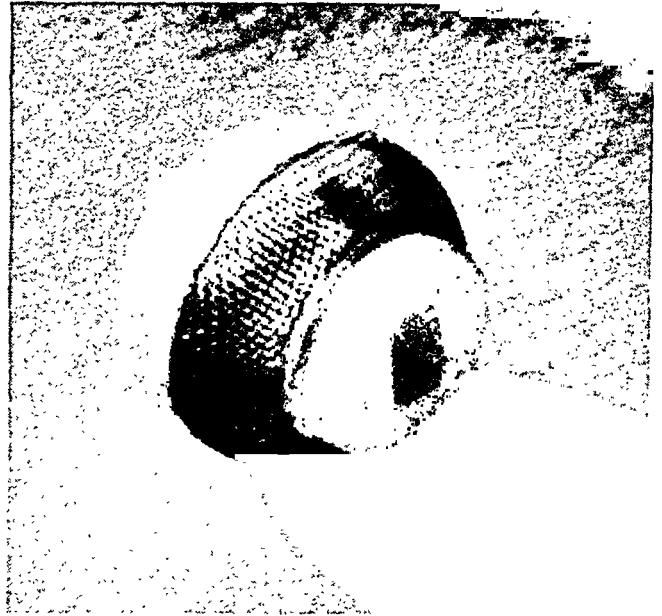
Fig. 12 (Guyton). Cutler's "universal" acrylic and tantalum mesh implant.

cedure has been attempted in the past by dental or orthopedic surgeons, no matter how small their unepithelized pin might be, sloughing invaribly has ensued."[207]

It seems probable that the excellent results so far obtained with tantalum-mesh attached implants will be permanent; but only long-term follow-ups can eliminate the possibilities of gradual late restriction of motility because of too heavy proliferation of fibrous tissue around the implants (such as noted by Whitney and Olson with buried implants of tantalum wire) or of late orbital infections occurring because of lack of epithelialization around the implant.

(To be concluded.)

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THE NONSURGICAL TREATMENT OF HETEROTROPIA*

RICHARD G. SCOBEE, M.D.

Saint Louis, Missouri

There are three objectives which may be attained by nonsurgical therapeutic means in the patient with heterotropia. They are: (1) The destruction of abnormal retinal correspondence, (2) the abolition of suppression amblyopia, and (3) some adjustment of the accommodation-convergence reflex. When these three objectives have been reached, the final goal in the treatment of all patients with heterotropia—fusion—may often be obtained in a surprising number of cases. The three objectives will be considered in the order mentioned.

ABNORMAL RETINAL CORRESPONDENCE

Corresponding retinal elements are those which have the same visual direction. In the person whose eyes are normal and who has normal retinal correspondence, imagine some object, O, located straight ahead as the object of gaze. The image of O will fall on corresponding retinal points in the two eyes. Any object whose image falls at A in the

right eye will be projected back into space to the point O and the same will be true of the point B in the left eye. Since A and B have the same visual direction, they are said
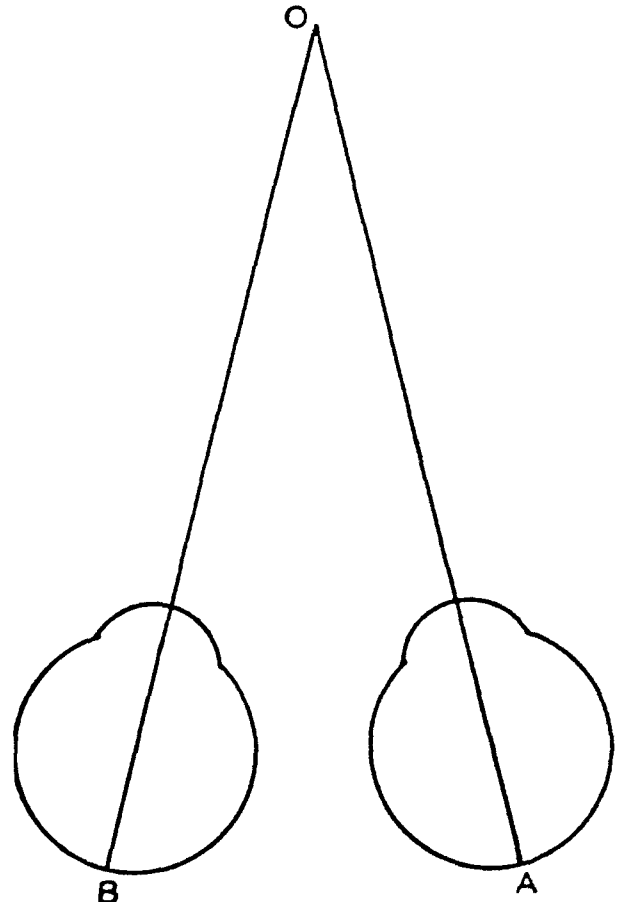
Fig. 1 (Scobee). Diagram showing corresponding retinal points.

to be corresponding retinal points. This is shown in Figure 1.

A person with esotropia, for example, has an entirely different situation, as shown in Figure 2. O is again the object of gaze of the right eye and the image of O falls at A; the left eye, however, is turned inward in esotro-
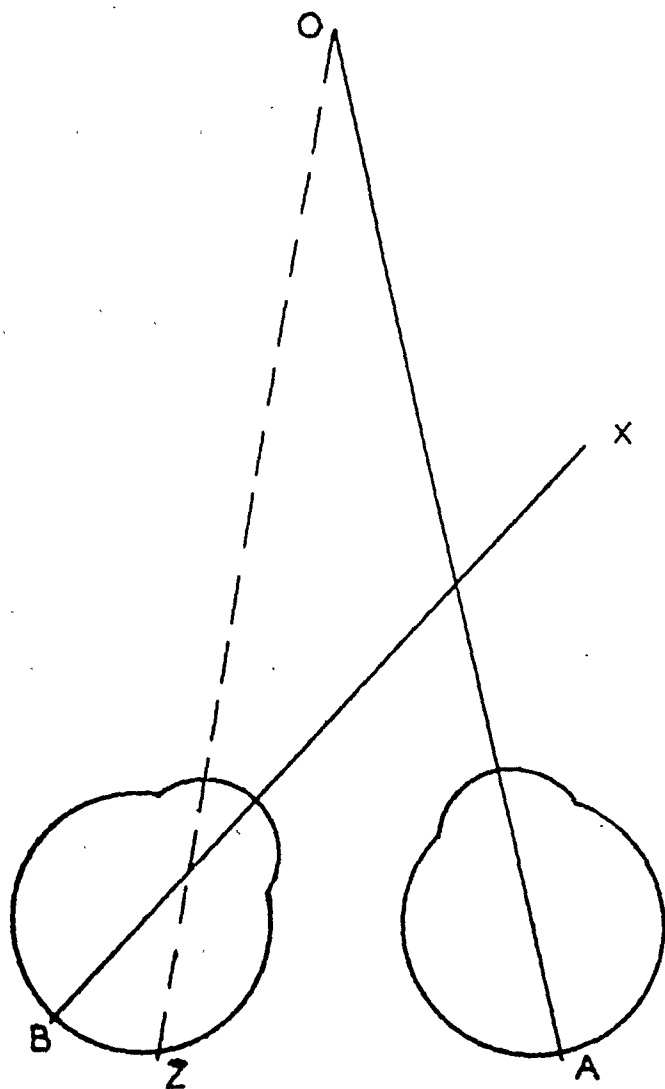
Fig. 2 (Scobee). Diagram showing abnormal retinal correspondence (esotropia).

pia and the image of O falls not on B but on the point Z.

In Figure 1, A and B, representing the two foveas, are seen to be corresponding points. In Figure 2, O is forming an image at A and at Z; A and Z are obviously not corresponding points because any object imaged at A will be interpreted as being straight ahead while any object imaged at Z will normally be interpreted as being located to the left of the midline.

Since the patient has esotropia, however, every time he looks at the object O, it is imaged at A in the right eye and at Z in the left eye. After countless repetitions of this situation, the patient finally learns to interpret images falling at Z as being straight ahead instead of to the left! A and Z have now become corresponding retinal points in that they have the same visual direction. A and B are normally corresponding retinal points and yet A and Z have developed an abnormal relationship of correspondence and the patient is said to have abnormal retinal correspondence.

The therapeutic problem in such a case is obviously first to destroy the abnormal relationship between A and Z and, secondly, to reëstablish the proper relationship between A and B.

Abnormal retinal correspondence is a conditioned reflex which has developed in response to a conditioning stimulus. Every time the patient looks at any object with the point A of his right eye, the point Z in the left eye is also stimulated and the relationship between A and Z is strengthened. If one would destroy a conditioned reflex, one must completely remove the conditioning stimulus. If the fixation of the objects with the right eye (actually, with the point A of the right eye) is the conditioning stimulus and the conditioning stimulus must be removed, then the fixation of objects with the point A of the right eye must be prevented at all costs. In other words, the right eye must be constantly occluded and thus prevented from fixing on any object at all.

Once the right eye is prevented by occlusion from assuming fixation, the left eye is forced to take up the task. The spot of greatest potential retinal sensitivity in the left eye is B, its fovea, even though it has not been used because of the abnormal position of the left eye in esotropia; the point Z in the left eye has been used in this instance as a matter of necessity. Once it is no longer necessary to use Z, the left eye will prefer to use the point B because B is

far more sensitive, potentially, than is Z. When Z is no longer used in conjunction with A, the abnormal relationship between these two abnormally corresponding points begins to weaken and will eventually disappear in most cases. Meanwhile, B—the normally corresponding point of A—is being used continuously. After the abnormal relationship between A and Z has been destroyed, the patient is free to develop a normal relationship between A and B provided the eyes can be held in such a position that this is possible.

While the foregoing paragraphs are somewhat of an oversimplification of the actual situation, nevertheless the idea as a whole is sound and should serve to clarify the problem. There is no question but that complete and constant occlusion of the nondeviating eye in the patient with heterotropia is the first and most important step in the destruction of abnormal retinal correspondence.

SUPPRESSION AMBLYOPIA

This may be defined as the apparent loss of vision in the crossing eye which develops in patients with monocular heterotropia. In the past, this visual loss has been somewhat erroneously called amblyopia ex anopsia or the blindness of disuse. In the first place, the visual loss is not a blindness of disuse because it does not occur in the retina itself but instead is localized at the level of the occipital visual cortex and is believed to occur as a result of active suppression in that area.

Suppression amblyopia occurs as the result of a conditioned reflex in the same way that abnormal retinal correspondence develops. It would not be incorrect to think of the two as developing simultaneously. To return to Figure 2, the patient is fixing an object O with the point A of the right eye; the deviating left eye has the point B (the normally corresponding point with A) aimed at some other object, X.

If the patient is to keep from seeing X and O superimposed at the same point in space—an impression which would obviously be very confusing—then the image falling either at A or at B must be ignored by the brain. The image falling at B, that is, the image falling at the fovea of the deviating or crossing eye, is the one which is invariably ignored and it is more than a passive inattention toward images falling at B; it is an actual suppression which is active and certainly not passive.

One cannot merely ignore a stick of dynamite with a lighted fuse lying nearby if one expects to continue in the efficient performance of the daily tasks of living; the fuse must be extinguished—in short, something active must be done about the situation.

The brain in actively ignoring images falling at B is "doing something" about the situation. Every time the patient looks at an object, such as O, with the point A of the right eye, the brain must ignore whatever object (such as X) that may happen to cast its image at B in the crossing left eye.

Thus, the stimulus for suppression in the brain connected with the point B in the left eye is the use of the point A in the right eye for fixation. Each time the patient looks at an object with A in the right eye, the point B in the crossing eye must be suppressed a little bit more. Suppression amblyopia is a conditioned reflex and the conditioning stimulus is the use of the point A in the nondeviating eye.

It has already been shown that the use of this same point A in the nondeviating eye is also the stimulus for the development of another conditioned reflex—that of abnormal retinal correspondence. As in this former instance, the treatment of suppression amblyopia is the destruction of the conditioned reflex which is responsible for its existence. This means removal of the conditioning stimulus.

The conditioning stimulus is easily eliminated by merely occluding the right eye and thus preventing the stimulation of the point A. This procedure forces the use of the left eye and its area of potentially greatest sensi-

tivity, the point B. With A out of the picture, there is no longer any need for the brain to ignore B but instead there is an actual demand for the recognition of objects falling at B. Thus may suppression amblyopia, a conditioned reflex, be destroyed by removing the conditioning stimulus, the latter being accomplished by occluding the habitually fixing eye.

It may now be appreciated that occlusion of the nondeviating eye in the patient with monocular heterotropia accomplishes two purposes simultaneously: (1) The disruption of abnormal retinal correspondence, and (2) the destruction of suppression amblyopia. In both instances, we have a conditioned reflex which is abolished by removal of the conditioning stimulus. In each case, the conditioning stimulus is the fixation of objects by the noncrossing eye. If a conditioned reflex is to be thoroughly abolished, the conditioning stimulus must be completely removed. This calls for constant and complete occlusion of the good or habitually fixing eye until both goals have been attained.

It is to be emphasized that wearing a patch over the habitually fixing eye for a few hours a day is not constant occlusion and is almost worthless. A conditioned reflex is extremely difficult to destroy if the conditioning stimulus is removed for only a few hours a day and is then allowed to act during the rest of the waking hours.

Atropinization of the better seeing eye instead of occlusion of that eye is of little value; the patient will continue to use the atropinized eye for distant fixation and use the poorer eye only for near objects.

A minimum trial period of six months of constant and complete occlusion should be insisted upon in every case. If the occlusion has been faithfully carried out and there is no improvement in vision at the end of this period, the occlusion may be discontinued and a tentative diagnosis made of congenital amblyopia.

Of the various types of occluders available on the market, the most satisfactory is the flesh-colored elastoplast patch. It is impossible for the patient to "peep" with this type of occlusion.

The patient with the better eye occluded should be encouraged to look at large, colored picture books, to play with large, brightly colored toys, especially large balls. The cheiroscope is an ingenious and useful instrument in stimulating the use of the poorer eye. Ruedemann has suggested the use of a kaleidoscope in these patients and the idea works well in practice; it is particularly important that the toy be held aimed at a sufficiently bright light source in order that the rapidly changing pictures may be properly illuminated.

ADJUSTING THE ACCOMMODATION-CONVERGENCE REFLEX

All of the remaining nonsurgical therapeutic measures in heterotropia may be gathered into this general classification. Included are the use of glasses, prolonged atropinization, prohibition of close work, certain forms of orthoptics, and more recently, the use of pilocarpine, eserine, and even of D.F.P. They will be discussed in the order named.

1. *Glasses.* Correction of any existing ametropia is the first step and an important part in the therapy of heterotropia because the majority of cases have an accommodative element, no matter how small. Because hypermetropia leads to compensatory accommodation and an associated excessive convergence, any hypermetropia found in patients with esotropia should be fully corrected; if exotropia is present and there is hypermetropia, only the minimum correction needed to secure clear vision is advisable. When myopia is present and there is esotropia, only the minimum correction needed to secure clear vision should be given; on the other hand, if there is exotropia and myopia, a very full or even a mild overcorrection of the myopia is indicated. Astigmatism, irrespective of type, should always be fully corrected, regardless of

whether the lateral deviation is one of eso-tropia or exotropia.

A word about what is meant by a "full" correction is necessary. A full correction means the entire refractive error as found under atropine cycloplegia. If a patient has esotropia and is found to have 4.25 diopters of hypermetropia, the full 4.25 diopters should be given in the prescription, deducting nothing for ciliary tone.

It is rare that one obtains complete cycloplegia in a child, even with atropine, and hence what appears to be a full correction is usually an actual undercorrection by an amount equal to the incompleteness of the cycloplegia. The deduction of even 0.5D. from the atropine findings will sometimes make a difference of as much as 10 degrees in the amount of deviation corrected by glasses.

We have discontinued entirely the use of atropine as an eyedrop in children and even adults with heterotropia for two reasons: (1) The cycloplegia is often incomplete because either tears quickly flush much of the drop from the sac or dilute it to a point where it is relatively ineffective, and (2) systemic reactions are frequently encountered in children.

In place of the atropine drop, atropine ophthalmic ointment (0.5 or 1 percent) is routinely used. Systemic reactions with the ointment are very rare and the ointment results in a higher concentration of atropine in the sac over a longer period of time, thus leading to much better cycloplegia.

If a parent has difficulty in getting any medicine into the child patient's eyes, the ointment is superior to the drop because even though it only gets on the lashes, it soon melts and runs into the eyes. The ointment is used three times daily for a minimum of three days prior to refraction.

A full correction is prescribed, no matter how small the error that is found, and the glasses are then worn constantly for a minimum of one month before any judgement of their effect in reducing the deviation is

attempted. The one-month interval is absolutely essential in order that the patient may establish a new accommodation-convergence ratio.

The routine just described often seems to work a hardship on the out-of-town patient and many oculists are wont to skip it in such instances. Their final results are proportionately bad. While such patients may at first seem to object, their final reaction is invariably one of satisfaction, the thought seemingly uppermost in their minds being that the doctor was thorough.

The occasional child who complains of blurred vision with his full correction will need to be atropinized by the use of the ointment once or twice daily for about two weeks.

A not uncommon occurrence is met with in patients whose esotropia is fairly well controlled by correcting lenses. They may suddenly seem to develop more esotropia in spite of the glasses. This is almost invariably an indication that the glasses need changing. These patients will be found to have outgrown a certain portion of their hypermetropia and a reduction in the amount of the plus sphere in their correction will, paradoxically enough, produce a corresponding reduction in the amount of esotropia.

The paradox is easily explained, however, when one recalls that a hypermetropic eye that is overcorrected—as is one that has outgrown some of its hypermetropia when the glasses are not changed—is an eye with blurred vision. The response to blurred vision is always an attempt to further accommodation with its associated convergence. Hence when vision blurs, the patient attempts to accommodate more in order to clear it and incidentally converges more in the process, thus increasing the esotropia.

Reducing the plus correction to the proper amount results in a return of clear vision and a decrease in the efforts at accommodation and incidental convergence.

2. Atropinization. Children with esotropia or marked esophoria will frequently be bene-

fited by from 3 to 6 weeks of atropinization during and immediately following systemic illnesses. The reason is obvious. The tonus of the bodily musculature as a whole is below par and the ciliary muscle is included. Excessive accommodative demands are needed in order to perform close work and excessive convergence automatically ensues.

Atropinization is also of value in high-strung children with esotropia normally corrected by glasses when they are undergoing periods of stress or strain, such as beginning school. Guibor advocates phenobarbital in small doses in such cases and it may indeed be of value in quieting a hypertonic convergence center associated with a tense central nervous system.

3. Prohibition of close work. The intelligent and high-strung child with esotropia will show an apparent increase of that esotropia during periods of stress. When this occurs, it is wise to prohibit all close work for a month, two months, or even three months. The goal of such prohibition is, of course, prevention of use of the eyes as much as possible during periods of actual esotropia and thus preventing both suppression and abnormal correspondence from developing. A child that is just on the borderline of fusion—fusing at times and at other times lapsing into tropia —should be prohibited from casual close work and confined to supervised orthoptics.

4. Orthoptics. Certain forms of orthoptics are aimed at adjusting the accommodation-convergence reflex. The goal is usually an attempt at at least a partial dissociation of accommodation and convergence. It is not within the scope of this paper to present the means by which this may be accomplished but it can be done successfully in many instances with gratifying results.

5. Pilocarpine, eserine, and D.F.P. Abraham* reports a series of cases whose treatment was based on an ingenious theory. He used miotics in patients with intermittent esotropia and reported good results in a surprisingly high percentage of such cases. He reasoned that miotics produced ciliary spasm which he chose to call "peripheral accomodative spasm" (as opposed to central accommodative spasm such as might occur in hypermetropia in response to a demand for clear images by the brain).

If such accommodation were produced artificially and peripherally, then there should be no demands centrally for accommodation and hence no associated convergence. Thus did Abraham explain the apparent beneficial effects of miotics in patients with intermittent esotropia. Attempts at confirmation of his work are not yet completed. The idea is a fascinating one for speculation, however.

SUMMARY

The nonsurgical measures in the therapy of heterotropia have been considered. Although approximately 60 to 70 percent of all patients with heterotropia require surgery before a final cure may be effected, still the remainder may be cured by nonsurgical measures properly employed. Many of the nonsurgical measures enumerated are important prerequisites of surgery in any event and it is well for the ophthalmologist who would treat patients with heterotropia to be fully cognizant of them all.

640 South Kingshighway (10).

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* Abraham, S. V.: The use of miotics in the treatment of convergent strabismus and anisometropia. Am. J. Ophth., 32:233, 1949.

NOTES, CASES, INSTRUMENTS

VITREOUS LESIONS OBSERVED IN BOECK'S SARCOID*

PHILIP H. LANDERS, M.D.†
Binghamton, New York

The purpose of this report is to describe vitreous lesions found in five eyes in a series of 13 patients having sarcoidosis who were observed at the Veterans Administration Hospital at Fort Howard, Maryland, during a two-year period ending July 1, 1948. A complete study from the ophthalmic viewpoint of the cases of sarcoidosis from this hospital, including the results of nitrogen-mustard therapy in selected cases, will be submitted at a later date.

Sarcoidosis, or the Besnier-Boeck-Schaumann disease, was estimated by Woods and Guyton[2] to constitute 2 to 3 percent of cases of endogenous uveitis. Longcope,[3, 4] Fisher[4, 5] and Michelson[6] have described the general features of the disease, and Walsh[7, 8] pointed out the relationship of sarcoidosis to Heerfordt's syndrome.

With the increasing recognition of sarcoidosis by clinicians in various fields, granulomatous uveitis and the other less common ocular manifestations are assuming a greater importance as links in the chain of diagnosis, and the severely damaged eyes, which may be almost the sole residual effect of the disease, pose a difficult problem to the ophthalmologist.

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* Published with permission of the chief medical director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or the conclusions drawn by the author. This group of patients was examined and followed as a part of a study of the effect of nitrogen mustard on sarcoidosis, which, with the approval of the National Research Council, was initiated by Dr. George E. Snider, and the preliminary report was made by him in January, 1948.[1]

† Resident in Ophthalmology, Veterans Administration Hospital, Fort Howard, Maryland.

The vitreous lesions consist of discrete grayish-white bodies occurring in the most dependent portion. They vary in size from dots to approximately one third of a normal disc diameter and are, for the most part, spherical. Frequently these bodies occur in chains like an isolated segment of a string of pearls. A few tubular forms have been noted, and occasionally other nondescript shapes. They may be seen with the ophthalmoscope focused on the retina, and focused in front of the retina up to a plus-10 reading. In all cases, they have been at least several disc diameters below the posterior pole, and are most numerous around the 6-o'clock position at the periphery. The bodies cast shadows from the ophthalmoscope light on the retina and the apparent distance of the bodies from their shadows indicates their relative position in the vitreous. It is almost impossible to see the lesions without fully dilating the pupil.

The patients studied were a group of 10 Negroes, two white men, and one American Indian. These veterans ranged in age from 21 to 35 years and all had generalized sarcoidosis including pulmonary lesions. All but one had peripheral node involvement. The various other sites included skin, lacrimal gland, epididymis, nasal mucosa, bone, and kidney. All diagnoses had been confirmed by one or more biopsies prior to examination by the ophthalmic department. Of the group of 13 patients, eight had eye involvement of some degree.

The three patients in whom the five eyes showed the vitreous lesions were young Negroes. All had chronic granulomatous uveitis characterized by greasy keratic precipitates on the posterior cornea, a positive aqueous flare, Koeppe and Busacca nodules, and a tendency to posterior synechia. The second eye of the third patient had a dense posterior synechia at the 6-o'clock position

which made it impossible to visualize the area in which the vitreous bodies might be expected.

The vitreous lesions have been observed only in the eyes of patients having relatively benign eye involvement. It is possible that the incidence of lesions in this group may be higher than has been indicated because, in the more severely involved eyes, it has been impossible to see the area in which they are to be found. Over a period of three months, there has been no marked change in the size, number, or character of the vitreous bodies in the five eyes, although in all cases the uveitis has become quiescent.

The present approach to the pathology of the vitreous lesions is necessarily indirect because all five eyes have useful vision. The area in which they are found suggests that they are of a higher specific gravity than the vitreous. The patient having the largest number of lesions was placed in a Trendelenburg position for three hours, and all patients were observed after periods of recumbency to check for drift of the bodies. However, no demonstrable change in their position was noted. It seems, therefore, that the specific gravity of the vitreous bodies must be essentially the same as that of the vitreous.

Two hypotheses as to the nature of these bodies have been considered; that they are similar in nature to Koeppe or Busacca nodules of the iris, which are collections of cells of the lymphoid series, and, that they are serous exudates which have been formed by an inflamed ciliary body and are therefore largely protein in composition. Up to the present, it has not been possible to prove or disprove either hypothesis.

Fig. 1 (Landers). The discrete, grayish white lesions were seen in the most dependent portion of the vitreous of a patient whose low-grade granulomatous uveitis was a manifestation of his generalized sarcoidosis.

It is possible that pathologic material may be available for the direct study of the vitreous lesions in sarcoidosis at a later date. In that event more tangible evidence will be brought to bear on this problem.

53 Main Street.

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Fig. 1 (Wholihan). The instrument case and its contents.

A COMPACT INSTRUMENT CASE*

JOHN W. WHOLIHAN, M.D.
Jackson, Michigan

Since ophthalmology requires so many instruments, the resident is at times puzzled as to what basic items he should have at hand to avoid omission of certain fundamental diagnostic steps.

The object of this article is to show that certain simple diagnostic instruments, drugs, treatment medication, and dressings can be readily carried in a small case. This instrument case is the outgrowth of several weeks of working with bulging pockets, frequent lapses in routine which necessitated revisits, and repeated trips to the supply room.

The convenience of the case is only one of its advantages. Besides making the taking of tensions a routine, unless contraindicated, it multiplied the number of interesting cases

seen. Several of the large wards at Wayne County General Hospital contain from 60 to 200 patients and frequently other residents, when on rounds, would ask for an
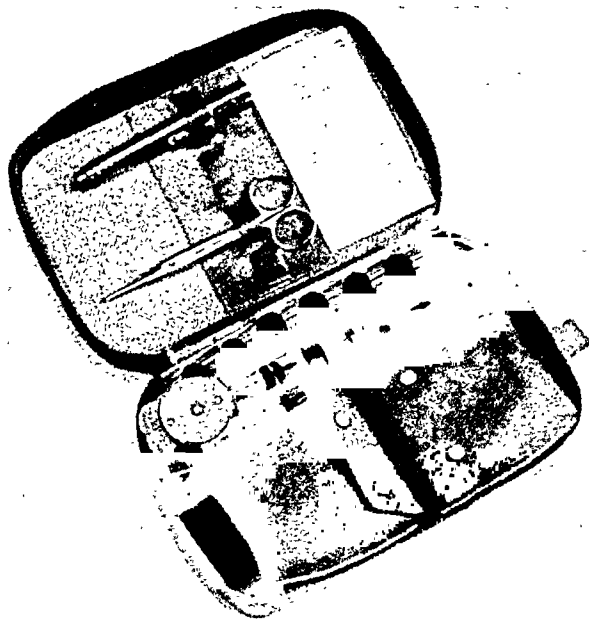
Fig. 2 (Wholihan). The case packed and ready to take on rounds.

* From the Wayne County General Hospital and Infirmary, Eloise, Michigan.

opinion or point out a case with unusual eye findings. The preliminary examination could be instituted on the spot rather than waiting until the resident had accumulated his "tools."

The photographs show the case which measures 9 by 6 by 3½ inches. The leather containers into which most of the smaller and less frequently used instruments fit are Schick razor cases. The contents of the case consist of:

1. Nine 0.5-oz., screw-top bottles containing frequently used diagnostic and therapeutic solutions.

2. Ophthalmoscope.

3. Tonometer.

4. Several visual acuity charts cut from a large chart and a near-vision, reduced Snellen chart.

5. A piece of exposed X-ray film, 5 by 15 cm. for screening.

6. Supply of sterile droppers.

7. Geneva lens measure, exophthalmometer, one-meter steel tape.

8. Several small instruments, epilation forceps, punctum dilator, syringe, and lacrimal canaliculus needle.

9. Condensing lens.

10. Roll of one-inch adhesive tape.

11. Supply of eye pads.

12. Supply of ointments.

13. Scissors.

14. Flashlight and extra batteries.

602 West Michigan Avenue.

EYE-DROP TRAYS

Max Kimbrig, M.D.
Huntington, New York

Errors caused by picking up the wrong eye-drop bottle, although rare, have occurred. One automatically checks himself several times before using any eye drops. This, and the fact that the bottle wanted is usually the last one picked up, means decreased office efficiency and annoyance.

The illustration shows an eye-drop tray which I designed and found to be an accurate and efficient aid in eye-drop selection. I made two identical trays for two treatment rooms. I am passing the idea along to anyone who is annoyed with time lost in searching for the right bottle; to anyone who wants to cut down the chances for error.

SPECIFICATIONS

Through a block of wood about 1 by 1½ by 11 inches, bore 10 holes, each ⅝ inch in diameter and about ⅜ inch apart. Glue a piece of cardboard on the bottom and set a ⅛ oz. dropper vial in each place.

A cellophane covered label in front of each hole matches the label on the vial, affording a double check on the vial's contents. This is really a triple check, for one can now reach for a bottle and know its contents by its location. The small vials can be filled from a stock bottle; or those seldom used, such as atropine, can be added to the vial in small quantities.

20 High Street.
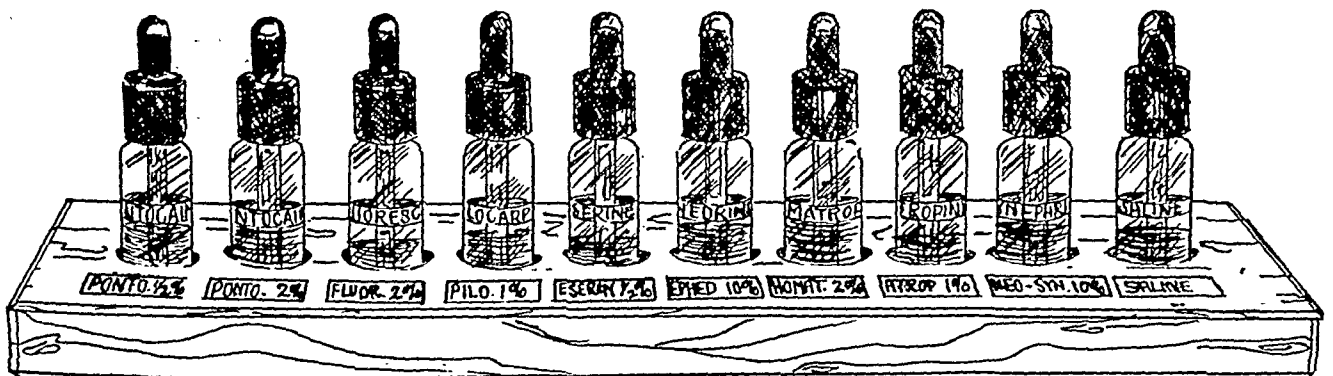
Fig. 1 (Kimbrig). An efficient eye-drop tray. (Drawing by S. M. Lee.)

SOCIETY PROCEEDINGS

Edited by Donald J. Lyle, M.D.

December 15, 1948

Dr. John E. Rice, *presiding*

Effect of Procaine upon the Sphincter
Mechanism

Dr. Harold G. Scheie of Philadelphia discussed this topic. His remarks are here summarized.

Retrobulbar injection of procaine hydrochloride was found temporarily to produce the effect of a ciliary ganglionectomy. The pupil on the injected side, in animals and humans, dilated widely and became fixed. The effect persisted in dogs for 80 to 90 minutes and in humans for 1 to 5 hours. During that period of time, physostigmine was ineffective in producing miosis, but pilocarpine remained effective.

Pupils constricted by physostigmine prior to retrobulbar injection of procaine dilated promptly following retrobulbar injection but pupils constricted similarly by pilocarpine remained miotic.

Pilocarpine, therefore, should be the postoperative miotic agent of choice when prompt miosis is desirable following operations done with retrobulbar anesthesia such as a cataract extraction through a round pupil. Pilocarpine should likewise be used preoperatively when miosis is desirable throughout an operative procedure when done with retrobulbar anesthesia. A peripheral iridectomy, for example, is easier to do when operating for narrow-angle glaucoma if the pupil remains miotic.

Caution should also be taken to instill pilocarpine or a substance with a similar pharmacologic action into an eye prior to the use of retrobulbar injection of procaine hydrochloride for the treatment of acute congestive glaucoma. Failure to do so, or the use of drugs with an escrinelike action alone, would permit mydriasis and very probable aggravation of the glaucomatous state by further obstruction of the angle of the anterior chamber.

Studies were also done to determine the effect of procaine when applied locally to the iris. Prompt pupillary dilatation was obtained in dogs and cats from the injection of 0.1 cc. procaine into the anterior chamber. Pupillary dilatation of some degree was also obtained in human subjects following the instillations of two drops of 10-percent procaine in 1:3,000 phemerol at five-minute intervals. This mydriasis lasted for two hours. A mild cycloplegic effect was also observed.

Pupils dilated by the injection of procaine into the anterior chamber were resistant to all types of miotic agents even those which stimulate the muscle cell directly, such as calcium ions. It was therefore concluded that procaine probably exerts a direct depressant action upon the cells of the sphincter muscle when applied locally. Procaine should probably, therefore, not be used beneath the subconjunctival flap where prompt postoperative miosis is desirable or when miosis is desirable throughout an operative procedure.

Discussion. Dr. David Cogan asked what effect procaine has on the sympathetic ganglion, as far as the pupils are concerned.

Dr. Scheie replied that he had seen Horner's syndrome preceded by injection of the sympathetic ganglion, and that procaine would block a sympathetic ganglion much as it would any other nerve or ganglion.

Dr. Paul Chandler: This paper just reflects the ignorance of the rest of us in regard to this subject—the fact that we are unable to discuss it—and it points up what an original and interesting piece of work it is.

S. Forrest Martin,
Reporter.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

Section on Ophthalmology

December 16, 1948

Dr. Perce DeLong, *chairman*

PLASMA CELL MYELOMA OF ORBIT

Dr. Joseph McEvoy (by invitation) said that tumors consisting of plasma cells occur quite frequently in the bone marrow and constitute one of the histologic types of multiple myeloma. Extramedullary plasma cell tumors, on the other hand, are of greater rarity.

A total of 128 cases of extramedullary plasma-cell tumors have been described in the literature. Most of these have been in the mucous membranes. The commonest site of occurrence is in the mucous membrane of the air passages and the next commonest site is in the conjunctiva, where 47 cases have been recorded. The only case involving the orbit that I have been able to find, other than the one described tonight, is the one described by Walsh, which he reports in his textbook on neuro-ophthalmology.

Histologically, the abundance of plasma cells is the outstanding feature of these tumors. The tumor cells are characterized by a large amount of cytoplasm and an eccentrically situated nucleus. The chromatin is arranged in cartwheel fashion, and a paranuclear unstained area is present. Cells with 2 or 3 or more nuclei are common. Other cells such as polymorphonuclears, lymphocytes, and histiocytes, if present at all, are never an essential part of the tumor.

When an isolated plasma-cell tumor is found, the question arises as to whether it is a solitary benign lesion, easily removed, or whether it is a part of the very malignant multiple myeloma. It seems that the microscopic appearance does not play an important role in predicting the clinical course of a given lesion. Even the appearance of mitotic figures in the cells does not indicate malig-

nancy. As long as the plasma-cell tumor is localized and confined to soft tissues and there is no other clinical evidence of multiple myeloma, cure can generally be obtained.

The case to be presented concerns an 80-year-old white woman who was admitted to the medical service of the Philadelphia General Hospital on May 26, 1948. She had no complaints, and was admitted simply for custodial care until admission to a nursing home could be arranged.

Physical examination revealed a well developed, but poorly nourished, anemic, old lady. The general physical examination revealed nothing of note other than the anemia which was hypochromic in type and thought to be nutritional. The right eye was blind. She had had a cataract extraction three years previously. The cornea was densely leukomatous. The left eye showed a senile cataract with vision of 6/60. There was a swelling of the right lower lid which felt like a firm mass extending into the orbit. This mass had been present about three months, was painless, and slowly progressing in size. There was no exophthalmos.

On June 16, 1948, surgery was performed under local anesthesia. The lower lid was incised along its entire length below the tarsus. Nothing was found in the lid itself. Within the septum orbitale was a reddish firm mass with a smooth, apparently encapsulated surface. By blunt dissection it was possible to separate the mass from the surrounding tissues, and follow it back into the orbit beneath the globe. It was shelled out, and removed in toto, measuring 3 by 1 by 1 cm. A large amount of hemorrhage was controlled with difficulty. A pressure dressing was applied. Postoperatively she developed a rather large hematoma of the operative site.

The pathologic report on this tumor is: The material consists of a homogeneous mass of uniformly dark, round cells—plasma cells. There is almost no stroma and practically no mitotic figures are seen. The diagnosis is plasma-cell myeloma.

X-ray examination of the skull, the orbit, the vertebras, the ribs, and the pelvis showed no evidence of bony myelomatous involvement. Repeated urinalyses showed no Bence-Jones protein. The serum calcium was 10 mg./100 cc. Examination of the sternal bone marrow showed no increase in cellularity and hematopoiesis was essentially normal. There was spotty infiltration throughout, with well-differentiated plasma cells.

The serum protein was 10.7 gm./100 cc. Of this 2.4 gm. were albumin and 8.3 gm., globulin.

This extreme hyperglobulinemia was thought to be highly suggestive of a diffuse myelomatous process in spite of the other negative findings.

The patient's right orbit was treated with two courses of irradiation of three doses each. The doses of X-ray therapy were 300 r., 600 r., and 900 r. at three-day intervals.

The postoperative hematoma completely absorbed in two weeks. No remaining tumor mass was discernible, and she was discharged from the hospital to a nursing home on August 24, 1948.

This case was presented as an example of an unusual orbital tumor and the difficulties of evaluation and prognosis of isolated plasma-cell tumors.

Discussion. Dr. Thomas Cowan: I have nothing to add as to the pathologic characteristics of this tumor, but the case does illustrate very well the difficulty of making a diagnosis before excision, and the desirability of excising so as to make a diagnosis. Clinically, the tumor impressed me as being benign by its appearance in the lid, and it had been so diagnosed elsewhere. As the orbit was entered, the characteristics of the tumor became more and more like those of a sarcoma. At its inner attachments it was so infiltrated among the tissues that it was very hard to remove surgically. Following the operation, the healing was very excellent for such an infiltrating tumor.

Dr. Perce DeLong: Plasmocytomas are not rare. However, few have been reported in the orbit.

The plasma cells are not easily recognized, because pathologically they present immature forms of the typical plasma cell, and for this reason are often referred to as myeloma cells.

The metabolic aspect of myelomatosis is interesting, in that it produces a protein in the urine which must be differentiated from albumin by the Bence-Jones test. If found, the diagnosis is quite conclusive. However, its presence is intermittent.

Dr. Joseph McEvoy: You mean the Bence-Jones protein test? Yes, we did it several times, and there was none found, but she did have an extremely high serum globulin.

ENDOTHELIAL MYELOMA (EWING'S TUMOR) OF ORBIT

CAPT. FRED HARBERT, (MC), U.S.N. (by invitation) AND COMMANDER GEORGE L. TABOR, JR., (MC), U.S.N. (by invitation) reported two cases of Ewing's tumor involving the orbit. The term Ewing's tumor is used to describe the clinical entity of a highly radiosensitive primary tumor of the bone which shows no true osteogenesis.

One of the cases presented was primary in the orbit with a rapidly fatal termination in spite of dramatic immediate improvement under radiation therapy. The other case was secondary in the orbit with complete replacement of osteolytic defects by normal cancellous bone following X-ray therapy.

The prognosis in a case of Ewing's tumor is considered to be inversely proportional to the degree of elaboration of recticulum. The histogenesis of Ewing's tumor and reticulum-cell sarcoma are considered to be identical.

Discussion. Dr. Perce DeLong: Ewing's tumors, by the majority of pathologists, are not considered a pathologic entity. It is a syndrome of a nonosteogenic, round-cell, radio-sensitive tumor, and this syndrome can be caused by many types of tumors.

The analysis of Ewing's tumors by many prominent pathologists showed that in a

majority of instances they were expressions of metastasis.

In the child and in the adolescent group, it was also found that they were not truly Ewing's tumors, but neuroblastomas, which proved to be metastatic, and finally, the ones that were primary proved in almost all instances to be reticulum sarcomas. If you notice, Dr. Harbert's second case was finally diagnosed as reticulum sarcoma. Ewing's tumor is not an entity, but a syndrome.

Dr. Fred Harbert: I must, of course, defer to your greater experience and judgment, but just from the standpoint of the clinician I think that Ewing's tumor is still a tenable diagnosis. What are you going to call the characteristic bony lesions when you cannot find a primary tumor, and throughout the subsequent course of the disease, you cannot ever find a primary soft tissue tumor? Ewing himself makes the absence of primary tumor a necessary criterion for diagnosis, so that at least it is a working diagnosis, and may have to remain even after postmortem. The differentiation between Ewing's tumor and reticulum-cell sarcoma is considered largely academic.

DIFFUSE INFILTRATION OF IRIS ASSOCIATED WITH NEVO-XANTHO-ENDOTHELIOMA

DR. GRACE R. NACHOD presented this paper which includes a brief discussion of the clinical and histologic picture of nevo-xantho-endothelioma together with a case report.

The case is that of a Negro male infant who was first seen because of a sore eye which proved to be due to a diffuse cellular infiltration of the iris and ciliary body with dislocation of the lens and secondary glaucoma. Shortly after the eye was enucleated, he developed multiple skin lesions, one of which was biopsied and diagnosed as nevo-xantho-endothelioma.

Although the cells that had infiltrated into the iris and ciliary body were somewhat similar to those seen in the skin lesion, no definite conclusions could be drawn as to their actual relationship.

Discussion. Dr. John Porter Scott: I speculate as to what would have happened had this eye not been removed. These lesions in the skin have the tendency to regress and disappear leaving no more scars than does chicken pox.

When I saw this child at the time the skin lesions first appeared, I thought that the eye had not been removed soon enough, because, in my ignorance, I assumed them to be metastatic lesions. At that time we had not received Dr. Fry's very excellent description of the tumor. Therefore, we were not sure just what the surgeon's diagnosis was.

Lesions of this type occur in some forms of storage disease. One of these is uncontrolled diabetes, in which xanthomatous lesions may appear. These are more yellow and less pink or salmon in color than the lesions in this child. As in this condition, they may disappear.

In Hand-Schüller-Christian's disease the lesions are yellowish, are larger, and have no tendency to disappear.

This case represents untrodden ground. I could not find any case in the literature in which the tumor was within the eye. One case was reported in which a tumor was in the orbit. I think the ophthalmologists should remember the appearance of this tumor. It would be extreme optimism to think that this tumor would have regressed as did the skin lesions. To repeat, I speculate as to what would have happened had the eye not been removed.

Dr. W. E. Fry: I think there are several features in regard to the eye specimen that might bear emphasis. The first is the infiltration of the iris which was very diffuse and very dense, and in which there were giant cells of the Touton giant-cell type similar in appearance to the Touton giant cells that appeared in the skin lesion, and which I understand are important for the diagnosis of the skin lesion. The eye had been

fixed and dehydrated in ether and alcohol so it was not possible to carry out fat stains. These would have been useful. Fat stains on the skin specimen showed a marked degree of fat.

The other feature that was important was the anterior dialysis of the retina through which apparently the dislocated lens had slipped. Just how this had occurred is entirely speculative. One possibility is that the lens dislocation could have been produced artificially when the eye was cut previous to embedding. This is unlikely, because, of hundreds of eyes that we do cut, if they are cut with reasonable care, no dislocation of the lens occurs, and if it does occur it is not dislocated behind the retina. The secondary glaucoma, probably caused by the dislocated lens behind the anterior dialysis, could have led to severe changes in the eye so that enucleation was indicated.

The question comes up as to whether these lesions in the iris regress. Probably they do, and this is probably why we have not seen them or they have not been reported to any extent before. In all probability, if the glaucoma changes had not occurred the eye might have cleared up, and the lesions regressed spontaneously.

Dr. Herman Beerman: I know the history of this patient and the pathologic findings very well, because I had the opportunity to study the cutaneous specimen, and Dr. Fry was good enough to allow me to study the eye slide. Although Dr. Blank, Dr. Eglick, and I have reported this case from the pediatric-cutaneous standpoints, I hope we have not interfered with Dr. Nachod's plans for publication of the ocular findings.

This is an extraordinarily rare case, and, as was previously mentioned, there is only one other instance in the literature in which eye complications have been noted. This was a patient reported in the discussion of Dr. Lamb and Dr. Lain's paper by Dr. Ellis of Baltimore. No further details are available on this case. Therefore, the present case is unique. I believe it is the first authentic

instance in which both cutaneous and ocular complications have occurred, and in which their identity was proved by pathologic examination.

I believe, in retrospect, that when one visualizes the amount of ocular damage present one cannot say the eye lesion would have regressed without necessitating enucleation. I do not believe, therefore, that anyone who handled this patient need fear criticism for the procedure employed.

Dr. A. G. Fewell: I thought the eye should come out, as the whole iris seemed to be thickened and infiltrated with the growth. The tension was rather high, and the eye was apparently blind.

Dr. Grace R. Nachod (closing): I am grateful to Dr. Fry and Dr. Fewell and Dr. Beerman for mentioning the fact that they thought the enucleation was indicated. I wondered about it a little bit myself; and am grateful to Dr. Scott for his discussion.

GENERAL ANESTHESIA IN OPHTHALMOLOGY

Dr. H. H. Stone (by invitation) read a paper on this subject.

Discussion. Dr. Edmund B. Spaeth: Some time ago, while discussing anesthesia for ophthalmic surgery with an anesthetist, not Dr. Stone, this statement was made by that anesthetist, "I do not understand the tremendous differences of opinion relative to general anesthesia which one observes when talking with different ophthalmic surgeons; I doubt whether there is anything more chaotic in surgery than that."

This observation has been made by other men. The fault, or perhaps the reason, for that state of affairs is not strange. There are three factors responsible. The ophthalmologist is only concerned with one of them, namely, his willingness to consider each case for surgery as an individual problem, and in each case whether the surgery indicated can best be done on the patient under consideration with local or general anesthesia.

The second factor is the brief, but rather essential, physical examination by an at-

tending internist, and the consideration of his recommendations as to which kind of anesthesia is to be used.

The third factor is the anesthetist's problem. Which type of anesthesia is to be used, inhalation anesthesia, intravenous anesthesia, or rectal anesthesia? All have optimum indications for use; each handles best a group of situations present. It is seldom, in recent years, that we suggest the type of general anesthesia to be used. Our wishes should be considered as to whether the surgery should be done under local or general anesthesia; but the anesthetist and the internist are responsible for the type of anesthesia to be used on each patient.

There is no doubt whatsoever but that the increase in the use of general anesthesia is directly proportional to the efficiency and the understanding of ophthalmic surgical problems by the anesthetist. We feel unusually fortunate to have Dr. Stone for our surgical cases.

Because of his efficiency and his department, we now view anesthesia quite differently. In the past, general anesthesia was used only when absolutely necessary. At the present time it has become the choice in many surgical procedures. Intraocular operations are still to be done under local anesthesia if possible; on the other hand, one need no longer dread them under general anesthesia, nor need one fear postanesthetic accidents and complications. This is quite a reversal in practice.

Plastic surgery, even the relatively minor procedures, can be done so much better without infiltration and/or block anesthesia otherwise necessary. Lacrimal-sac surgery, with its rather exacting anatomic dissections, is definitely simpler when performed under general anesthesia.

All types of muscle surgery, regardless of the age of the patient, are shortened in operating time and simplified without injections into the capsule sheaths which are necessary to make that surgery painless. Surgery for retinal separation, which can vary from a relatively brief period of operating time to hours on the operating table, when done under general anesthesia is far less taxing to the patient, and very much easier for the surgeon.

These procedures need little if any change in essential techniques regardless of the type of anesthetic which is used. Intraocular surgery, when done under general anesthesia, must have certain rather important changes in the surgical technique, connected with fixation of the globe and the support of the lids. This is outstanding with corneal grafts; in fact, it is so important with this latter type of surgery that it is used also at the first dressing of the patient's eye.

In the final analysis, a paper such as Dr. Stone has just given us has greater significance to anesthesiology than to ophthalmology. The anesthetist cannot take care of ophthalmic cases unless we are willing to permit it, and to coöperate with him at the same time. General anesthesia should play a bigger role in ophthalmic surgery than it does, considering, naturally, the availability of trained medical specialists in anesthesiology.

Dr. H. H. Stone (closing): Up to the present time we have had no fatalities. We occasionally do get into difficulty, and I think you get into difficulty no matter what type of anesthesia you use. We have seen difficulty with local anesthesia. Not especially in eye surgery, but we have had two fatalities when general surgeons were using local anesthesia. The expert should give the anesthetic for ophthalmic surgery.

I feel there is not a more difficult case than the cataract extraction under general anesthesia, not barring chest surgery. It takes far greater skill to keep these patients breathing yet not coughing or sneezing when the cataract is removed, and keep them well oxygenated throughout the entire procedure, than is required for a 5 or 6 hour pneumonectomy.

M. Luther Kauffman,
Clerk.

CHICAGO OPHTHALMOLOGICAL SOCIETY

December 20, 1948

DR. A. C. KRAUSE, *president*

CLINICAL MEETING

Presented by the Department of Ophthalmology, Northwestern University Medical School.

CONVERGENCE INSUFFICIENCY

DR. BRUCE MCCLELLAN presented a 37-year-old man who was first seen at the eye clinic about one month ago, with a complaint of headache associated with eyestrain and a "drawing sensation" about the right eye. His eyes have turned out since he was a child, but medical advice had not been sought until the symptoms became worse.

Examination showed 20/20 vision in each eye; refraction showed a +0.75D. sph. with a small cylinder for each eye. On the screen test for distance he measured 45 prism diopters divergence for distance and 65 for near, with a left heterotropia of 4 diopters for distance and 2 for near; these measurements have been repeated on three successive tests. His near point is remote; however, this is not a true case of heterotropia because he can fuse; he can fuse for near, the near point being forced to 110 mm. on the first examination, and, on the second, to 90 mm. with the right eye deviated. He prefers the left eye for distance and for near. There is marked underaction of both superior recti muscles, the right more so than the left; also underaction of the medial rectus muscles.

The diagnosis in this case was convergence insufficiency, secondary to divergence excess, also bilateral superior rectus paresis with overaction of both inferior oblique muscles.

Discussion. Dr. Beulah Cushman felt that the convergence insufficiency is secondary to the divergence excess, which always becomes a complication sooner or later. It becomes apparent as the accommodative power is reduced. This patient at the age of 37 years is having difficulty maintaining single vision for near work; the divergence for distance has been present since youth. The vertical anomaly is the primary factor. Surgery will include first the correction of the convergence insufficiency with resection of the medials and recession of the overactive oblique; at the second step there will be recession of the laterals.

Dr. E. H. Merz said the surgery mentioned will correct the vertical anomaly and the horizontal can be corrected at a later date. As Weidman states, most horizontal errors are secondary to vertical abnormality. It has been reported that these conditions can be corrected with tenotomies of the inferior oblique or recessions.

Dr. Kirby and Dr. White have commented on conditions where complete tenotomy has resulted in complete paralysis of the inferior oblique. If there is complete paralysis of the inferior oblique and of the superior rectus, there is a posterior head tilt which is undesirable.

Dr. Scobee has reported a case of bilateral paralysis following surgery in which pseudoptosis resulted because of the marked back tilt of the head. The congenital paresis is due to an error in cleavage of the common premuscle mass. These conditions are not uncommon. White, Kirby, and Dunnington say they are the most common of all muscle conditions. The superior rectus muscle differentiates from the group later than any other, and for that reason more congenital anomalies are found in that muscle.

FRACTURE OF FRONTAL BONE

DR. PAUL R. IRVINE reported a 10-year-old girl with a history of a fall from a bicycle. Whether she suffered a concussion is not clear; she was said to have struck the right side of the head on the handlebar or a rock. At the time, nothing was noted except slight discoloration at the right outer canthus. Approximately one hour after the accident some

swelling was noted about the eye. This became more marked and, 48 hours later, she was seen by an oculist. On the suggestion that a hematoma was present a conjunctival incision was made but no blood drainage resulted. About five days later nausea and dizziness occurred and she was put to bed, without improvement.

Ten days ago she was first seen at Passavant Memorial Hospital. On examination the right eye was proptosed and depressed. Vision was: R.E., 20/200; L.E., 20/20. Palpation over the lacrimal gland revealed a mass which was thought to be a dislocated lacrimal gland; a smaller mass was noted nasalward. X-ray films showed fracture of the frontal bone extending into the roof of the orbit. Neurologic consultation advised conservative management; they felt there was not only a hematoma but a cerebrospinal leak. On dismissal she had no diplopia.

Discussion. Dr. Derrick Vail said that this case emphasizes that one should not be too hasty in entering an orbit for acute proptosis even with the practical certainty that it is due to subperiosteal hematoma from injury. It is not unusual to find reports in the literature of acute proptosis due to hemorrhagic extravasation under the periosteum in patients who had scurvy, particularly infants.

When the X-ray films in this case were received from the family doctor, surgery was scheduled. As a precaution, however, further X-ray studies were made which showed the fracture and the operation was therefore cancelled. The fracture, as shown on the slides, extended into the roof of the orbit. The family doctor had mentioned that, on inserting a needle, he had withdrawn about 0.5 cc. of clear fluid; that report should have led to the suspicion of a leak through the roof of the orbit of cerebrospinal fluid. It is, however, not unusual to obtain some fluid from the orbit on diagnostic puncture in cases of acute proptosis; fluid from edema, for example, can be drawn into the syringe.

Certainly, in this case, conservative treatment was well worthwhile. The neurosurgeon feels that the crack will heal fairly well and if, at the end of six weeks or so, there still remains definite proptosis, particularly if a swelling is palpated in the roof of the orbit, a small incision to see if there is an encapsulated hematoma is probably justified.

PROGRESSIVE MENINGIOMA

DR. R. D. TEBBETT presented two cases. The first was that of a 54-year-old white woman who complained of gradually increasing weight for 17 years, blindness of the left eye for 10 years, and failing vision in the right eye for one year. In 1931, she weighed 131 pounds and at present she weighs 245. In 1940, she got something in the right eye and as she rubbed it she noted that the left eye was completely blind. Apparently the cause for the loss of vision was primary optic atrophy, but the cause was not determined. She was told that the right eye would probably never be affected. In January, 1948, she noted decreasing vision in the right eye, with what she described as a gray area in the lateral part of the field. Glasses were prescribed which improved the vision somewhat.

When she entered the hospital in July, 1948, vision in the right eye was 20/70. The left eye showed a cataract and primary optic atrophy. The right disc was pale; the scotoma descended from above laterally to the fixation point. Neurologic examination was essentially negative; spinal fluid was normal. X-ray studies of the skull showed proliferative changes of the inner table of the frontal bone and the rostral and dorsal portion of the sphenoid. It was decided that she had a meningioma which had probably been progressive for 10 years or more. Surgery was not advised.

TUMOR OF ORBIT

The second patient, presented by Dr. Tebbett, was a 33-year-old white woman who had had proptosis of the left eye, apparently of mild degree, for 3 or 4 years. Ten days prior

to entry she noted increase in the proptosis; in fact, the eye herniated between the lids. She entered the hospital for observation, and a lateral tarsorrhaphy was done to prevent further herniation of the eye. Previous X-ray studies were reported as negative.

Eye examination was essentially negative with the exception of the proptosis which measured: R.E., 13 mm., L.E., 27 mm. The eye was proptosed directly forward without lateral displacement. Visual fields were normal. Neurologic consultation was essentially negative. There was no bruit over the proptosed eye. There was a question of frontal-lobe disturbance because of the slightly disturbed judgment of the patient during questioning. X-ray films at this time showed marked erosion of the optic foramen on the left side, erosion of the lesser wing of the sphenoid, and erosion of the greater wing of the sphenoid.

Operation was performed by the neurosurgical service and a dumbell-shaped tumor was found, the greater part of the mass lying in the middle fossa extending up through the left optic foramen and into the orbit. The entire multiloculated tumor was removed at the time of operation. The pathologic report is, as yet, debatable. It has been reported as a neuroma and also as a meningioma.

Discussion. Dr. Derrick Vail felt that these two patients were most instructive for demonstration because they emphasize so clearly the point that one cannot ignore optic atrophy or dismiss it lightly without being satisfied that every possible avenue of investigation has been exhausted—even then it should be considered as an unsolved crime, which should cause concern to the ophthalmologist. If the first patient had had the proper diagnosis, early surgery could probably have been done. After 10 years of obesity, increased blood pressure, cardiac and arteriosclerotic changes she was not a suitable neurologic risk.

This woman's youngest child is about 8 years old and she feels, as does the surgeon,

that it probably would be best, with a slowly-developing malignant tumor—not malignant in the sense of metastasis but in destroying the adjacent tissues—to go on, with the possibility of keeping a small degree of sight, gradually getting worse, but at least keeping her life during the next few critical years of bringing up this child. She knows the whole story, has the utmost courage, and has faced the issue most cheerfully. Had surgery been attempted the neurosurgeon felt that a fatal result was pretty certain.

The second case is an example of the same situation. The patient had proptosis for 10 years, gradually getting worse, and more or less ignored the condition. Five years ago she consulted an ophthalmologist who found some proptosis, but the X-ray report was negative and he felt that there was no particular reason to account for the proptosis. An interesting feature of this case is that the proptosis is directly forward, which would indicate disturbance in the muscle cone; also that the vision is entirely normal in each eye and, third, that the optic nerveheads were entirely normal; the fields of vision were entirely normal; and there was no interference with ocular movements and no diplopia.

The situation became critical when she had sudden herniation of the eye, a catching of the upper lid behind the proptosed eye, which alarmed her considerably and she sought help. The X-ray film shows a striking phenomenon; complete erosion of the entire outer wall of the optic foramen. To take a picture of the optic foramen requires special technique and the X-ray man must be instructed to get a good view of the optic foramen. Extensive erosion of the sphenoid wings is also shown. Not many conditions produce such a picture—proptosis with erosion of the optic foramen and sphenoid wings.

The first thing to be considered is meningioma, and meningiomas are not unusual in females particularly. The second thing is

aneurysm, but there was no suggestive history and aneurysm would have undoubtedly interfered with some of the ocular movements. In view of the experience of Dandy, Cushing, and Eisenhardt—whose monograph is one of the classics of ophthalmic literature —it was felt that to perform an orbital operation in this case would be a mistake, and that the transfrontal approach was necessary.

Almost all cases are not purely local in the orbit, but secondary, by extension through the apex of the orbit from a meningioma arising usually on the lesser wing of the sphenoid. To give the patient every chance possible, the transfrontal approach must be used because, if there is proptosis plus bone changes, it is evident that an intracranial tumor extending into the orbit is present. To do an orbital exenteration only is but half the job; whereas, by transfrontal approach the neurosurgeon skilled in his work can unroof the roof of the orbit and find the tumor, as was done beautifully in this case.

It is a mistake, therefore, for the ophthalmologist to carry out orbital exploration, particularly in view of the possibility of meningioma. It is gratifying to report that this woman is recovering well, the proptosis has entirely receded and it is now just a matter of complete convalescence to be followed later by opening the lids.

These two cases should, therefore, emphasize that one should not be content with a purely objective diagnosis of optic atrophy, but should seek the cause, and should not be satisfied until that cause is found.

Dr. James E. Lebensohn: The first case, in which there was optic atrophy in one eye and central scotoma with expansion temporally, is probably one phase of the Foster-Kennedy syndrome; in fact, the Foster-Kennedy syndrome is more often found with suprasellar meningiomas than with frontal-lobe tumors.

The development of field changes is interesting. Pressure produces primarily a central scotoma which expands centrifugally, hence

producing first a temporal pallor and then the picture of primary optic atrophy. On the other hand, the papilledema on the contralateral side shows primary loss in the peripheral field, continues with centripetal contraction until finally secondary optic atrophy results. Among the significant findings that distinguish secondary optic atrophy of this type are occasionally concentric rings around the optic disc.

Pituitary adenoma is only one of the possible causes of bitemporal hemianopia. Similar effects on the chiasm may be produced by meningiomas, glioma of the chiasm, aneurysm of the anterior cerebral artery or its communicating branches, and chiasmal arachnoiditis. Careful study should indicate the differential diagnosis in any particular case.

SCIENTIFIC PROGRAM

PRIMARY LIPID DYSTROPHY OF THE CORNEA

DR. DANIEL SNYDACKER presented the case of a Negress, aged 20 years, with an unusual bilateral, symmetrical, ring-shaped corneal opacity. The appearance of the lesion, the lack of a demonstrable etiology, and the presence of an elevated blood cholesterol pointed to the diagnosis of a primary lipid dystrophy of the cornea.

Discussion. Dr. J. V. Cassady mentioned a similar case which he had had under observation. The patient was a 56-year-old woman who had a central type of xanthomatosis of the cornea rather than the peripheral type presented by Dr. Snydacker. There was a deep, central, yellow, vascularized corneal opacity in one eye, which had gradually developed without antecedent trauma or inflammation. Occasionally it was irritated and red, but usually without subjective symptoms other than blurred vision. Katz and Delaney described a similar central lesion in lipid dystrophy of the cornea. Dr. Robert von der Heydt confirmed the diagnosis in this case. The Wassermann and Mantoux tests were negative; the patient had 225 mg. blood

cholesterol, hypercholesterinemia. Vision in the other eye was normal, although many cases are bilateral.

Dr. Peter C. Kronfeld had observed for some time a patient whose eyes are similar to those of Dr. Snydacker's patient. Little was known of the history in this case. Her two sisters were blind from a gross form of this dystrophy and, while he had not seen them, they had been described by an eye doctor in their home town, and the corneas were completely opaque. In the two sisters, the disease took the same course as in the woman under observation. All have marked hypothyroidism and all are much overweight, none weighing less than 220 pounds. The symptoms started during the third decade of life. The patient under observation still has 20/20 vision in each eye. She has been put on a diet of 1,000 calories a day, plus vitamins. Her blood cholesterol is high, and the determination on one of the sisters was also high.

Dr. Robert W. Zeller said that, after a previous admission at Cook County Hospital in 1946, this patient again came under observation in 1948. In 1946 there was a flareup of the keratitis following injection of tuberculin; it was felt that the keratitis might have been on an acid-fast basis. She was not seen for two years when she returned because of a fractured vertebra.

The basal metabolic rate was then −23; subsequent determination were −17 and −9. The first determination was probably the most significant of the three. Total cholesterol was 186 mg., within normal limits. Total protein determination was 7.6, albumin was 4.2, and globulin, 3.4, which is rather high. The cephalin flocculation was 1+ positive. Thymol determination was 7.4 units; the upper limits of normal at County Hospital Laboratory is 5 units.

The biochemist felt that these determinations indicated possible minimal liver damage; he also said that the thymol determination had to do with determination of lipids

in the blood and, if elevated, might substantiate the diagnosis of lipid dystrophy.

This case was seen by Professor Van Ness who was here from Finland. He has apparently had a case of true lipid dystrophy, one of the seven reported. He felt that this was a case of lipid dystrophy also. It might be worth while to use choline in this patient, following Dimitry's suggestion. It is known to be a fat solvent, and might possibly bring about dissolution of the opacities.

Dr. Daniel Snydacker (closing): In answer to Dr. Zeller's question about the use of choline, it is doubtful if this would be of value because the opacities are deep and the choline probably could not reach them, and the basis of the treatment involves actual contact.

CHOICE OF OPERATION IN ACUTE GLAUCOMA SECONDARY TO SWELLING OF THE LENS

DR. PAUL STERNBERG AND DR. SAMUEL J. MEYER presented a paper on this subject and discussed choice of operation for an eye in which glaucoma is secondary to lenticular intumescence. It is believed that the acute, congestive glaucomatous attack which is said to be secondary to lens swelling occurs in an eye that may be termed preglaucomatous. The opposite eye is frequently of the preglaucomatous description, with a narrow entrance to the angle of the anterior chamber.

An iridectomy, if done early, or, if done later, an iridencleisis are the operative choices for reducing the increased intraocular pressure. An intracapsular cataract extraction is performed subsequently with use of corneoscleral sutures.

Discussion. Dr. Derrick Vail agreed with Dr. Sternberg that, in one's experience, glaucoma due to an intumescent cataractous lens will be encountered sooner or later. The essayists have given clear indications for various types of surgery in this condition, but he differed on some of the points expressed.

The glaucoma is due entirely to the swol-

len lens; that is a mechanical fact. Whether or not the angle is narrow prior to development of the intumescent lens is not pertinent to this discussion, because in any cataract case, if the lens is allowed to remain and become intumescent, there will be a rise in intraocular pressure at some time or other.

This occurs when the swelling of the lens reaches its maximum and may not precipitate an acute attack, but will result in a period of increased intraocular pressure followed in time by decrease in pressure as the intumescence recedes.

A mature cataract undergoes a varying process of evolution, eventually leading to the morgagnian type where the nucleus falls to the floor. If the morgagnian cataract is permitted to remain, the milky lens material eventually absorbs if it does not leak out through a spontaneous rupture of the anterior or posterior capsule, in which case there is bound to be considerable difficulty in the eye with iridocyclitis and secondary glaucoma. If the capsule remains intact the milky substance generally absorbs, leaving the condition that has been described in the literature: a shrivelled nucleus held between two collapsed capsules; in which case, of course, the glaucoma is not a problem because, if it did exist, it had spontaneously taken care of itself.

The point about the narrow angle as a provocative condition deserves considerable emphasis. It certainly should make one more careful in the study of these cases, particularly so far as the opposite eye is concerned. In ordinary acute glaucoma due to an intumescent lens, the lens should be removed as the primary cause of the glaucoma. In the literature there are described the use of pilocarpine and preliminary operations such as iridectomy and iridencleisis, which are apparently not necessary; in an experience with 10 or more such cases, the cataract has been removed successfully even in the presence of high intraocular pressure and a congested eye. The lens may be removed in

its capsule by the Smith method and, on the second or third day following, the eye is white and obviously grateful for the surgical interference. As Colonel Smith has said, the lens in such cases may be dislocated almost by "an angry look." To try to deliver the lens with capsule forceps is almost futile, because it is like trying to pick up a piece of soap in the bathtub.

A procedure recently advised by Dr. Daily is to prick the capsule with a small needle, letting out some of the material which, in turn, reduces the intumescence and permits grasping the capsule with forceps. Another method described is to open the capsule with a diathermy coagulation needle as a preliminary step. That seems rather involved when a needle will serve the purpose. Some men have had success with the erisophake, but in his own hands the Smith operation for this type of case is ideal.

An illustrative case is one of a patient operated on, in 1915, by Dr. Derrick T. Vail, Sr., at which time a cataract was removed from the right eye. The patient was satisfied with the result, he saw well, and was advised to have the lens removed from the other eye, which advice he ignored and went on for 10 years; the lens, of course, becoming more and more mature.

When seen at that time the lens was becoming hypermature and removal of the cataract was again advised. Six or eight months later he came in with an acute attack of glaucoma. He was almost 80 years old, had a vascular hypertension of 200+, he had had a coronary attack about two years before, he had nephritis, and could not possibly have been a worse risk.

However, although the problem was approached with fear and trembling, the incision was made ab externa, as so ably described by Dr. Meyer, the incision was enlarged with scissors, sutures were placed, and an iridectomy was done.

In doing the iridectomy the lens came forward and it was just a matter of touching

it gently through the cornea to deliver it by the Smith method. Surprisingly, an expulsive hemorrhage did not occur and the eye turned out very well indeed; the second day following operation it was as white as in the ordinary case and the patient made a complete recovery without any complications whatsoever. Thus, in certain conditions, one is justified in performing an intracapsular operation even in the presence of a high degree of glaucoma.

{ Possibly one reason why iridectomy has failed in these cases is because anterior peripheral synechias have developed, as pointed out by the essayists. It is not certain that an iridencleisis in these cases is advisable, because the angle is already blocked by the intumescent lens, and although the essayists have demonstrated that this is a theoretic objection, it is conceivable that one will temporize and delay and lose valuable time in permitting filtration to function. Such an eye is subjected to two procedures rather than one. *{|*

INTRAORBITAL ANEURYSM

DR. ROBERT F. HEIMBURGER (by invitation), DR. H. ROBERT OBERHILL (by invitation), DR. H. ISABELLE MCGARRY, AND DR. PAUL C. BUCY (by invitation) presented a paper on this subject and reported a case of exophthalmos due to aneurysm of the lacrimal artery contained entirely within the orbit. Transcranial exploration of the orbit and removal of the aneurysm of the lacrimal artery resulted in the patient's recovery.

A survey of the literature shows no other verified case of aneurysm of the lacrimal artery and, consequently, the criteria for differential diagnosis cannot be set up. Unilateral exophthalmos without pulsation but with evidence of venous obstruction, increased intraocular pressure, and failing vision were the clinical manifestations of the case presented.

Discussion. Dr. Paul Bucy was surprised to find that these are such uncommon lesions and that even those cases so listed in the literature are practically all questionable. In view of that fact it is even more remarkable that Dr. Kronfeld made the correct diagnosis preoperatively. This is an interesting problem, one which can be best dealt with if the lesion is in full view, as is possible with a transfrontal operation.

Dr. Peter C. Kronfeld recalled that when this patient was first seen she had progressive exophthalmos, ocular hypertension refractory to everything that was tried, limitation of ocular motion, swelling of the disc, and retinal hemorrhages. By this neurosurgical operation she has been cured. The present function of the eye is normal. One thing that was perhaps omitted was a more thorough study of the ocular hypertension. It apparently was a case of hypertension due to interference with venous outflow; somehow the aneurysm interfered with outflow of one or both ophthalmic veins; it would have been interesting to study this more in detail. It looked alarming and since it was felt that it was probably an aneurysm, the patient was referred to the neurosurgeon. In watching the operation, it is apparent that there is no possibility of exposing such a lesion equally satisfactorily through the anterior aperture of the orbit. While the great advantages of the transfrontal, transcranial approach to the orbit have been appreciated, this particular case is convincing proof that many cases of orbital tumor deserve the transcranial approach.

Richard C. Gamble,
Secretary.

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EPILOGUE

Flying 25,000 feet above the Atlantic ocean; behind, two weeks of American hospitality; in front, the old routine of work; it seems a good moment—the first opportunity in two weeks to sit back and relax—to send American ophthalmology a "thank you."

These two weeks have indeed been full to overflowing—one at the academy meeting at Chicago, a week-end at St. Louis with the local ophthalmological society and the American Board of Ophthalmology, followed by a week with the American College of Surgeons again at Chicago—two weeks of scientific papers and exhibitions, of social and academic functions, a whirl of events guided with what appears to be effortless efficiency, from companionable breakfasts through the crowded sequence of the day to the boundless hospitality of the evening and the good fellowship of the early morning.

This was the first academy meeting I have attended. I have taken part in many meetings in many countries; but there has been none like this. My main impressions were of the vastness of the meeting and the ordered rush of 4,000 members (all so enthusiastic)

and almost 4,000 wives (all so delightful); the immense caravanserai of a hotel that absorbed them into its interstices like a hydrophilic gel, apparently without effort or disturbance of its normal routine; the crowd of events that can be fitted into a day; the excellence and variety of the scientific program; the amount and the modernity of the scientific equipment on exhibition; and finally, and by no means least, the value and comprehensiveness of the courses of instruction—a feature unique to the academy which must be of immense educational value to the more isolated practitioner, whereby each year he can refresh himself in fundamental procedures and acquaint himself with recent advances at the hands of acknowledged authorities. But the most pleasant time of each day was the hour before dinner when everyone "visited" and I met intimately the many friends who have now become an accepted part of my life.

Without doubt the academy is one of the most important influences in American ophthalmology. The atmosphere of the meeting with its nice balance between professional and social activities, between what is new (as seen in the papers presented) and what is established in ophthalmology (as seen in the instruction courses), is an immense stimulus to the visitor and must be an equal stimulus to those practicing in a country wherein distances are measured in thousands of miles; but one hopes that it will not become much bigger and busier lest it topple over by its own weight or explode. So far as the present meeting was concerned, the burden thrown upon its organizers must be immense, but it is a burden that they can obviously carry and it was a pleasure to witness the effortless ease with which Conrad Berens presided over it, aided immensely by the charm of his wife.

The American College of Surgeons formed a second week of equal interest, but with 5,000 delegates instead of 4,000—the same high standard and breadth of scientific proceedings and the same good fellowship.

The highlight of this meeting was the colored television—a thousand people at a time could follow in its detail an operation for cataract carried out, with a running commentary by the surgeon, in a hospital in another part of the city. In this meeting, however, ophthalmology occupied a small corner. Is that wise? If ophthalmology stands alone outside the umbrella of general medicine and surgery, it will lose much of its inspiration and philosophy.

In both these meetings the outstanding impression carried away by the European visitor is their vastness. For example, at the convocation of the college almost 1,000 candidates were initiated into the fellowship at one time. This is the greatest difference between America and Europe. In Europe the standards are as high and the men as good; but the mass and weight of America must give it an immensely preponderating influence in world medicine. With this comes responsibility—a responsibility which America must accept, and is indeed accepting with enthusiasm and confidence.

Stewart Duke-Elder.

PIGMENTED TUMORS

The beautiful exhibit of Dr. Arnold Zimmerman at Atlantic City which displayed the results of the work of an anatomist on a dermatologic problem is of the greatest interest to ophthalmologists. His preparations showed clearly that the pigmentation of the skin does not arise by synthesis of melanin in the epithelial cell. Instead it is elaborated in specialized branched cells called melanophores which invade the embryo skin from afar and transfer their melanin to epithelial cells.

It seems not unreasonable to speculate that the cells of the choroid also receive their pigment from specialized pigment-bearing cells if, indeed, the melanophores of this membrane are not actually similar cells that have originated in the embryonic neural crest. If this is true, then the tumor known

clinically as sarcoma of the choroid is actually a neurogenic tumor.

A dozen years ago Georgiana Dvorak-Theobold (Tr. Am. Ophth. Soc., 1937) thoroughly reviewed the subject and suggested that the most tenable hypothesis is that of Masson in whose opinion the cells of these tumors, as well as of nevi, are derivatives of the cells of the sheath of Schwann. There still is doubt about the origin of the cell. Recent studies of the origin of melanoblasts, or cells that elaborate melanin, are most suggestive and may point the way to a solution of the complex problem.

There is of course no conclusive evidence that the origin of the pigment-bearing cells of the choroid have the same origin as the melanophores elsewhere in the body but it is at least probable that this is true. It has long been accepted by zoologists that the pigment-producing cells of amphibia and birds arise from the embryonic neural crest. The melanoblasts of mammals were thought to have a different origin.

The recent experimental work of Mary E. Rawles (Physiol. Zoöl., 20:248, 1947; Physiol. Rev., 28:383, 1948), however, supports the view that this is not true. She tested the potency of various portions of mouse embryos of a homozygous black strain ranging in age from 8 to 12 days' gestation by isolation and transplantation into the celom of white-leghorn chick embryos of 60 to 65 hours' incubation. In this site the transplants were allowed to grow until the host hatched. Isolations were made at various axial levels of the embryo in such a way as to test tissues of the central nervous system, adjacent tissues of the somite, and lateral plate and limb-bud regions for pigment-cell production in the grafts.

It was clearly shown that melanophores can be produced only from tissues that contain presumptive neural crest, histologically recognizable neural crest, or cells in migration from the neural crest. Skin and hairs that were completely normal except for the absence of pigment and pigment cells grew in all the grafts whenever neural crest had been excluded.

The development of structurally normal white hairs from a potentially pigmented mouse is conclusive proof that the formation of melanin pigment in the ectoderm and its derivative, the hair, is entirely dependent on one particular type of branched pigment-forming cell, the melanophore, which originates in the neural crest. Several hundred grafts were made.

That epithelial pigment in man also arises in neural melanoblasts was shown by Zimmerman and Cornbleet (J. Invest. Dermat., 11:383, 1948) who studied the development of epidermal pigmentation in the Negro fetus. Specimens of skin were taken from the scapular and abdominal region of 50 fetuses obtained by abortion.

Dendritic melanoblasts, with incompletely elaborated melanin, appear in the third month and from their first appearance do not resemble epithelial cells. They give a faintly positive dopa reaction which indicates that they elaborate an oxidase that is essential to the synthesis of the melanin, and epithelial cells do not. The melanoblasts progressively pervade the epidermis through the intercellular spaces and form an intricate pattern by their long processes. The epithelial cells acquire melanin secondarily by transfer from the dendritic processes of the melanoblasts.

Carcinomas that arise from the pigmented basal layer of the skin are only moderately malignant; whereas, the melanoblastic neoplasm is wildly malignant. The latter has a tendency to spread in sheets along preformed surfaces. The sheath cells, which are thought to be the cell from which choroidal sarcoma originates, are indeed sister cells of the melanoblasts but they give rise to sarcomas that are sparsely pigmented, if at all.

It is also interesting to note that workers in diverse areas of thought are uncovering interesting related data on the origin of pigment cells and that their findings all sup-

plement and support each other without essential reservation.

That this is true justifies the belief that in time the work now in progress will also clarify the specifically ophthalmic problem of pigmented tumors.

F. H. Haessler.

TRAINING IN OPHTHALMOLOGY

The American Board of Ophthalmology examinations afford an excellent opportunity to evaluate the present-day training available for men wishing to enter ophthalmology. Here it is possible to compare the knowledge acquired by the candidate in the various training facilities.

In certain circles there is the opinion that unless a man has had a regular residency in one of our better-known training centers there is little opportunity for him to acquire sufficient knowledge to become a "safe ophthalmologist." The examinations have shown that this is not the fact.

The individual who has a regular residency has definite advantages. His time is planned and the work in the basic sciences is supervised and often spread out over a sufficiently long time to make it simpler for him to acquire the knowledge. He is assigned to the laboratories where, at his leisure, he may work and study. Time is set aside during which various men in the department devote their energy in teaching him the clinical aspect of the specialty. He is taught to write and present papers. He has the advantage of working in the clinic and hospital in company with other residents. His evenings are free to study or, in some centers, to attend lectures. All in all it is an ideal and pleasant method of obtaining training.

Unfortunately, not all residencies live up to this ideal method. In some clinics the resident is used for the benefit of the organization without the organization giving its fair share in return. From the examination of candidates from such institutions it is apparent that little time has been spent in

supervision or teaching. That this supervision is necessary is very apparent. There have been some instances where the chief of the department lost interest in the teaching of residents and the candidates coming up for examination under this regime show lack of proper training.

What of the man who has been denied the privilege of a residency and who must depend upon a preceptorship for his training? The examinations have shown that it is possible to obtain an excellent training by this method. It does, however, require a longer time. In addition, there must be the "will to win" as the man must do his studying at night when he is fatigued from a hard day's work at the office. The examinations have also brought out the fact that in most instances it is necessary for the student to take a course in the basic sciences. Whether it be one of the longer courses or the very concentrated course of the Ophthalmological Study Council (The Lancaster Course) appears to make little difference.

In the preceptorship much depends upon the preceptor. If the candidate is to be properly trained the preceptor must be a sound ophthalmologist who is willing to take the necessary time to teach the clinical aspects of ophthalmology. One of the candidates, who received his training from a short basic-science course and a preceptorship and who was given one of the highest average grades, was asked regarding his training. His preceptor, in one of the small communities in Texas, spent a certain amount of time each evening after office hours discussing the cases of the day that offered unusual problems, thus allowing the student the opportunity to acquire clinical knowledge and judgment.

Thus the examinations have brought out the fact that, while a carefully supervised residency is the ideal method of obtaining a training in ophthalmology, it can be obtained from a combination of a basic-science course and a preceptorship. The examinations have also shown that a man may go through a

poorly supervised training to make him a safe ophthalmologist. It therefore becomes evident that those in charge of the training of younger men in ophthalmology, whether in a residency or a preceptorship, assume a grave responsibility in making certain that these men receive the necessary personal supervision and instruction.

Frederick C. Cordes.

GOETHE AND COLOR

During his life, and even more since, Johann Wolfgang von Goethe has excited homage and adulation. His family home has been quickly rebuilt after the war's destruction. The mineral, goethite (hydroxide of iron), was named in his honor. The bicentennial of his birth, August 28, 1749, received world-wide attention. A universal man of genius, like Leonardo da Vinci and Benjamin Franklin, Goethe was a writer, poet, statesman, theatre director, and naturalist.

Before completing his law course at Strasbourg, in 1770, Goethe had a serious pulmonary hemorrhage and, during his lengthy convalescence, pored over books on occult philosophy, alchemy, astrology, and religious mysticism. Converted finally to the philosophy of Spinoza, he henceforth considered individual creeds and dogmas unnecessary.

While in his student boarding house, he was impressed by the enthusiasm of the students of medicine. . . . "These, as is well known, are the only students who discuss with energy out of school hours their science and profession." He visited the clinics, watched Schilling in his expert cataract surgery, and observed attentively as Lobstein performed a type of dacryocystorhinostomy on his companion, Herder. Goethe felt strongly that "The physician must be creative if he is really going to heal. If he is not creative then he . . . will be a mere bungler at his work."

Goethe's literary productions from 1771 to 1775 gave him renown and influential friends. In 1775, he was appointed state councilor at the Saxon capital of Weimar, and his concern with the productive capacity of the duchy restimulated his interest in the natural sciences. His scientific thinking was speculative, poetic, and intuitive rather than empirical, analytical, and critical. Everywhere Goethe sought for and found continuity. "The plant goes from knot to knot, closing at last with the flower and the seed. So the tapeworm, the caterpillar, goes from knot to knot and closes with the head. Man and the higher animals are built up through the vertebrae, the powers being concentrated in the head." Goethe had the view that all variations in plants and animals were only metamorphoses of a primitive archetype, and not evolved one from the other, as Darwin later enunciated.

Being an amateur artist, Goethe studied pictorial art in 1768 and from this stemmed his interest in anatomy and color. Peering through a prism at the broad luminous surface of a sheet of paper on a dark background, he noted that he saw the colors only where the white paper and the dark background had a common boundary. He immediately concluded that Newton's theory is false, and that every color was merely the mixture of light and darkness in new proportions. The prism only served to move light and darkness over each other. He rejected the "artificial" theory of seven colors —the fundamental colors were just black and white. Color was solely a problem of sensory perception and he abhorred the intrusion of mathematics and physics into the subject. "Nature refuses to be unveiled by force. What she does not reveal to your mental sight you will not wrest from her with levers and screws." He refused to admit that yellow is red-green, that white is red-green-blue, and that black is a negative sensation.

He first advanced his theories in 1791 and would not be dissuaded by criticism from the completion of his monumental work, *Zur Farbenlehre*, in 1810—a two-volume

octavo of 1,510 pages and 16 colored plates. The observations recorded are astonishingly numerous and varied, from which artists have derived great benefit, as exemplified, to note only one instance, by their frequent discriminating use of colored shadows. Of this opus, Goethe wrote: "As for what I have done as a poet I take no pride whatever . . . but in my century I am the only person who knows the truth in the difficult science of colors—of that I say I am not a little proud." Two English translations have appeared, the first by Charles Locke Eastlake, the second by John Tyndall.

Though disdained by scientists, the monograph created a great sensation, and Goethe's views were widely accepted by philosophical writers, such as Hegel and Emerson. Herman Grimm declared, "Considered as a book . . . the *Theory of Colors* is truly enchanting." Lord Brougham, in his formal review, called the work a case of hallucination. The French Academy, at the advice of Cuvier, refused to consider it seriously. Helmholtz has labelled it as "the extravagancies of a great genius wandering out of his sphere."

Purkinje's dissertation on subjective visual phenomena, in 1819, won for him the friendship of Goethe, and partly through Goethe's influence Purkinje was appointed professor of physiology at the University of Breslau in 1823. Goethe's work inspired a psychologic school in which sensation rather than physical stimuli were stressed, with Purkinje, Brücke, Aubert, and Hering as typical representatives. The psychologic difficulties of accepting a purely physical interpretation of color have inspired several theorists to compromise hypotheses, such as those of Fick, Hering, and Ladd-Franklin.

On the night of his death, March 22, 1832, Goethe's last distinct words were "Mehr Licht! Noch mehr Licht!" and his keen eyes then closed forever.

James E. Lebensohn.

CORRESPONDENCE

ELECTROCOAGULATION OF THE SCLERA

Editor,
American Journal of Ophthalmology:

I have read with interest the article in your June number by Dr. Harold G. Scheie and Dr. Bourne Jerome on this subject, and agree with the conclusion they draw that electrocoagulation causes shrinkage of the eye. This fact will be known to all surgeons who have operated on a detached retina and who have found that the cornea becomes hazy from raised intraocular pressure after several diathermy applications. This corneal haze caused by scleral shrinkage and raised pressure is relieved immediately if a scleral perforation is made.

The point of this letter, therefore, is to question the conclusions of your authors that shrinkage of the globe by this means might be employed as an alternative to scleral resection in the treatment of some detachments.

Electrocoagulation causes a severe intraocular reaction and for that reason can only be applied to the eye with safety in very limited amounts. To carry out this treatment over half the circumference of the globe and so produce sufficient shrinkage is an unwise procedure causing too much damage to the eye, and it is for this reason that scleral resection, which causes no severe intraocular reaction at all, is used in those severe detachments too extensive for diathermy to replace.

It will be known to those surgeons who have carried out scleral resection that the intraocular reaction is less than that of an ordinary diathermy operation.

I, therefore, give the opinion that while there is no doubt that electrocoagulation causes shrinkage of the sclera, this same method cannot replace surgical removal of a strip of sclera where this treatment is indicated.

(Signed) Seymour Philps,
London, England.

Dr. Scheie's reply

Editor,
American Journal of Ophthalmology:

The communication received from Mr. Philps serves to emphasize points brought out in our paper "Electrocoagulation of the sclera: Reduction in ocular volume and pathologic changes produced," AMERICAN JOURNAL OF OPHTHALMOLOGY, volume 32, part II, June, 1949, pages 60-78.

We demonstrated rather marked changes in the animal eyes used in our experiments with surface electrocoagulation. Engorgement of the retinal vessels, particularly in the nerve-fiber layers, associated with hemorrhagic phenomena was striking. The final retinal atrophy was considerable.

We concluded by stating, "although surface diathermy produced a high degree of scleral shrinkage, the associated pathologic changes were of such a severe nature that clinical application to this same extent would probably be inadvisable." Further work is now in progress on the problem.

(Signed) Harold G. Scheie,
Philadelphia, Pennsylvania.

Pterygium surgery

Editor,
American Journal of Ophthalmology:

In your issue of July, 1949, Dr. H. Saul Sugar paid me a graceful compliment by saying that it was the stimulus of my paper in the *British Journal of Ophthalmology* in February, 1948, that led to the writing of his paper on the "Surgical treatment of pterygium."

In return I would like to congratulate Dr. Sugar on his own well-conceived operation; I will pay him the practical compliment of performing his operation in Australia.

It would appear that Dr. Sugar is substantially in agreement with me, with the addition of certain very sound amplifications of his own, as to the essential nature of pterygium.

He feels, however, that my procedure of removing the whole of the subconjunctival tissue from the cornea to the plica semilunaris is fraught with danger to the internal rectus muscle.

Here I must beg to differ from my distinguished colleague for two reasons:

Firstly, as the subconjunctival tissue is dissected away from the uplifted conjunctival mucosa, held up vertically with fixation forceps by an assistant, interference with the underlying muscle cannot very well occur.

Secondly, over a period of some 10 years, no interference with the action of the internal rectus muscle has been noted, either by myself or by such of my Australian colleagues who use my technique.

In conclusion, however, this stimulating thought remains with me: how pleasant it is that an American surgeon, presenting his own excellent views on a subject, should give generous credit to a paper by an Australian, printed in a British journal.

(Signed) Arthur D'Ombrain,
Sydney, Australia.

First human electroretinogram

Editor,
American Journal of Ophthalmology:

As a footnote to the centennial perspective on "Electrophysiology," editorially noted by Dr. James E. Lebensohn in the August, 1949, issue of the JOURNAL, it may interest your readers that an account of the first human electroretinogram was published by R. H. Kahn and myself (Arch. f. Ophth., 114:304, 1924). In Karpe's recent monograph on human electroretinography (1948), this priority is acknowledged. With grief I must add that my dear friend, R. H. Kahn, perished in Prague during the war.

(Signed) Arnold Loewenstein,
Glasgow, Scotland.

ELECTRICAL CONTROL FOR ASTIGMATIC CROSS

Editor,

American Journal of Ophthalmology:

In the September, 1949, issue of the JOURNAL, Dr. Horace L. Weston has an interesting account of an electrical method for revolving his astigmatic cross. Since I set up an arrangement similar to his four years ago, some suggestions may be of interest to others thinking of building such a remote control system.

One transmitter (control unit) may be made to drive an additional receiver—thus an astigmatic dial may be mounted in front of a pointer, the latter being rotated so as to indicate the most prominent line on the dial. As this receiver is driven in synchronization with the one turning the pointer, further setting of the pointer is minimized.

There is no need to use mechanisms which hum and require transformers for the surplus market is still glutted with fine units operating silently on 115-volts, 60-cycle A. C. These units are known as servo mechanisms. The two types are called transmitter and receiver. General Electric calls its units Selsyns (self synchronizing motors).

If the pointer and cross are not made extremely light, annoying chatter or oscillation will occur.

(Signed) Lee S. Sannella,
Petaluma, California.

BOOK REVIEWS

OCULAR SIGNS IN SLIT-LAMP MICROSCOPY. By James Hamilton Doggart. St. Louis, C. V. Mosby Company, 1949. 98 pages, cloth binding, 93 illustrations, 85 in color; bibliography, index. Price, $6.75.

In recent years there has been no small adequate textbook on slitlamp microscopy that has been available to the resident or student in ophthalmology. The text by Berliner is too ponderous and expensive. The monumental volumes written by Vogt are so difficult to obtain that they are not available for the student. The German language difficulty of the first two volumes is an additional handicap.

Thus Doggart's book fills a long-felt need, as a textbook for practical slitlamp microscopy for the postgraduate student.

As the author states in the preface, "bearing in mind the requirements of postgraduate students, the present writer has relegated the history of slitlamp microscopy to a short final chapter, and mathematical optics he has altogether eschewed. The apparatus is described in an appendix, and in order to forestall the criticism that this is the wrong approach, I would emphasize that such descriptions are seldom of interest, save to those who already know something about the apparatus. Therefore it is intended to plunge immediately into the clinical aspects of slitlamp microscopy with the object of helping the beginner."

The book is divided into nine chapters which discuss the value of the slitlamp technique of examination, the normal eye, corneal abnormality, aqueous disturbances, pathologic signs in the iris, lenticular changes, changes in the vitreous, and the evolution of slitlamp microscopy of the living eye.

On the whole the text is excellent. The chapter on the technique of examination is clear and concise and will be very helpful to the beginner in learning to use the instrument. The author's advice that slitlamp microscopy of the living eye should always be preceded by "naked-eye inspection" and by examination with the simpler methods is a factor that is all too often overlooked by the present-day student of ophthalmology. In discussing the pathologic changes a little more detail would seem to have been worthwhile.

In any textbook on slitlamp microscopy, colored illustrations are important. Of the 93 illustrations the book contains, 85 are in color. Some of the illustrations have been used in other books and publications of the author. Most of the pictures, however, are published in this volume for the first time. The original drawings are excellent and are

very well reproduced. They add a great deal to the value of the book.

The bibliography is comprehensive and is a good source of references for anyone interested in doing further work in some phase of slitlamp microscopy. Those books or journals giving further references to the literature are marked.

The index is complete and is an additional valuable factor in the book. The format and binding are excellent.

The book is a must for every student of ophthalmology.

<div align="right">Frederick C. Cordes.</div>

Revista de Oftalmologie. July-September, 1948, volume 1, pp. 1-204.

In this first volume of Rumania's new journal of ophthalmology, Bailliart publishes his reflections on the theories of vision, a subject for which he suggests a program of ophthalmic investigation. He also emphasizes the importance of a clear understanding of the specific photochemical and electrical reactions in the retina for other fields of science such as television which uses a mechanism similar to that of the retina.

Little is known of the details of the chemical composition or action of rhodopsin and its allied substances, of the functions of the rods and cones, the intercommunicating fibers of the different retinal layers, of the relative differences in the perceptive powers of the nasal and temporal retina, of the details of color vision, and of the shadow formation on the neuro-epithelium of the retinal vessels.

G. Bietti considers the etiology of trachoma and the effects of the sulfonamides and anitibiotics on this disease. The elementary and initial bodies cannot be considered to be Rickettsia because they are affected by the sulfonamides but are resistant to para-amino-benzoic acid which is specific for the Rickettsia. They cannot be interpreted as degenerated and phagocytized bacteria because they react to the sulfonamides and pencillin but not to streptomycin,

in spite of the equal antibacterial effect of these substances. They are not degenerative reactions of the cells but are vital elements. All studies seem to suggest that the elementary and initial bodies are the corpuscular form of the trachoma virus.

A. Bussacca's article on pericorneal and corneal vascularization in keratitis is a chapter from his monograph on the pathology of the eye. He discusses the limbal network, superficial and deep vascularization, the exact localization and variation of corneal vessels and their involution. The paper is accompanied by several very good photographs and schematic figures.

In the longest paper of this volume, N. Blatt and M. Athanasiv report their study of the optic canal, a detailed and painstaking work in which they hoped to clarify the relation of the optic canal to diseases of the optic nerve. This paper contains a survey of the literature, a report on 10,000 adult and infant skulls, numerous tables, figures, X-ray pictures, and drawings. It discusses every possible variation in the appearance of the optic canal as found in 124 adults and 12 infants.

A. Franceschetti and C. Balavoine describe their method of keratoplasty. They use round corneal flaps, removed, if possible, within one hour after death and preserved in Ringer's solution on a specially constructed glass disc.

A. Kettesy proposes to standardize the examination of visual acuity. V. J. Munteanu describes three cases of dacryocystitis treated with pencillin. D. Lazarescu and P. Toporas discuss the physiologic variations of intraocular pressure. V. Sabadeanu and C. Henter contribute a paper on epidemic keratoconjunctivitis. N. Zolog stresses the allergic factor in phlyctenular keratoconjunctivitis and reports his experience with 25 patients treated with a hormone of the reticuloendothelial system which appears in large amounts in the blood of animals blocked by electronegative colloidal solutions.

<div align="right">Alice R. Deutsch.</div>

ABSTRACT DEPARTMENT

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

11
RETINA AND VITREOUS

Santoni, A. Seasonal variations and frequency of retinal detachments. Giorn. ital. oftal. 1:418-424, Sept.-Oct., 1948.

A statistical analysis of 610 cases of retinal detachment studied in the period from 1936 to 1947, showed a peak of incidence during the months of June and July, slightly less during May and August, and least in December. The possible significance of this finding is discussed.

Vito La Rocca.

Sautter, Hans. Experimental spasm and the effect of vasodilators on retinal vessels. Klin. Monatsbl. f. Augenh. 114:333-346, 1949.

Visible contraction of retinal arteries can be brought about by intravenous injection of adrenaline. The dose necessary for this effect usually kills the animal. Injection into the vitreous leads at once to an ever increasing interruption of the retinal circulation. The vascular constriction is followed by a dilatation with secondary diapedesis of blood through the damaged capillary walls. The milky opacity during the constrictory phase is a pure ischemia. Intercellular edema is manifest during the phase of dilation as pseudocircinate retinitis caused by capillary damage. Hemorrhages and intercellular edema occur only during incomplete interruption of the flow of blood, never in complete embolism. Late effects of intravitreal injection of adrenaline into rabbits' eyes were degenerative changes in the choroid and pigmentary disturbances in the retinal periphery similar to retinitis pigmentosa. Vasodilators like acetylcholine and similarily acting agents were usually incapable of relieving the arterial spasm or the edema, even when injected into the vitreous. They were even less effective or seemed to increase the constriction if given in combination with atropine. The desirability of a new agent which dilates the vessels, but does not lower the blood pressure is stressed for the treatment of thrombosis and embolism. (8 figures, references.)

Max Hirschfelder.

Scheerer, R. Retinal diseases from the viewpoint of the constitution theory of Kretschmer. Klin. Monatsbl. f. Augenh. 114:319-328, 1949.

The two basic types in Kretschmer's theory of constitution are the leptosome type and the pycnic type. The fundus of leptosomes usually shows thin arteries, a physiologic ischemia, a thin retina and a sclerotic choroid. The pycnic type shows a "moist" retina with broad vessels, and slight transparency and tends to approach the picture of a hypertonic fundus. Influence of general constitution is noted in several ocular diseases. Venous thrombosis is more frequent in the pycnic type with arteriosclerosis and other circular disturbances. Albuminuric retinopathy is more frequent in pycnic types, while chronic nephritis occurs in leptosomes. In glaucoma simplex one finds more leptosomes and in only 14 percent of them was vasoneurosis or arterial hypertension found. On the other hand, 67 percent of the patients with acute glaucoma, most of them of the pycnic type, had this finding. Life expectancy with acute glaucoma seems to be ten years less than with chronic simple glaucoma. Senile macular degeneration, found in "dry" retinas of chronic nephritis, occurs in leptosomes, whereas disciform degeneration of Kuhnt-Junius belongs to the "moist" retina of general vascular hypertension. (7 figures, references.)

Max Hirschfelder.

Scuderi, Giuseppe. **Macular retinitis of brown color.** Rassegna ital. d'ottal. 18:82-96, March-April, 1949.

In 1946 Dejean and Laporte described a peculiar form of tuberculous retinitis of the macula and perimacular region. Its four stages are 1. a reddish-yellow alteration of the macular area of round or oval form, 2. the color changes to brick-red and the disc becomes hyperemic, 3. grayish nodules appear around the macula, 4. after several years black pigment spots are seen in a ring around, and in the macula. Scuderi's patient was a youth, 17 years of age, whose father had died of tuberculosis. Evidences of pulmonary changes were noted in the patient. The right eye only was affected. The article is illustrated with 8 figures, 4 in color, and 2 diagrams made by autoendoscopy by the patient. Eugene M. Blake.

Stown, M. N. **Hyperplasia of the pigment epithelium of the retina simulating a neoplasm.** Tr. Am. Acad. Ophth. pp. 674-677, July-Aug., 1949.

The ocular condition in the left eye of a white man, aged 49 years, had been clinically diagnosed as von Hippel's disease ten years ago. Now sections showed marked proliferation of the pigment epithelium in a mass over the optic nerve head where bone changes also occurred. Some sections resembled neoplasm because of the marked proliferation of retinal epithelium. Lymphocytes, plasma cells and plasmacytoid cells diffusely infiltrated the anterior choroid. The retina was detached. Chas. A. Bahn.

Verzella, Mario. **A new therapy for retinitis pigmentosa. Juxtabulbar injections of nicotinic acid.** Giorn. ital. oftal. 1:331-358, July-Aug., 1948.

The author explains the characteristics of a new therapeutic technic based on intense hemo-dynamic action by massive local injections of nicotinic acid on the eye. After describing the technical modifications of injections, and trying to clarify the mechanism of action, the author reports concisely the history of 12 patients and the results obtained. He comments briefly on the favorable functional changes. Vito La Rocca.

12
OPTIC NERVE AND CHIASM

Bedell, A. J. **Perineuritis optica.** Tr. Am. Ophth. Soc. 46:399-411, 1948.

Four cases in which unusual signs

temporarily confused the diagnosis are reported and illustrated with serial fundus photographs. Serial fundus photography was also valuable in establishing the diagnosis in an unusual senile macular degeneration in a myope with hyperpiesia, a rare form of optic neuritis with a sharply localized edema of part of the nerve head in multiple sclerosis, syphilitic neuroretinitis simulating occlusion of the central retinal vein and traumatic retinal angiopathy, and tuberculous retinitis with severe optic nerve reaction and complete resolution of the focus with restoration of function.   David O. Harrington.

Blatt, N. **The value of malarial therapy in syphilitic optic atrophy.** Ann. d'ocul. 182:513-520, July, 1949.

The results of treatment in 387 cases of syphilitic optic atrophy during 20 years are analyzed. It can be easily seen that the prognosis of syphilitic optic atrophy is much worse in those treated with malarial therapy than in those treated by other methods or even untreated.
                            Chas A. Bahn.

Dresner, E., and Montgomery, D. A. D. **Primary optic atrophy in von Recklinghausen's disease (multiple neurofibromatosis).** Quart. J. Med. 18:93-104, April, 1949.

The authors described three cases of optic atrophy in which multiple neurofibromatosis was the cause. Two of them occurred in uniovular twins. The third patient came to autopsy and an astrocytic glioma of the optic nerve was found. Primary optic atrophy has been found with von Recklinghausen's disease in 46 instances. In 41 cases in which histologic studies of the optic nerve were made there were 35 primary gliomas of the nerve or chiasm.   R. Grunfeld.

Friemann, W. **Hereditary optic atrophy**

in women. Arch. f. Ophth. 149:266-274, 1949.

A pedigree is presented with familial optic atrophy in women of two generations. In Leber's optic atrophy men are usually affected.   Ernst Schmerl.

Paufique, L., and Etienne, R. **Depressed colobomata of the papilla.** Ann. d'ocul. 182:605-615, Aug., 1949.

This unusual developmental anomaly is usually unilateral and seldom multiple. The color of the depression is usually gray, involves $\frac{1}{8}$ to $\frac{1}{3}$ of the temporal part of the papilla, and its depth varies from 1 to 6 mm. Pulsation from the central retinal vessels may be observed. Vision is variably affected and central and paracentral scotomata may be present. In some cases a hereditary factor has been established, and other ocular degenerations such as macular cysts, congenital cataracts and microphthalmus may be coexistent. This anomaly is caused by an imperfect invagination of the primary optic cup. Two cases are described.
                            Chas. A. Bahn.

13
NEURO-OPHTHALMOLOGY

Capolongo, Giuseppe. **Chronaximetry in ophthalmology.** Riv. oto-neuro-oftal. 23:371-386, Sept.-Dec., 1948.

The phosphene from an electric stimulus occurs at the level of the occipital cortex where the retina and the optic nerve are not intact and its chronaxy cannot be considered indicative of the functional state of the retina and the optic nerve.   Melchiore Lombardo.

Cibis, P., and Lazar, O. **Disturbances of the lower visual functions in injuries of the brain.** Klin. Monatsbl. f. Augenh. 114:346-356, 1949.

In this statistical evaluation of 157 pa-

tients with brain injuries in World War II it was found that over one half of them had injuries to the posterior part of the skull. Of all the injured, 94 percent had better than half vision in the better eye and none was completely blind. Two of the patients had injuries of the optic tract with complete hemianopsia. The functioning half of the visual field reacted normally to adaptation tests, which is never found in injuries to the occipital lobe. About one third of the injured showed hemianopsias in the peripheral field, half of which were bilateral. A great majority showed "sparing of the macula" in the presence of peripheral hemianopic defects. The "spared area" showed damage of adaptation as well as of color distinction, which is ascribed to a change in the function of the cones in the area of central vision. (References.)

Max Hirschfelder.

Grignolo, Antonio. A case of Claude Bernard-Horner syndrome from zona ophthalmica. Riv. oto-neuro-oftal. 23:387-392, Sept.-Dec., 1948.

A man, 57 years of age, soon after an attack of herpes zoster of the first branch of the trigeminus was found to have ptosis, miosis and enophthalmos on the same side. There was a spasm of the orbicularis, hypesthesia of the cornea and sluggish reaction of the pupil to light. The pupil became dilated after instillation of atropin and adrenalin but not of cocaine. This indicates that the lesion was between the superior cervical ganglion and the pupillary dilator just where the sympathetic fibers come in contact with the Gasserian ganglion. It is probable that the Horner syndrome was in this case caused by a diffusion by contiguity of the herpetic process from the trigeminus to the ocular sympathetic fibers.

Melchiore Lombardo.

Ohm, J. The optokinetic tracts of the anterior corpora quadrigemina. Arch. f. Ophth. 149:248-265, 1949.

The author compares his own studies with those by Spiegel and Scala.

Ernst Schmerl.

Pampiglione, Giuseppe. The electroencephalographic research in intracranial tumors. Riv. oto-neuro-oftal. 23:353-370, Sept.-Dec., 1948.

Many electroencephalograms are shown to demonstrate the importance of this test in the diagnosis and the localization of the cerebral neoplasms. (12 figures, references.) Melchiore Lombardo.

Poos, F. Paradoxical adrenaline mydriasis. Ophthalmologica 118:127-136, Aug., 1949.

The term paradoxical adrenaline mydriasis is applied to the well-known phenomenon of greater efficacy of topically applied adrenaline solutions in sympathetically denervated eyes. Instillation of adrenaline hydrochloride in 0.1-percent concentration produces appreciable mydriasis in the sympathetically denervated, but not in the normal eye. According to the conventional explanation of this phenomenon the denervated effector cells are more sensitive to adrenaline than the normally innervated dilator cells. The author is opposed to this concept of sensitization of the denervated muscle and adduces new evidence which suggests a different explanation. His main point is that the pupillomotor impulses elicited by changes in the light adaptation of the retina raise the threshold concentration of any mydriatic. The true threshold concentrations should be determined on sightless but otherwise normal eyes (a state apparently produced by severing the optic nerve close to the globe). A different and considerably higher threshold con-

centration is obtained if one determines the smallest concentration of a drug that overcomes the pupillomotor impulses serving retinal adaptation. Adrenaline in 0.1-percent concentration produces marked mydriasis in blind rabbits' eyes in which the retina no longer exerts its dominating effect upon the pupil. Even in normal rabbits' eyes a mydriatic effect of instillations of 0.1-percent adrenaline can be demonstrated if the observations are made at very low degrees of illumination.

The specific case of a marked change in the size of a sympathetically denervated pupil in man after the instillation of 0.1-percent adrenaline which produces no measurable change in the opposite, normal, eye may be explained as a result of the existing anisocoria. The width of the normal pupil is chiefly governed by retinal influences. A weak mydriatic would have to overcome these retinal influences in order to dilate the pupil. In the denervated, relatively miotic eye the weak mydriatic can produce a measurable dilation of the pupil without having to overcome the retinal pupillomotor factor and, moreover, the absorption of drugs from the conjunctival sac, the author believes, is better on the denervated than on the normal side. Peter C. Kronfeld.

Weekers, R., and Roussel, F. The mode of action of retrobulbar injections of alcohol. Ophthalmologica 118:115-126, Aug. 1949.

The authors review the anatomy, physiology and pharmacology of the sympathetic and parasympathetic innervation of the anterior uvea. In order to elucidate the mode of action of retrobulbar alcohol injections in man, the authors have performed such injections in rabbits. The effects of these injections have been very uniform and consisted of mydriasis, dim-inution or abolition of the light reflex of the pupil, hypersensitivity to topical application of mecholyl and insensitivity to eserine. In most cases these effects have been transient and followed by complete recovery. The retrobulbar injection apparently produces a postganglionic, predominantly parasympathetic, reparable lesion. The sympathetic fibers escape injury because of their more dispersed course within the orbit. After retrobulbar alcohol injections in man, lasting pupillary disturbances are very rare. The authors report four such cases with pupillary reactions closely resembling those of Adie's syndrome. Some, but not all cases of Adie's syndrome are due to postganglionic parasympathetic lesions.

Peter C. Kronfeld.

14
EYEBALL, ORBIT, SINUSES

Heimburger, R. F., Oberhill, H. R., McGarry, H. I., and Bucy, P. C. Intraorbital aneurysm; a case of aneurysm of the lacrimal artery. Arch. Ophth. 42:1-13, July, 1949.

A case of exophthalmos due to aneurysm of the lacrimal artery contained entirely within the orbit is reported. The lesion was removed by the transcranial route, and the patient is entirely well, over a year after operation, with normal vision and normal ocular movements. A survey of the literature revealed no other verified case of aneurysm of the lacrimal artery. Reports of six intraorbital aneurysms seen either at operation or at autopsy are reviewed, but in none is the diagnosis without question. The case presented is evidence that orbital aneurysm can be manifest clinically by unilateral exophthalmos without pulsation, but with evidence of venous obstruction, increased ocular tension and failing vision.

Ralph W. Danielson.

15
EYELIDS, LACRIMAL APPARATUS

D'Ermo, F. Further contribution to the surgical treatment of the jaw winking phenomenon. Boll. d'ocul. 28:207-215, April, 1949.

After discussing previous approaches to this problem, D'Ermo describes two patients, aged 22 and 23 years, who were satisfactorily operated on according to the method of G. Bietti. His method is a combination of the technics advocated by Hess and by Angelucci. It was published by Bietti in the Boll. d'ocul. 21: 721, 1942. A large skin pocket is prepared by undermining the skin of the lid and separating it from the orbicularis muscle, beginning at the eyebrow and ending above the lid border. Separating the orbicularis fibers gives access to the levator muscle which is isolated and cut one half centimeter from its tarsal insertion. The distal muscle end is secured by three catgut sutures which are led through the frontalis muscle three centimeters above the eyebrow. Here, two more catgut sutures may be added on both sides of the original three sutures in order to strengthen the hold of the muscle stump in its new position. Two double-armed silk sutures are passed through the lid skin 4 millimeters from the lid border, from the outside towards the pocket, and led through the frontalis muscle to come to the surface 3 to 4 centimeters above the eyebrow. When the sutures are knotted, the two lower thirds of the cornea must remain uncovered by the upper lid. Regulation of the pull during the early postoperative period is indicated. The silk sutures are removed after 8 to 10 days. In both cases, the cosmetic result was satisfactory and the synkinetic movements with opening of the mouth, chewing, and lateral movement of the jaw were abolished. (12 figures, references.)

K. W. Ascher.

Nuti, F. Etiologic explanation of a case of mycotic dacryocanaliculitis (Conistreptothrix Försteri). Boll. d'ocul. 28:169-178, March, 1949.

A 33-year-old woman developed purulent discharge from both canaliculi of her right eye one year after dacryocystectomy was performed. The opened canaliculi yielded numerous grayish-yellowish concrements some of which were inoculated into the anterior chamber of a rabbit, the remainder cultivated on aerobic and anaerobic media. In the rabbit eye the germ provoked a mild inflammatory process of the posterior corneal layers. The cultures proved the presence of a Conistreptothrix, most probably Försteri. Nuti raises the question whether some similar case previously attributed to actinomyces might have been caused by the same Conistreptothrix. K. W. Ascher.

16
TUMORS

Negri, L., and Alajamo, A. Tumors of the uveal tract and their cytogenesis. Giorn. ital. oftal. 1:289-316, July-Aug., 1948.

In a histologic study of 24 tumors of the choroid and one of the ciliary body stained with hematoxilin-eosin and a trichromic stain to show the reticulum, it was found that the pigmentation of the tumors is not enough for differential diagnosis on the basis of cellular morphology. They agree with Callender and Wilder that abundance in silver-staining fibers indicates less malignancy. The hypothesis of the origin of these tumors from a proliferation of the cells of the sheath of Schwann of the ciliary nerves deserves consideration, but requires further study.

Vito La Rocca.

Wolff, E. The nature of the malignant choroidal melanomata. Brit. J. Ophth. 33: 445-452, July, 1949.

To support the theory that malignant choroidal melanoma is a sarcoma and that it is derived from the cells of Schwann of the ciliary nerves, Wolff points out that melanoma, like sarcoma, does not produce a local tissue reaction as does carcinoma. Blood vessels in sarcoma and melanoma are like new-formed vessels in that they have no walls of their own but are surrounded by tumor tissue. Teased tissue preparations show that the chromatophore and not the epithelioid cell is the essential cell of the melanoma. (6 figures.)

Morris Kaplan.

17
INJURIES

Ghose, Nirmal Kumar. Unusual ocular foreign body. Brit. J. Ophth. 33:520-521, Aug., 1949.

The author describes an unusual irritating foreign body, a small snail that was removed after it emerged from under the conjunctiva. This organism easily survives in the sheltered subconjunctival tissue but rapidly dies upon exposure to air.   Orwyn H. Ellis.

Schreck, E. Gas gangrene and the eye. Klin. Monatsbl. f. Augenh. 114:364-370, 1949.

The clinical, bacteriologic and histologic data on a patient who developed an intraocular infection with gas bacillus after perforation with a piece of metal are reported. Early panophthalmitis with rapid amaurosis and ocular hypertension and necrosis of the wound margins aid in the clinical diagnosis. Gas formation can sometimes be observed with the slit lamp or during operation. Gangrene of the ocular tissues with edema and necrosis as well as hemolysis and formation of methemoglobin were the pathologic characteristics. The patient received gas gangrene serum, sulfonamides and penicillin and recovered uneventfully after the

enucleation of the bulbus. (3 figures, references.)   Max Hirschfelder.

18
SYSTEMIC DISEASE AND PARASITES

Ashton, N. Vascular changes in diabetes with particular reference to the retinal vessels. Brit. J. Ophth. 33:407-420, July, 1949.

Histologic studies of vessel changes throughout the bodies of 21 diabetics were made and minutely compared. Tissues examined included those of the retina, choroid, ciliary body, iris, conjunctiva, brain, meninges, pleura, pericardium, omentum, peritoneum, bladder mucosa and the capsules of the kidney and liver. The details of fixing and staining all tissues are described. The suggestion that the lesions in the retina are micro-aneurysms is confirmed and it is shown that these dilatations occur in no other tissue. They occur mainly in the inner nuclear layer and are possibly caused at least partly by a venous stasis in this area brought about by fluctuations in ocular tension although this explanation is unsatisfactory and more work remains to be done. The retinopathy and the intercapillary glomerulosclerosis are very closely related etiologically and result from the same pathologic process whose manifestations differ in the eye and the kidney because of the different anatomic pattern of the retinal and glomerular vessels. (25 photographs.)

Morris Kaplan.

Botasso, Giovanni. Posthemorrhagic amaurosis. Rassegna ital. d'ottal. 18:121-129, March-April, 1949.

Loss of sight from hemorrhage occurs most often from gastrointestinal and uterine hemorrhage, repeated blood-letting, epistaxis and hemoptysis, in the order mentioned. In only 12 to 15 percent of cases is the ocular involvement uni-

lateral and women are oftener affected than men. The author reports an instance of bilateral blindness occurring in a 45-year-old woman after a severe metrorrhagia. Eugene M. Blake.

Di Ferdinando, R. A. **A case of palpebral leishmaniasis.** Giorn. ital. oftal. 1:359-364, July-Aug., 1948.

The author describes a case of palpebral leishmaniasis observed in a baby, 2 years of age, in the province of Pesaro-Urbino, where such disease occurs epidemically. He confirms the rarity of this dermatosis in comparison to its frequent appearance in other exposed parts of the body, which may be ascribed to local conditions of defense that hinder the action of the transmitting agent. Vito La Rocca.

Hartmann, Edward. **Psychosomatic phenomena in ophthalmology.** Brit. J. Ophth. 33:461-476, Aug., 1949.

The author presents numerous case reports to illustrate psychosomatic problems in ophthalmology. Various responses such as esotropia in children and glaucoma in adults are produced. Functional disturbances are often associated with organic conditions and it is often important that the psychosomatic disturbance be alleviated before the organic condition will respond to treatment. (42 references.) Orwyn H. Ellis.

vom Hofe, K. **Participation of general factors in inflammations of the uvea and cornea.** Arch. f. Ophth. 149:220-229, 1949.

Among the general diseases most often found in uveitis are rheumatism, tonsillitis, furunculosis, pneumonitis, otitis media and appendicitis.
Ernst Schmerl.

Ridley, A. **Toxoplasmosis, a summary of the disease with report of a case.** Brit. J. Ophth. 33:397-407, July, 1949.

Prenatal infection of the eyes of human infants by the protozoon toxoplasma is being recognized and reported with increased frequency in all countries, and here the third case to be reported in England is presented. First discovered in 1908, the toxoplasma is an intracellular parasite whose presence is easily demonstrated in post-mortem material of most of the tissues and in vivo in the spinal fluid. In man, the severity of the disease and its predilection for the eye seem to vary inversely with the age of the patient. The eye manifestions include searching nystagmus, microphthalmos, persistent pupillary membrane, strabismus, lens opacities and, most seriously, focal choroiditis which is often in both macular areas. There is usually an associated focal encephalitis with multiple areas of calcification which are demonstrable on X-ray films. A diagnostic serologic test needs refinement. Treatment is disappointing although the combination of sulphonamides and emetine is recommended. (6 illustrations.) Morris Kaplan.

19
CONGENITAL DEFORMITIES, HEREDITY

Anderson, B. **Familial central and peripapillary choroidal sclerosis associated with familial pseudoxanthoma elasticum.** Tr. Am. Ophth. Soc. 46:326-347, 1948.

A family pedigree is presented in which three of four siblings and one collateral relative have choroidal sclerosis and pseudoxanthoma elasticum. The sibling not exhibiting pseudoxanthoma elasticum presented angioid streaks and a retinal lesion resembling retinitis punctata albescens. The literature is reviewed. The hypothesis is advanced that the choroidal sclerosis is due to or associated with degeneration of the elastic membrane of the vessel wall. It is further postulated that the choroidal degeneration is due to localized anoxemia produced by the

changing pattern of the posterior ciliary arteries in the development of the orbital vascular and osseous system. The cases reported seem to substantiate the thesis that choroidal sclerosis is a clinical entity, a familial and probably a hereditary disease. Failure of the elastic tissue system may be the common denominator in angioid streaks, retinitis punctata albescens, choroidal sclerosis, pseudoxanthoma elasticum and retinitis pigmentosa.

David O. Harrington.

Azzolini, U. **The Laurence-Moon-Bardet-Biedl syndrome and similar clinical forms.** Riv. oto-neuro-oftal. 23:309-340, Sept.-Dec., 1948.

The author differentiates a chronic arachno-diencephalic form of this syndrome which he ascribes to an inflammatory meningeal process in a tissue predisposed by heredity, whereas the usual manifestation is purely heredodegenerative. A clinical case is reported for illustration.   Melchiore Lombardo.

Burns, R. A. **Hereditary myopia in identical twins.** Brit. J. Ophth. 33:491-494, Aug., 1949.

The detailed case studies and family pedigree of hereditary myopia in identical twins is reported. The twins were identical in all characteristics except for a difference in the refraction. The right eyes were almost alike but not the left. The family pedigree showed a dominant type of transmission which, however, did not appear in a later generation.

Orwyn H. Ellis.

Hepner, W. R., Krause, A. C., and Davis, M. E. **Retrolental fibroplasia and light.** Pediatrics 3:824-828, June, 1949.

The effect of light as a causative factor of retrolental fibroplasia in premature infants was studied. The authors conclude that light is not a cause of this condition.

Donald T. Hughson.

Stadlin, W. **Chorioretinal changes in two sisters with Freidrichs' heredoataxia.** Ann. d'ocul. 182:489-508, July, 1949.

This rare manifestation of this unusual disease is illustrated by two sisters whose parents were first cousins. The genealogy is traced through six generations of which they were in the fourth. The older sister was born in 1900 and the younger in 1903. Both were in good health until approximately the age of 15 years, when weakness developed in the lower extremities after an acute infection. Ataxia, scoliosis, loss of some reflexes, and ocular abnormalities slowly followed. Nystagmus was observed in both sisters about 1924. Now vision in the older sister is .1 in each eye and in the younger, .6 in each eye. The macular regions are irregularly pigmented and more so in the older. In the equatorial region the fundi contain 10 to 20 yellowish areas of various size and shape located in the external retina and choriocapillaris, most of which show moderate pigment migration. The discs and retinal vessels look normal, but the fields are moderately and concentrically contracted. The chorioretinal changes are slowly progressive. Their inflammatory or degenerative origin and the classification of tapeto-retinal degenerations alone or co-existent with cerebral and/or spino-cerebellar degenerations are discussed thoroughly.

Chas. A. Bahn.

Wilson, W. M. G. **Congenital blindness (pseudoglioma) occurring as a sex-linked developmental anomaly.** Canad., M. A. J. 60:580-584, June, 1949.

The author constructed the pedigree of six generations of an Indian family in which several males were born blind. All the females except one were free from the disease. The transmission of the defect thus revealed sex-linked characteristics. Eyes that came to enucleation from three males showed the presence of gross de-

velopmental anomalies. The eyes of males that were seen in early infancy proved to have pseudoglioma due to excessive congenital detachment of the retina.

R. Grunfeld.

20
HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Csapody, I. Writing and the surgeon. Szemészet 2:85-91, 1949.

Surgical skill often manifests itself in handwriting. Three types can be distinguished: the ease in the writing of born artists' hands, the more expressive writing of energetic people, and the small letters of careful people. Security associated with ease is the common feature of suitable hands. Consciously nice writing is a good training for both skill and will. Analysis of writing may be employed in judging candidates.   Gyula Lugossy.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

DEATHS

Dr. John Arthur Spengler, Geneva, New York, died August 12, 1949, aged 81 years.

MISCELLANEOUS

GRADY CLAY MEMORIAL EYE CLINIC

On September 15th dedication ceremonies for the Grady Clay Memorial Eye Clinic were held at the Grady Clay Memorial Hospital, Atlanta, Georgia. The Grady Clay Memorial Eye Clinic is the result of the work of friends of the late Dr. Grady Edward Clay, professor of ophthalmology, who died July 12, 1946.

From the time of his appointment as head of the department of ophthalmology in 1939 until his death, Dr. Clay worked to develop an outstanding graduate training program in ophthalmology at Emory University.

Dr. Phinizy Calhoun, Sr., emeritus professor of ophthalmology at Emory University, delivered the dedication address and was followed by Dr. J. Mason Baird, director of the Grady Clay Memorial Clinic. The Grady Clay Memorial Eye Clinic building was accepted by Dr. R. Hugh Wood, dean of the Emory University School of Medicine and Dr. Alton V. Hallum, acting head of the department of ophthalmology.

The Grady Clay Memorial Eye Clinic is a two story, air-conditioned, brick building. It houses the out-patient clinics for the department of ophthalmology and the Montgomery Ophthalmological Laboratory, under the direction of Dr. Phinizy Calhoun, Jr. Instruction and conference rooms for graduate and undergraduate education and a library for ophthalmology, which is a part of the Emory University Medical Library, are also housed in the building.

Dr. Morgan B. Raiford, is fulltime clinical director of the clinic. Glaucoma and motility clinics have been organized.

ESTELLE DOHENY EYE LECTURE

The third Estelle Doheny Eye Lecture presented by the Estelle Doheny Eye Foundation will be given by Dr. Phillips Thygeson, at Los Angeles on January 17, 1950. Dr. Thygeson is associate professor of ophthalmology at the University of California Medical School in San Francisco. The subject of the address will be "The etiology and treatment of phlyctenular keratitis."

The lecture, an integral part of the foundation's functions, is named for Mrs. Edward Laurence Doheny, the foundation's benefactress. Dr. Alan C. Woods delivered the first annual lecture on December 17, 1947, and Dr. Cecil J. O'Brien, the second lecture on November 8, 1948.

SOCIETIES

WASHINGTON OFFICERS

New officers of the Washington, D.C., Ophthalmological Society are: President, Dr. J. Thomas Schnebly; vice-president, Dr. Thomas A. Egan; secretary-treasurer, Dr. Everett S. Caldemeyer; directors, Dr. Joseph Desoff and Dr. Jerome A. Sansoucy.

The meeting dates for the 1949-1950 season are November 7th, January 9th, March 6th, and May 1st. The March 6th meeting will be held jointly with the Baltimore Ophthalmological Society.

On November 7th, a dinner meeting was held at the Kennedy-Warren Hotel. Dr. Raynold N. Berke of Hackensack, New Jersey, spoke on "Ophthalmology in India," and films depicting the status of ophthalmology in India were shown.

AKRON OFFICERS

Recently elected officers of the Akron Academy of Ophthalmology and Otolaryngology are: President, Dr. C. R. Anderson; vice-president, Dr. Daniel Mathias; secretary-treasurer, Dr. A. L. Peter.

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